

立百病毒感染症面面觀

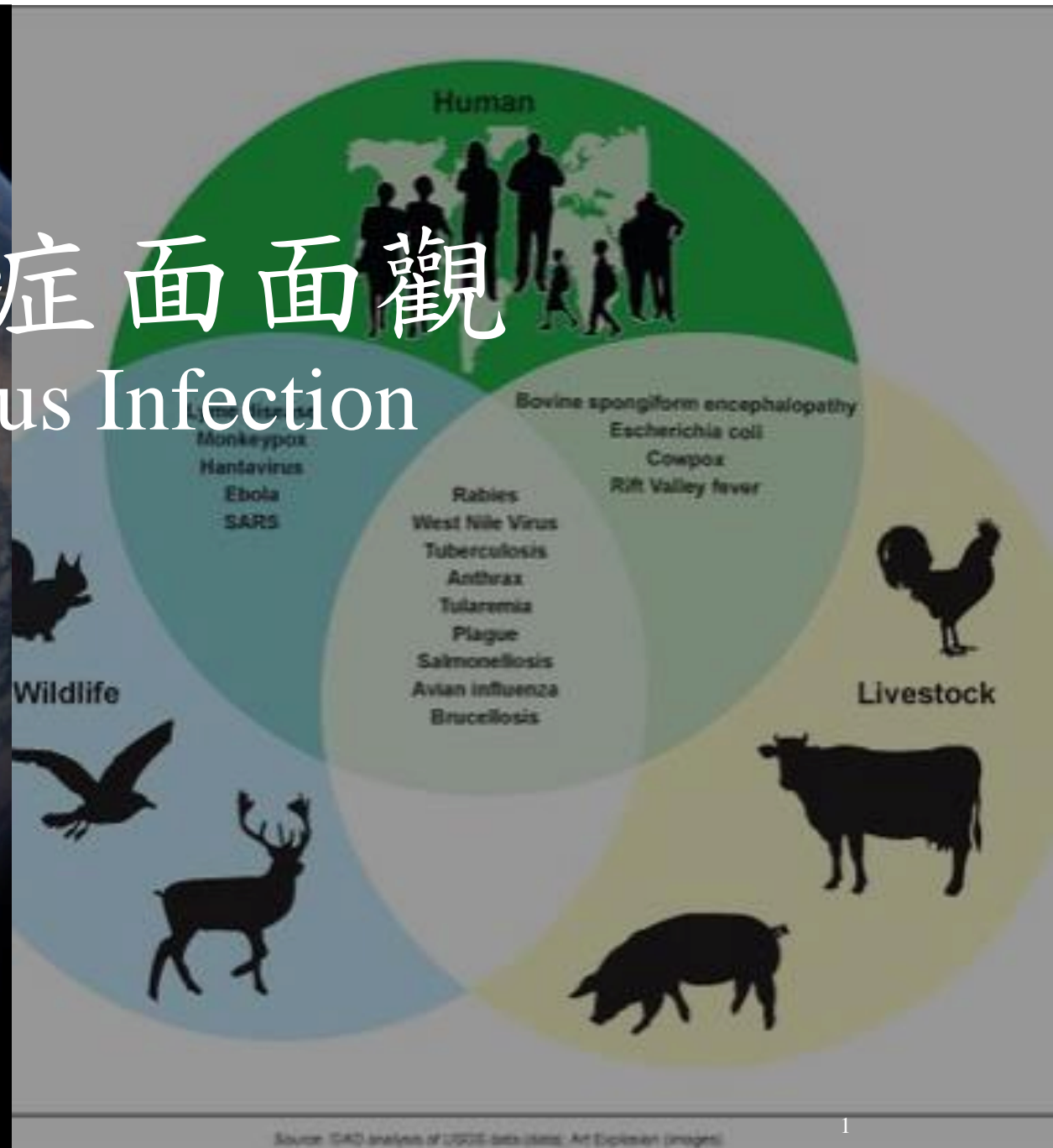
A Review of Nipah Virus Infection

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2021-9-30



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前言

疾病管制署列入「**重點監視項目**」-立百病毒感染症 (Nipah virus infection)

防檢局依法定動物傳染病分類列入「**乙類動物傳染病**」-立百病毒腦炎 (Nipah virus encephalitis)



The Role of Comparative Pathology in the Investigation of Zoonoses

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Abstract

Emerging and re-emerging zoonoses have raised great concerns in both human and animal health worldwide in the past 20 years. Rudolph Virchow proposed a "one medicine" discipline and emphasized the importance of cooperation 150 years ago. In the face of emerging threats from unpredictable zoonoses, human medicine and veterinary medicine should not be separate and independent sciences. Anatomic pathologists who are capable of analyzing and interpreting anatomical manifestations of diseases to obtain a definite diagnosis or exclude a wide variety of diseases play an important role in the diagnostic team. Although disease-associated microbes are numerous, morphologic patterns of tissue reaction caused by microbes are limited. Therefore, the interactions between microbes and host determine the histological changes in the target tissues. The contributions of anatomic pathology, with its use of morphologic similarities and special techniques, are important in zoonosis diagnosis. This can be seen in retrospective case studies of recent zoonoses such as multinucleated syncytial giant cells in severe acute respiratory syndrome and mouse hepatitis virus infection, syncytial cells in *Hemiparvovirus* infection and paramyxovirus, neuronal vacuolation in bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease, and *Streptococcus suis* type 2 meningitis. In Taiwan, the Chinese Society for Comparative Pathology, which was established in 1994, provides for this interaction. Interlaboratory cooperation plays an important role in the diagnosis, surveillance, and control of emerging and re-emerging zoonoses. (Tzu Chi Med J 2007;19(3):127-133)

人畜共通傳染病 (Zoonosis)

- 在動物和人之間自然傳播的感染與疾病。(Those diseases and infections which are naturally transmitted between animals and man.)

(WHO)

比較病理學在人畜共通傳染病扮演的角色

世界動物衛生組織
(OIE) 「強化獸醫學教育以建構更安全的世界」 (Evolving Veterinary Education for a Safer World)
全球獸醫教育會議
(2009/10/12-10/14)

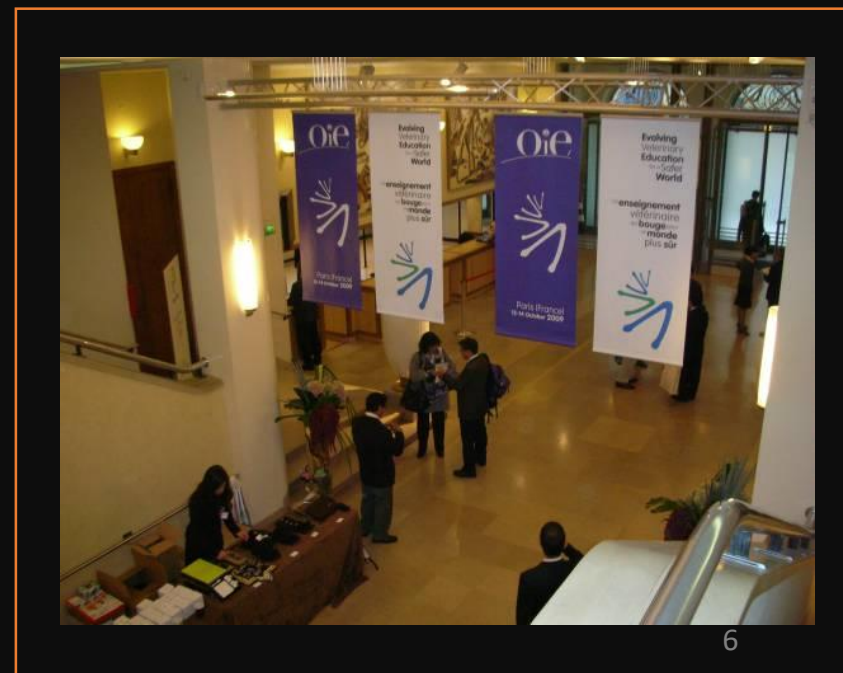
2021/9/30

- 面對急遽變化的世界，獸醫學而求
對育必需的修正時去迎對新社會的挑戰需
持續的修時去迎對新社會的挑戰需
— 新興疾病及再浮現疾病威脅、物醫
新現、環境變及動物與食品安福利
全球流通衛生和動物與食品安福利
- 適當的教育的與訓練可直接影響
獸醫服務的品質與表現
- 獸醫師繼續教育為強化獸醫服
務體系的重要手段
- 受過良好教育及訓練的公務及
私人執業獸醫師，將可以協助
OIE完成全球的使命-強化全球動
物健康。

「強化獸醫學教育以建構更安全的世界」主軸

- 主題演講
 - 全球性獸醫教育對於滿足社會需求之重要性
 - 如何提升全球動物之健康
- 預防及控制跨界疾病、人畜共通傳染病、新興傳染病
- 早期發現、通報及監測
- 獸醫公共衛生及“獸醫服務”的概念
- 食品安全
- 動物福利
- 全球對獸醫教育的基本需求
- 獸醫課程及國際認證文憑的全球性協調與評估

2021/9/30


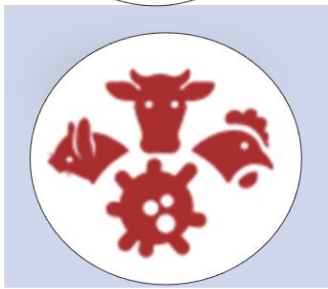
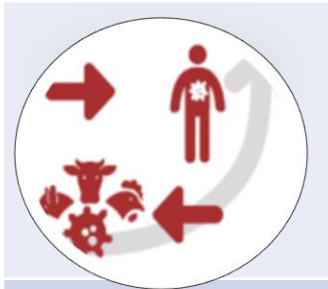
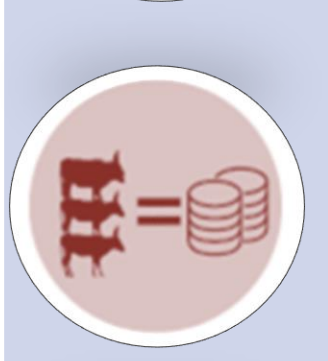


公共衛生：強化 全球性人畜共通 傳染病防治與監 控及保障畜產品 的安全與衛生

2021/9/30

- 因為SARS、H5N1及H1N1等疾病的發生，瞭解到世界一體的衛生概念及獸醫師控制好地區動物疫病減低對全球衝擊的重要性
- 世界銀行擬利用已開發先進的獸醫技術去訓練開發中國家的獸醫師及獸醫佐理人員，並設立評估系統，以協助監控與防治動物傳染病及解決公共衛生等問題。
- 新浮現的傳染病大都來自於動物，因此控制新興與再浮現的傳染病須要以多面向的整合與考量。為防治這些疾病的傳播，獸醫學與人類醫學必須攜手合作，但也須要彼此瞭解各自的文化與專業。

全球健康風險及未來挑戰 (OIE)

	<ul style="list-style-type: none">• 世界衛生	<ul style="list-style-type: none">• 引起人類疾病病原，60% 來自家畜或野生動物。• 75% 新興人類病原來自動物。• 80% 生物恐怖攻擊病原來自動物。
	<ul style="list-style-type: none">• 食物安全	<ul style="list-style-type: none">• 在2050年預估人口98億，需要額外生產70%動物性蛋白質。• 全世界超過20%動物產品損失來自於動物疾病。
	<ul style="list-style-type: none">• 環境	<ul style="list-style-type: none">• 了解生物多樣性、生態系統及傳染病之間關係是必要的。
	<ul style="list-style-type: none">• 經濟	<ul style="list-style-type: none">• 動物疫病對依賴家畜生產的農村社會造成收入的直接威脅。• 全世界十億人口，超過75%賴以糊口農業及飼養家畜而獲得每日少於美金2元為生。

獸醫師三大職責



傳染病病原

- **病毒 (Virus)**
- 細菌 (Bacteria)
- 真菌 (Fungus)
- 原蟲 (Protozoa)
- 蠕蟲 (Helminth)
- 立克次體 (Rickettsia)
- 黴漿菌 (Mycoplasma)
- 披衣菌 (Chlamydia)
- 普里昂 (傳染性蛋白，
朊蛋白) (Prion)

傳染病三角論

病原 (Pathogen)

- 使用殺滅病原藥物
- 消毒
- 例行監控

環境
(Environment)

- 維持生態平衡
- 勿食野生動物
- 消毒
- 蟲媒

宿主
(Host)

- 自衛防疫
- 提高免疫力-疫苗、抗體



THE VETERINARIAN
(www.nlm.nih.gov)

全球飼養

家畜 (約33
億)

牛9.8億，豬6.8億，
綿羊10億，山羊5億

雞 (240億)

伴侶動物
約 (10億)

犬4.7億，貓3.7億

重要人畜共通傳染病大事紀

- 1986 英國爆發牛海綿狀腦病 (BSE)
- 1994 英國發生人類新型庫賈氏病 (vCJD)
- 1994 澳洲發生人與馬感染亨德拉病毒 (Hendra virus)
- 1998 馬來西亞爆發人與豬感染立百病毒 (Nipah virus)
- 1999 美國發生人、馬與鳥類感染西尼羅熱 (West Nile fever)
- 2002 爆發嚴重急性呼吸道症候群 (SARS)
- 2003 亞洲地區發生H5N1流感 (俗稱禽流感, Avian flu)
- 2005 大陸四川發生豬第二型鏈球菌 (*Streptococcus suis* type 2) 感染症
- 2009 H1N1 新型流感
- 2012 中東呼吸症候群冠狀病毒感染症(MERS)
- 2013 臺灣鼬獾狂犬病
- 2014 非洲伊波拉病毒 (Ebola virus)
- 2019 2019冠狀病毒性疾病 (COVID-19)

全球人類及動物傳染病影響因素

- 跨界動物傳染病
(Transboundry animal diseases)
- 近年來人畜共通傳染病
 - 75%來自野生動物。



建立早期病毒預警制度!

DVM (Doctor of Veterinary Medicine)

- Doctors of Very Many Species
- Doctors of Very Many Situations
- Determinators of Very Many Scenarios

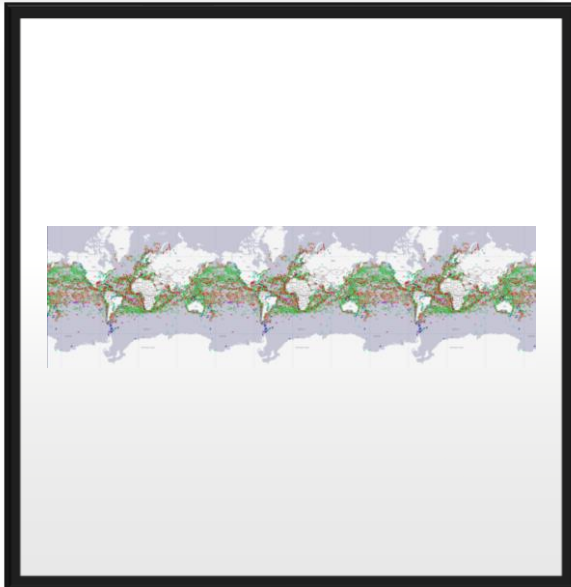
(Dr. Brian EVANS)



Mass deforestation risks more deadly global pandemics, scientists warn

▶ A UN summit will hear from leading biologists that there is now clear evidence of link between environmental destruction and deadly new diseases

This file picture taken on May 29, 2019 shows an aerial view of an agriculture field next to a native Carrado (savanna) in Formosa do Rio Preto, western Bahia



跨界動物傳染病 (Transboundary animal diseases, TAD)

- 許多國家使用外來 (exotic) 或海外 (foreign) 動物疾病來指一些疾病，如果進入其領土將會產生災難性的後果。
- 以聯合國的觀點，全球疫病戰場上，沒有什麼是外來的，必需全世界共同聯防。
- 世界糧農組織 (FAO) 動物衛生緊急預防系統關注約12-14種跨界疾病（口蹄疫、牛瘟、傳染性牛胸膜肺炎、綿羊和山羊痘、小反芻獸疫、高病原性禽流感、裂谷熱、新城病、非洲和古典豬瘟、馬腦炎，以及在某些情況下狂犬病和布魯氏菌病）及新興傳染病（大部分是人畜共通傳染病）。

蝙蝠，又名蠟蟻（音同「職墨」）



- 對翼手目（學名：Chiroptera）動物的通稱，翼手目是哺乳動物中僅次於齧齒目動物的第二大類群，現生種共有19科185屬962種，除極地和大洋中的一些島嶼外，分佈遍於全世界。蝙蝠是唯一會飛的哺乳類。數量僅次於齧齒類。
- 蝙蝠基因組裡面有更多有關基因修復的基因，並且表達量遠遠高於其他哺乳動物。
- 這些DNA修復基因在抑制病毒複製方面有著顯著的作用，所以雖然蝙蝠攜帶很多致命病毒，但是病毒的複製在蝙蝠的體內是被嚴重抑制的。

Viral zoonoses through bats

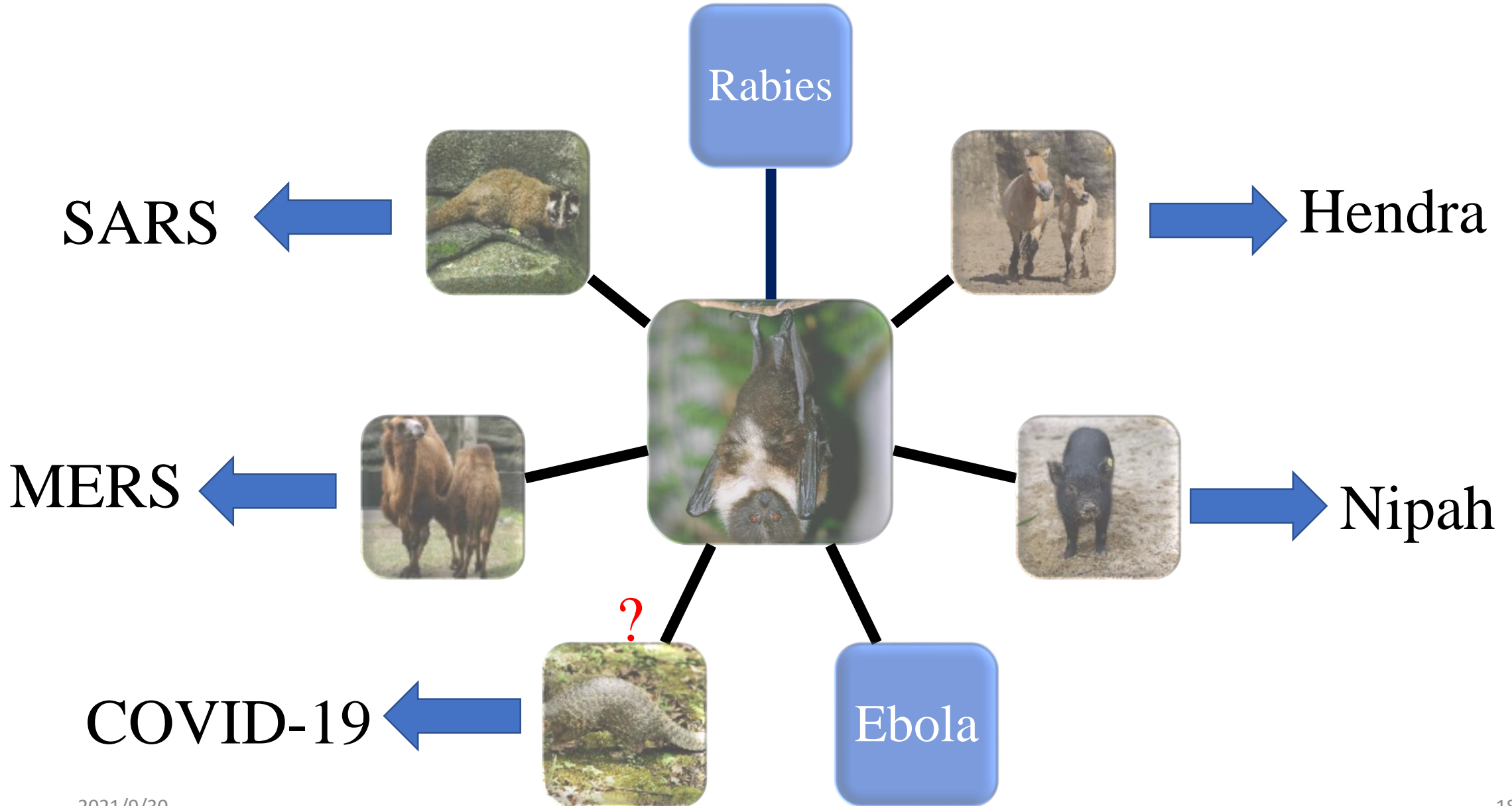


Table 2 – Emerging zoonotic diseases associated with bats

Virus	Host	Location	Reference
Hantaan virus	Common serotine bat (<i>Eptesicus serotinus</i>) horseshoe bat (<i>Rhinolophus ferrumequinum</i>)	Korea	Hoar et al. (1998)
Rift Valley fever virus	<i>Micropteropus pusillus</i> and <i>Hipposideros albae</i>	Republic of Guinea	Hoar et al. (1998)
Yellow fever	Old World fruit bat <i>Epomophorus</i> sp.	Ethiopia	Hoar et al. (1998)
Venezuelan equine encephalitis virus	Bat species	Guatemala	Hoar et al. (1998)
St. Louis encephalitis virus	Bat species	Guatemala	Hoar et al. (1998)
Eastern equine encephalitis virus	Bat species	Guatemala	Hoar et al. (1998)
Bat-variant rabies virus	Bat species	USA	McColl et al. (2000)
Australian bat Iyssavirus	Flying foxes <i>Pteropus</i> spp. yellow-bellied sheath-tail bat <i>Saccolaimus flaviventris</i>	Australia	Hanna et al. (2000)
Hendra virus	Flying foxes <i>Pteropus</i> spp.	Australia	Field et al. (2001)
Menangle virus	Flying foxes <i>Pteropus</i> spp.	Australia	Philbey et al. (1999)
Nipah virus	Flying foxes <i>Pteropus</i> spp.	Malaysia, Thailand, Cambodia, Bangladesh	Johara et al. (2001), Olson et al. (2002), Hsu et al. (2004), Wacharapluesadee et al. (2005)
Severe acute respiratory syndrome (SARS)-like coronavirus	Horseshoe bats (<i>Rhinolophus</i> spp.)	China	Lau et al. (2005) and Li et al. (2005)
Ebola virus	Old World fruit bats <i>Hypsignathus monstrosus</i> , <i>Epomops franqueti</i> , <i>Myonycteris torquata</i>	Gabon, Republic of Congo	Leroy et al. (2005)

國際組織在2015年確立避免「歧視」疾病命名原則

- 疾病命名經世界衛生組織 (WHO)、世界動物衛生組織 (OIE) 及世界糧農組織 (FAO) 這三個聯合國組織確立「五不」原則，避免五個類別的字眼出現，包括：

1. 地方名字

2. 人名

3. 特定類別的動物或食物名字

4. 跟文化、人口、產業或職業有關（例如「退伍軍人症」）

5. 引起不必要恐慌（例如「不明」、「致命」）

Table B

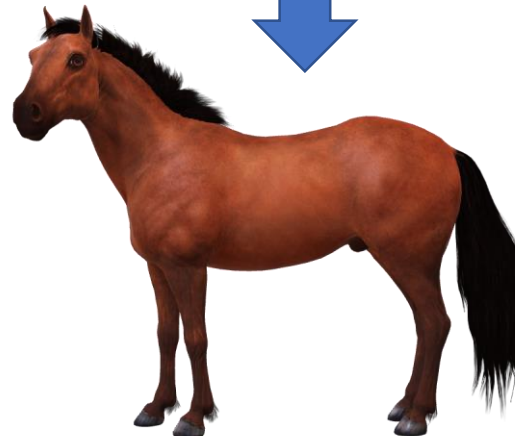
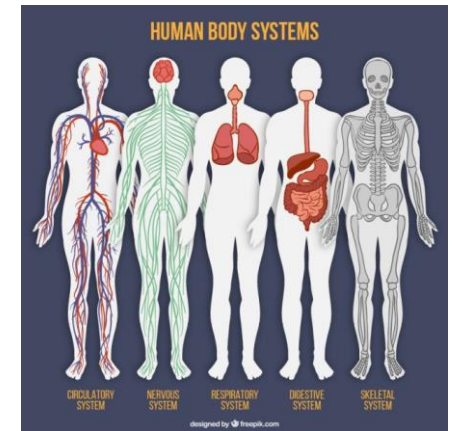
Disease names may NOT include:	Examples to be avoided
Geographic locations: Cities, countries, regions, continents	Middle East Respiratory Syndrome, Spanish Flu, Rift Valley fever, Lyme disease, Crimean Congo hemorrhagic fever, Japanese encephalitis
People's names	Creutzfeldt-Jakob disease, Chagas disease
Species/class of animal or food	Swine flu, bird flu, monkey pox, equine encephalitis, paralytic shellfish poisoning
Cultural, population, industry or occupational references	Occupational, legionnaires, miners, butchers, cooks, nurses
Terms that incite undue fear	Unknown, death, fatal, epidemic

*Superscripts indicate those terms further described below

- A. "Severe" is appropriate to use for diseases with a very high initial case fatality rate (CFR), recognising that the CFR may decrease as an event progresses.
- B. "Novel" can be used to indicate a new pathogen of a previously known type, recognising that this term will become obsolete if other new pathogens of that type are identified.
- C. A date (year, or month and year) may be used when it is necessary to differentiate between similar events that happened in different years

歷史

亨德拉病毒感染 Hendra virus infection



歷史

- 1994年在澳洲Brisbane的Hendra開始出現馬及類嚴重且常致命的呼吸和神經系統疾病。
- 截至2020年6月，Queensland and New South Wales共發生64起亨德拉病毒疫情，85匹馬確診死亡，20匹疑似感染死亡。另有7人感染，5人死亡，人類病例死亡率為71%，馬死亡率為75%。
- 2011年，一隻犬有HEV抗體。
- 沒有證據顯示直接從蝙蝠傳染給人類，人類感染似乎只通過中間宿主-馬發生。
- Flying fox (*Pteropus poliocephalus*)是亨德拉病毒的自然宿主。新南威爾士州政府於2014年批准摧毀飛狐群落。
- 疫病初期被稱為Equine morbillivirus, Bat paramyxovirus

2021/9/30



Hendra

City in Queensland

Hendra is a suburb of the city of Brisbane, Queensland, Australia. It lies roughly six kilometres north-east of Brisbane central business district. The streets of Hendra are lined with Jacaranda and Royal poinciana Trees. As with its neighbouring suburbs, Hendra is predominantly a family-oriented community. [Wikipedia](#)

Postal code: 4011



Summary of human cases of Hendra virus infection

Case 1 and 2	In 1994 In Hendra, a 49-year-old horse trainer died after a fulminating pneumonic illness, and a 40-year old stable worker survived an influenza-like illness.
Case 3	In 1995 in Mackay, a 36-year-old horse trainer died from encephalitis.
Case 4	In late 2004 in Cairns, a veterinary practitioner aged in her 20s, performed a post-mortem examination died of Hendra virus infection.
Case 5 and 6	In July 2008, a veterinary hospital at Redlands (a suburb of Brisbane), two of the staff members caring for the horses, One of them subsequently died.
Case 7	In August 2009, at an equine nursery at Cawarral near Rockhampton, central Queensland, a 55-year-old veterinarian died of encephalitis.

澳洲Hendra virus發生時間及地點



A relatively small number of horse owners indicated they were undertaking measures to reduce interactions between their horses and flying foxes. |

PHOTO CREDIT: WITTMANN/REUTERS



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



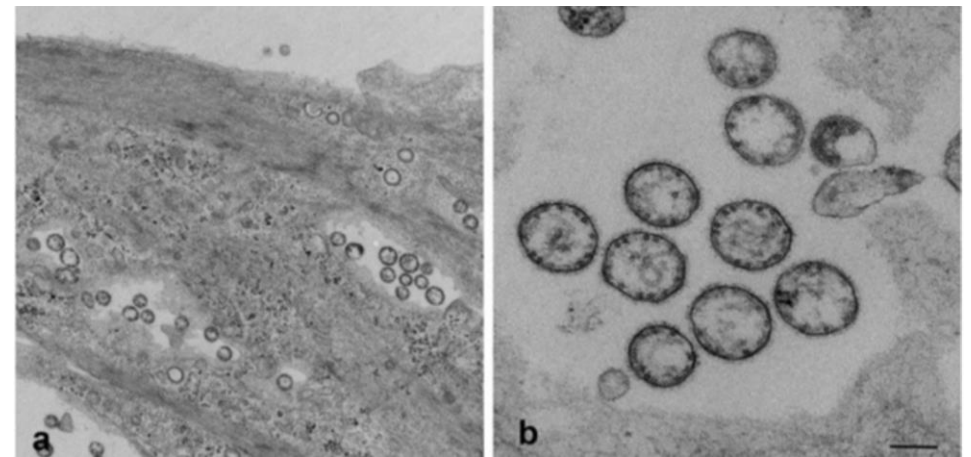
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病原

Hendra virus (HeV) is a member of the family *Paramyxoviridae*, genus *Henipavirus*. 與 Nipah virus 同屬 *Henipavirus* ◦

Henipaviruses are zoonotic, enveloped, negative-sense, single-stranded RNA virus ◦

- Serological evidence of Hendra virus infection was endemic in all four species of flying fox on mainland Australia (*Pteropus. alecto*, *P. poliocephalus*, *P. scapulatus* and *P. conspicillatus*)
- Flying foxes were a natural host and probable reservoir of this virus.



傳播

- 馬感染被懷疑是因為吃了牧場上被蝙蝠糞尿或流產/生產胎組織污染的草。
- 馬之間的傳播主要是通過呼吸分泌物及污染器械。
- 馬傳人。

疾病病理學 習網站

- Joint Pathology Center (JPC)網站
- 舉例:鍵入“JPC and Hendra virus”
- https://www.askjpc.org/vspo/show_page.php?id=Q3JROXZibGN5SU53cG1JMUhIT1Rsdz09

JPC SYSTEMIC PATHOLOGY
RESPIRATORY SYSTEM
October 2017
P-V26

Signalment (JPC #2641092): Adult horse, breed and gender unspecified

HISTORY: This horse was experimentally inoculated with Hendra virus. Seven days post-inoculation the horse developed tachycardia, tachypnea, anorexia and lethargy.

HISTOPATHOLOGIC DESCRIPTION: Lung: Multifocally, alveolar septa are thickened up to 10X normal by fibrin, edema, increased numbers of macrophages and lymphocytes and small aggregates of brown globular pigment within macrophages (hemosiderin). Endothelial cells lining small to medium caliber blood vessels and alveolar capillaries often form viral syncytial cells with up to six nuclei. Occasionally, endothelial cells are shrunken, with bright eosinophilic cytoplasm and a pyknotic nucleus (necrosis). Remaining endothelial cells are often hypertrophic and the tunica media is infiltrated by low numbers of macrophages and lymphocytes with mild edema. Diffusely, perivascular and peribronchiolar connective tissues, interlobular septa and pleura are markedly expanded by homogenous, pale eosinophilic to clear fluid and ectatic lymphatics (edema), and low numbers of lymphocytes, plasma cells, macrophages, hemosiderin-laden macrophages and fewer neutrophils. Multifocally, smaller bronchi, bronchioles and alveolar lumina contain variable amounts of edema admixed with a cellular exudate composed of lymphocytes, macrophages and hemorrhage. Multifocally, alveolar septa are ruptured with blunt clubbed ends forming large confluent airways (emphysema). Within the interstitium there are aggregates of macrophages which contain a black spiculated pigmented material (anthracosis).

MORPHOLOGIC DIAGNOSIS: Lung: Pneumonia, interstitial, multifocal, subacute, moderate, with endothelial viral syncytial cells and perivascular, interlobular and alveolar edema, breed not specified, equine.

HISTOPATHOLOGIC DESCRIPTION:

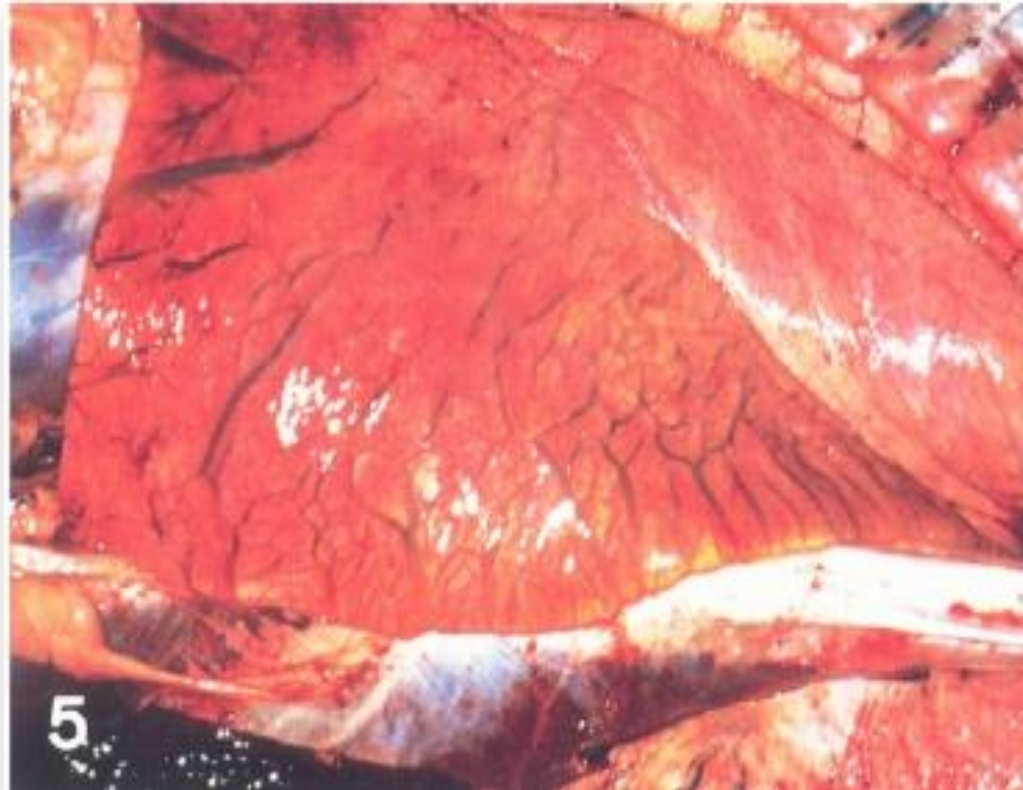
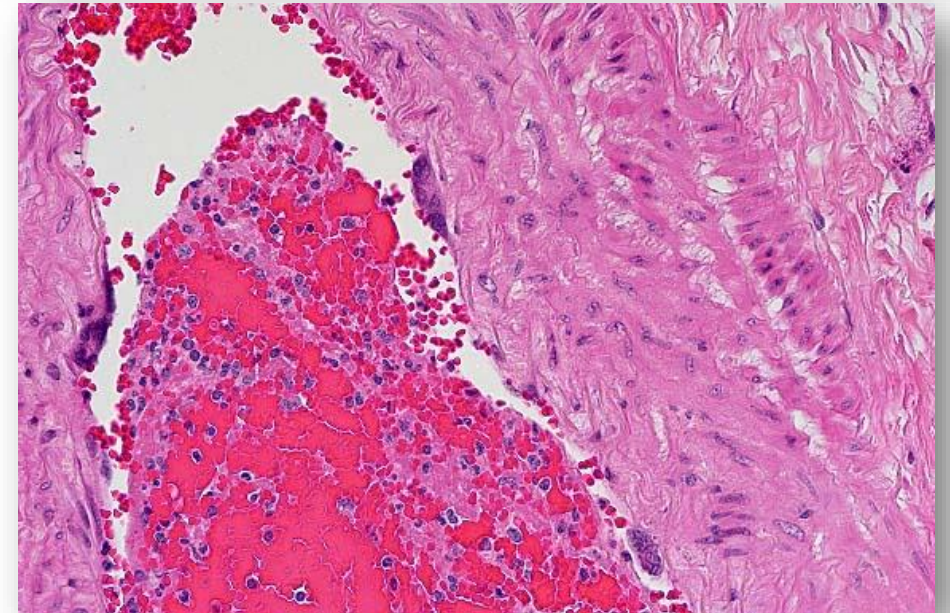
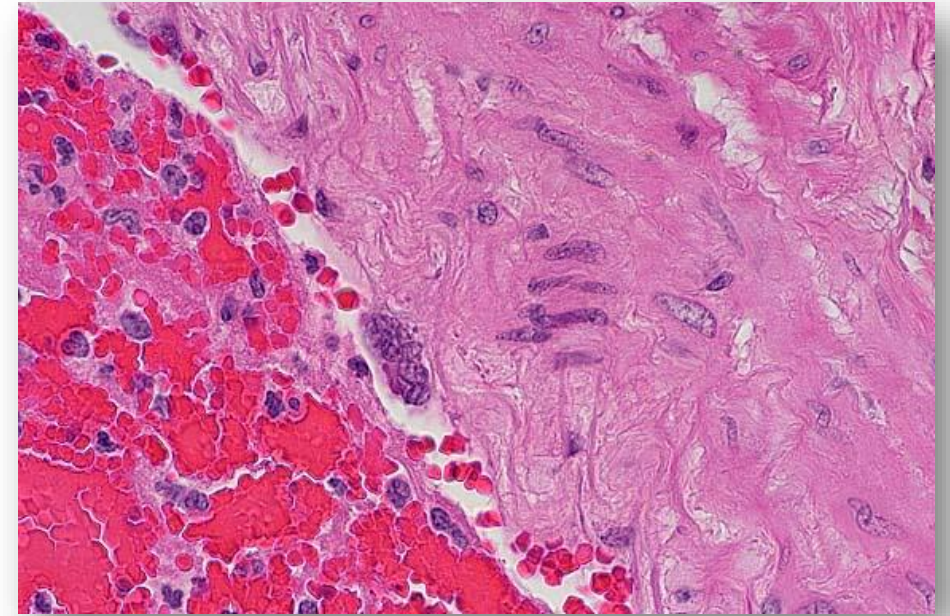
馬臨床症狀

- Incubation period: 8 - 11 days (maximum of 16 days)
- Clinical course: short with high mortality; death occurs in approximately three days
- Acute respiratory distress, anorexia, fever, depression and ataxia
- Copious yellow frothy nasal discharge, ataxia and head pressing are common in the terminal stages
- **Coughing is not a feature**

馬肉眼病變

- Notable absence of upper respiratory tract lesions
- Marked pulmonary edema and congestion with gelatinous distention of sub-pleural lymphatics; ventral consolidation of the lungs; excess thoracic and pericardial fluid
- Petechial hemorrhages on pleural surfaces; patchy hemorrhages of varying sizes within the parenchyma
- Fluid may ooze from cut surfaces; airways are often blocked by white to blood-tinged foam; trachea may contain abundant froth
- Other gross findings: visceral edema and petechial and ecchymotic hemorrhages in the perirenal tissue, stomach and intestines

Eosinophilic intracytoplasmic inclusion body



Severe pulmonary edema characterized by gelatinous distension of lymphatics.

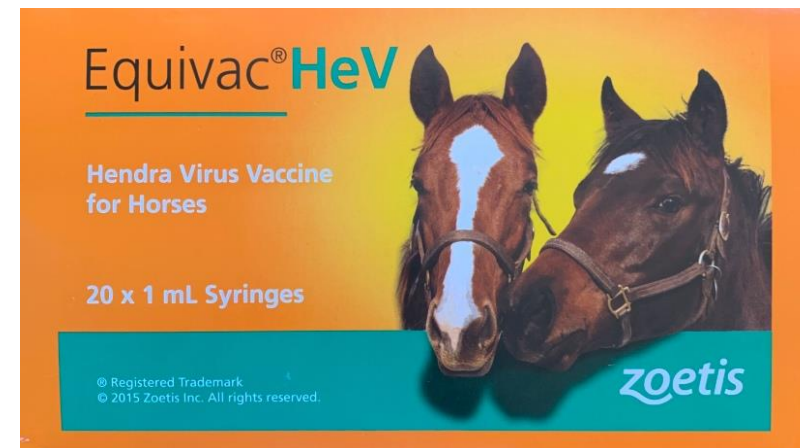
**Pulmonary artery:
Endothelial syncytial cells**

馬組織病理

- **Diffuse serofibrinous alveolar edema with vasculitis**, capillary thrombosis, ectatic lymphatics, hemorrhage and **increased numbers of alveolar macrophages**
- **Endothelial syncytial cells are inconsistently present in small blood vessels and alveolar capillaries**
- Suble vascular lesions may be present in a wide range of organs including lung, heart and kidney
- **Inclusion bodies are not visible by light microscopy** (except in Guinea pig neurons)

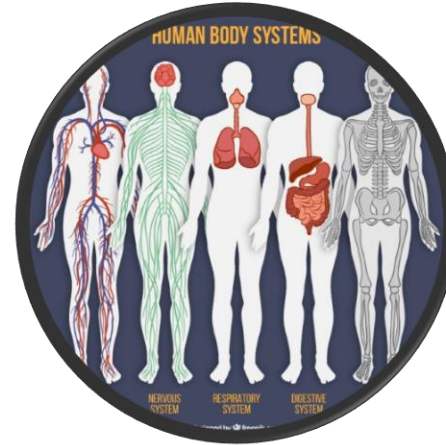
疫苗

- 在接種兩次疫苗，可以保護馬匹免受亨德拉病毒的侵害長達六個月。
- Equivac[®] HeV vaccine for horses (Zoetis, Parkville, VIC., Australia)
 - 馬的血清監測證明可以誘發高力價中和抗體。
- 尚未有人用疫苗。



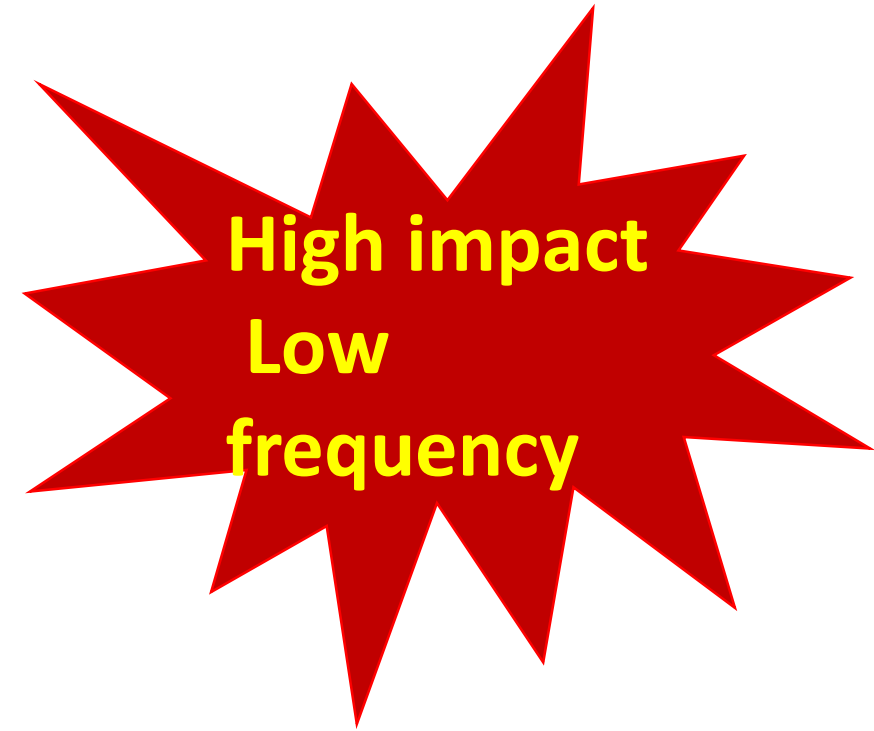
立百病毒感染症 (Nipah virus infection)

- **Nipah Virus Encephalitis**
- Porcine Respiratory and Encephalitis Syndrome
- Porcine Respiratory and Neurologic Syndrome
- Barking Pig Syndrome



Nipah Virus International Conference 2019

- The Nipah Virus International Conference was held from 9 to 10 December 2019 in Singapore.
- This 2-day conference is co-organised by the Coalition for Epidemic Preparedness Innovations (CEPI, 流行病預防創新聯盟), Duke-NUS Medical School, WHO and NIH.



2021年9月，印度喀拉拉邦科日科德市一名12歲男孩死亡。



Health workers and relatives carrying the body of Nipah virus victim Muhammad Hashim to the burial ground in Kozhikode. (AP Photo)

Nipah virus disease – India (WHO) 24 September 2021

- On 29 August, a 12 year-old boy developed low grade fever.
- On 4 September, the presence of Nipah virus in the plasma, cerebrospinal fluid was confirmed
- On 5 September, the patient died.

疫情爆發



- 立百病毒的發生開始自1998年9月起至1999年4月，首先在馬來西亞北部霹靂州怡保（Ipoh）地區，出現養豬戶或與豬有密切接觸的人員發生腦炎甚至因而死亡的案例。因豬隻移動再發生於距160公里外的森美蘭州及新加坡。
- 283人感染得腦膜腦炎 (93%與養豬產業有關)，109人死亡。撲殺上百萬隻豬，造成至少400萬美元的經濟損失。
- 新加坡屠宰場11個工人感染，1人死亡。

診斷過程：日本腦炎及立百病毒腦炎

News

European Commission proposes public health department

Rory Watson, *Bussels*

The European Commission is being urged to establish a specific department to handle public health issues.

The idea has been launched by Euro MPs at a meeting this week. They believe that the creation of a special health directorate general under the direct responsibility of one of the 20 commissioners would help to ensure that health concerns are placed at the heart of all European policy areas, ranging from agriculture to consumer affairs.

Supporters of the move acknowledge that responsibility for the organisation and delivery of health services will remain the

exclusive responsibility of national governments. But they point out that the coming into force of the new Amsterdam Treaty containing the latest changes to the EU's constitution in the next few weeks will commit the 15 member states to ensuring "a high level of human health protection."

The British Labour MEP Clive Needle, who won the support of the European parliament for the concept of a health commissioner, has also called for a European decade of health from next year.

Euro MPs believe that three priorities should now feature prominently on the Union's

health agenda: improvements in public health information, ensuring an ability to react rapidly to threats to health, and tackling health determinants through health promotion and disease prevention. To these will be added an increasing emphasis on the need to help raise health standards in those countries of Eastern and Central Europe that are hoping to join the Union.

The MEP's recommendations will now be taken into account by EU governments as they finalise the Union's second health programme, which is due to start next year.

The suggestion coincides with moves to overhaul the European Commission's own internal bureaucracy, after the unprecedented mass resignation in mid March of the full team of 20 commissioners. □

Open letter disputes WHO hypertension guidelines

Richard Woodman, *London*

Over 400 doctors, pharmacists, and scientists from 42 countries have signed a letter on the internet, expressing fears that the World Health Organisation's new hypertension guidelines will result in "increased use of antihypertensive drugs, at great expense and for little benefit."

The letter, to WHO Director General Gro Harlem Brundtland, says that there is insufficient evidence to justify the recommended guideline of restoring blood pressure to levels defined as "normal" (<130/85 mm Hg) or "optimal" (<120/80 mm Hg). "As far as we

know, there is only one trial that has aimed to investigate the level of optimal target blood pressure, the Hypertension Optimal Treatment (HOT) study (*Lancet* 1998;351:1755-62). About the HOT study, the guidelines state:

"Comparison of outcomes between the three randomised blood pressure target groups in the HOT study (diastolic blood pressure <90, 85 or 80 mm Hg) was unable to detect significant differences in the risk of cardiovascular disease between adjacent target groups. We have also reviewed the HOT paper and found no evidence to recommend aiming for a blood pressure below 140/90 in non-diabetic patients."

"The justification for the recommendation seems to be that the HOT study indicates that there is no increase in cardiovascular risk in patients randomised to the lowest target groups (<80 mm Hg). In our view it is necessary to prove benefits, not lack of harm, when making such a recommendation."

Ingrid Martin, the team coordinator for cardiovascular disease at the WHO in Geneva, commented: "The recommendations represent the guidelines committee's interpretation of the totality of the available evidence from epidemiological studies and from randomised trials." □

The letter can be read at www.who.int/letter/

Outbreak of Japanese encephalitis hits Malaysia

Adam Easton, *Malacca*

More than 50 people have died and hundreds of thousands of pigs—the possible carriers of the infection—have been slaughtered in Malaysia after an outbreak of Japanese encephalitis.

There have been 154 reported cases of Japanese encephalitis, of which 42 have been confirmed, and 56 deaths in Negeri Sembilan, 90 km south of the capital, Kuala Lumpur, and in Perak. Many of the victims were adult male pig farmers or workers. The outbreak has spread to neighbouring Singapore, where eight cases and one death have been reported.

The disease outbreak has caused panic among sections of the population. Up to 700 soldiers have reportedly entered three villages in Negeri Sembilan and begun shooting 300,000 pigs. The pigs are the reservoir for the virus, which is commonly transmitted to humans via the *Culex* mosquito. Both Singapore and Thailand have banned the import of pigs from Malaysia.

Malaysia has suffered outbreaks of the virus previously and has adequate resources to

deal with the current one, according to the World Health Organisation's regional adviser in vector borne diseases, Dr Kevin Palmer. The country generally reports a handful of seasonal cases of Japanese encephalitis each year. The area currently affected has the highest density of pigs in South East Asia and an unusually large number of mosquitoes. Sanitation is also extremely poor, and some observers have been surprised that an outbreak has not occurred previously. Dr Palmer

commented: "It's filthy; there is no sanitation there. The pigs are kept in sheds, and the ditches are full of stagnant water for mosquitoes to breed in. It's like a bomb ready to go bang."

Japanese encephalitis is the leading cause of viral encephalitis in Asia with 30,000 to 50,000 cases reported annually. Acute cases can end in paralysis, coma, and death. Fatalities usually occur among the very young and older people. The condition is untreatable, although it can be prevented through vaccination. □



Pigs are being slaughtered to halt the spread of Japanese encephalitis

- 人檢體送日本-JE
- 依日本腦炎方式滅蚊及消毒-無效
- 美國CDC: Nipah virus
- 兩者豬疾病之區別

立百 (尼帕) 病毒感染症

- <https://youtu.be/MSuWYB3FnFQ?t=7>
- <https://youtu.be/VS8F6SXVpQs?t=6>



大愛電視
大愛電視

前往

圖片可能受版權保護。瞭解詳情

相關圖片



立百病毒浩劫20年·病毒襲村从此无...
chinapress.com.my



一场夺命病毒肆虐宜麦养猪区走向没...
kwongwah.com.my



立百病毒20周年特辑·星洲·1/7】立...
khalid.com.my



双溪立百新村的故事- 人间烟火



NIPAH Virus (lacc microbiology 020)

印度及孟加拉疫情

- 2001年至2004年底有十數起腦炎病例發生於孟加拉（Bangladesh），此後幾乎每年都發生疫情。尤以2004年三月發生34例群聚感染，而造成24人死亡案例最為嚴重。
- 2001年起在印度東部有75人群聚感染，造成45人死亡疫情，繼後也陸續發現該疾病。



History of Nipah virus outbreak (1998-2021)

TABLE 1 Morbidity and mortality in humans due to NiV infections^a

S. No	Year/Month	Country	Location	No. of cases	No. of deaths	Case fatality rate, %
1	Sep 1998-April 1999	Malaysia	Perak, Selangor, Negeri Sembilan states	265	105	39.6
2	Mar-1999	Singapore	Singapore	11	1	9
3	Jan-Feb 2001	India	Siliguri	66	45	68.2
4	Apr-May 2001	Bangladesh	Meherpur	13	9	69.2
5	Jan 2003	Bangladesh	Naogaon	12	8	66.7
6	Jan-Apr 2004	Bangladesh	Rajbari, Faridpur	67	50	74.6
7	Jan-Mar 2005	Bangladesh	Tangail	12	11	91.7
8	Jan-Apr 2007	Bangladesh	Kushtia, Naogaon, Natore, Pabna, Thakurgaon	18	9	50
9	Apr 2007	India	Nadia	5	5	100
10	Feb-Apr 2008	Bangladesh	Manikganj, Rajbari	11	9	81.8
11	Jan 2009	Bangladesh	Gaibandha, Nilphamari, Rangpur, Rajbari	4	1	25
12	Feb-Mar 2010	Bangladesh	Faridpur, Gopalganj, Kurigram, Rajbari	17	15	88.2
13	Jan-Feb 2011	Bangladesh	Comilla, Dinajpur, Faridpur, Lalmonirhat, Nilphamari,	44	40	90.9
14	Jan 2012	Bangladesh	Joypurhat	12	10	83.3
15	Jan-Apr 2013	Bangladesh	Gaibandha, Manikganj, Naogaon, Natore, Pabna,	24	21	87.5
16	Jan-Feb 2014	Bangladesh	13 districts	18	9	50
17	Mar-May 2014	Philippines	Philippines	17	9	52.9
18	Jan-Feb 2015	Bangladesh	Faridpur, Magura, Naogaon, Nilphamari, Ponchoghor, Rajbari	9	6	66.7
19	2018 May	India	Kozhikode and Malappuram	18	17	94.4
Total				643	380	59

^aAdapted from WHO data.²⁹

2019 Kerala, India. A 23-year-old student was infected and discharged.

2021 Kerala, India. A 12-year-old boy was dead.

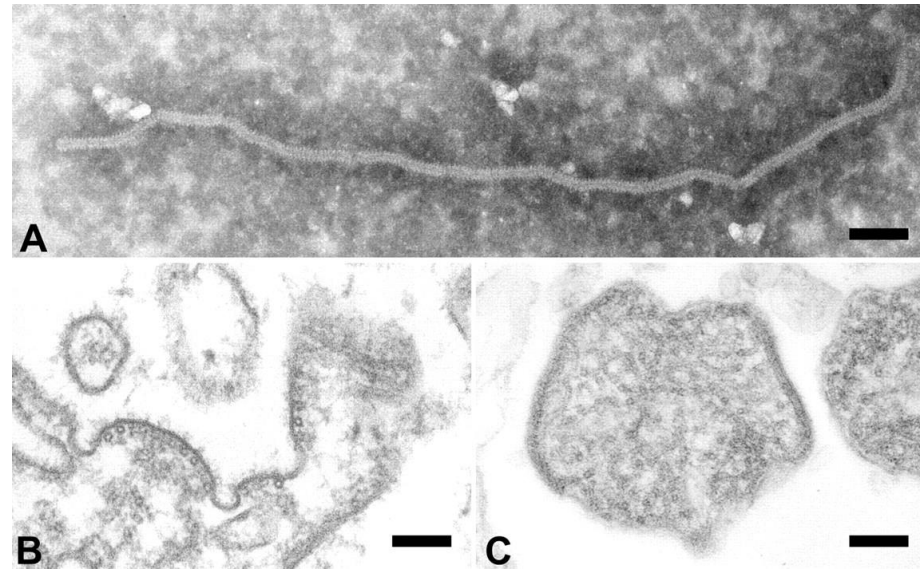
菲律賓疫情 (?)

- 2014年，菲律賓爆發了一起 Nipah virus 感染（根據血清學和部分基因組序列懷疑為 NiV）。
- 疑似馬傳人及人傳人，導致 17 例人感染，82% 的死亡率。
- 10 匹馬死亡。
- 可能還有一隻犬和幾隻貓被餵食馬肉而感染。

發生地區

- 迄今為止，只有馬來西亞、孟加拉和印度有報告。新加坡屠宰場工人的人類病例與1998年首次報告的疾病有關。
- 菲律賓未有正式報告。
- 在已知的天然宿主狐蝠屬蝙蝠以及柬埔寨、迦納、印尼、馬達加斯加、菲律賓和泰國等一些國家的其它若干蝙蝠種類中存在立百病毒。

病原



Chua *et al* 2000

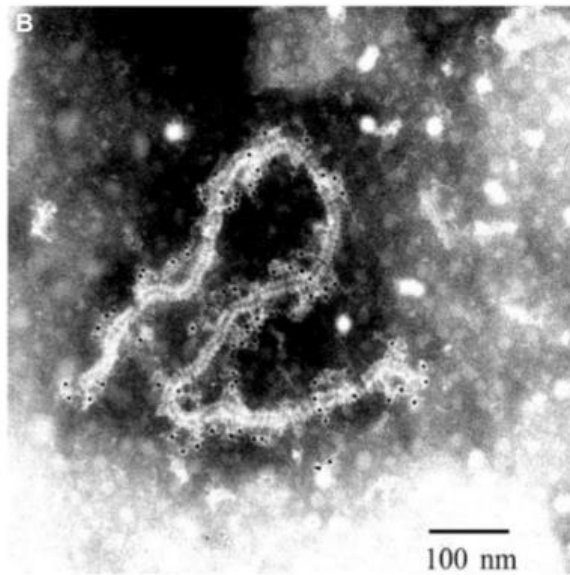
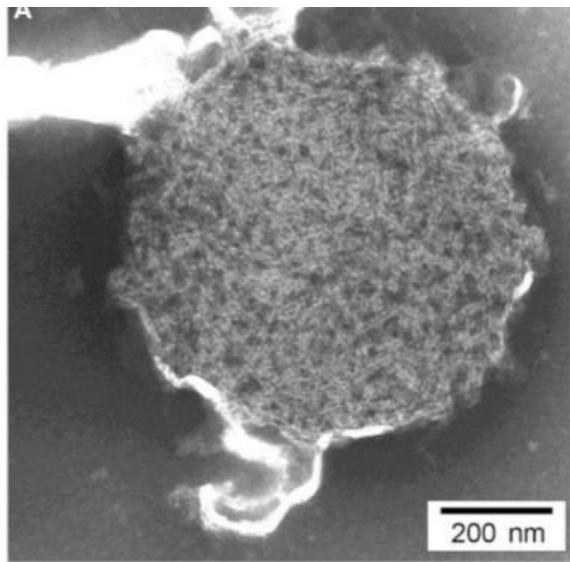


Figure 2 Structure of the Nipah virus virion core.

Notes: (A) Nucleocapsid core with residual envelope; (B) herringbone-shaped fragment of the nucleocapsid with immunogold labeling of P proteins. Images are

- Nipah virus is an enveloped, negative-sense, single-stranded RNA, a member of the genus Henipavirus in the family Paramyxoviridae.
- Two major strains were isolated from pigs in Malaysia, and the strains that cause human cases in Bangladesh and India differ from outbreak strains isolated in Malaysia.
- A henipavirus that recently caused an outbreak in the Philippines is also thought to be Nipah virus, based on RT-PCR results. It appears to be most similar to the viruses from Malaysia

Henipavirus (ICTV) virus

Taxonomy: 2019 Release, EC 51, Berlin, Germany, July 2019

Email ratification March 2020 (MSL #35)

- *Henipavirus*: 5 species

Genus: *Henipavirus*

Species:	<i>Cedar henipavirus</i>
Species:	<i>Ghanaian bat henipavirus</i>
Species:	<i>Hendra henipavirus</i>
Species:	<i>Mojiang henipavirus</i>
Species:	<i>Nipah henipavirus</i>

Blood and tissue samples were collected from 324 bats from 14 species and *P. vampyrus* and *P. hypomelanus* were identified as likely natural and reservoir hosts due to the high percentage of individuals showing antibodies to Nipah virus. (Johara et al., 2001)^{2021/9/30}

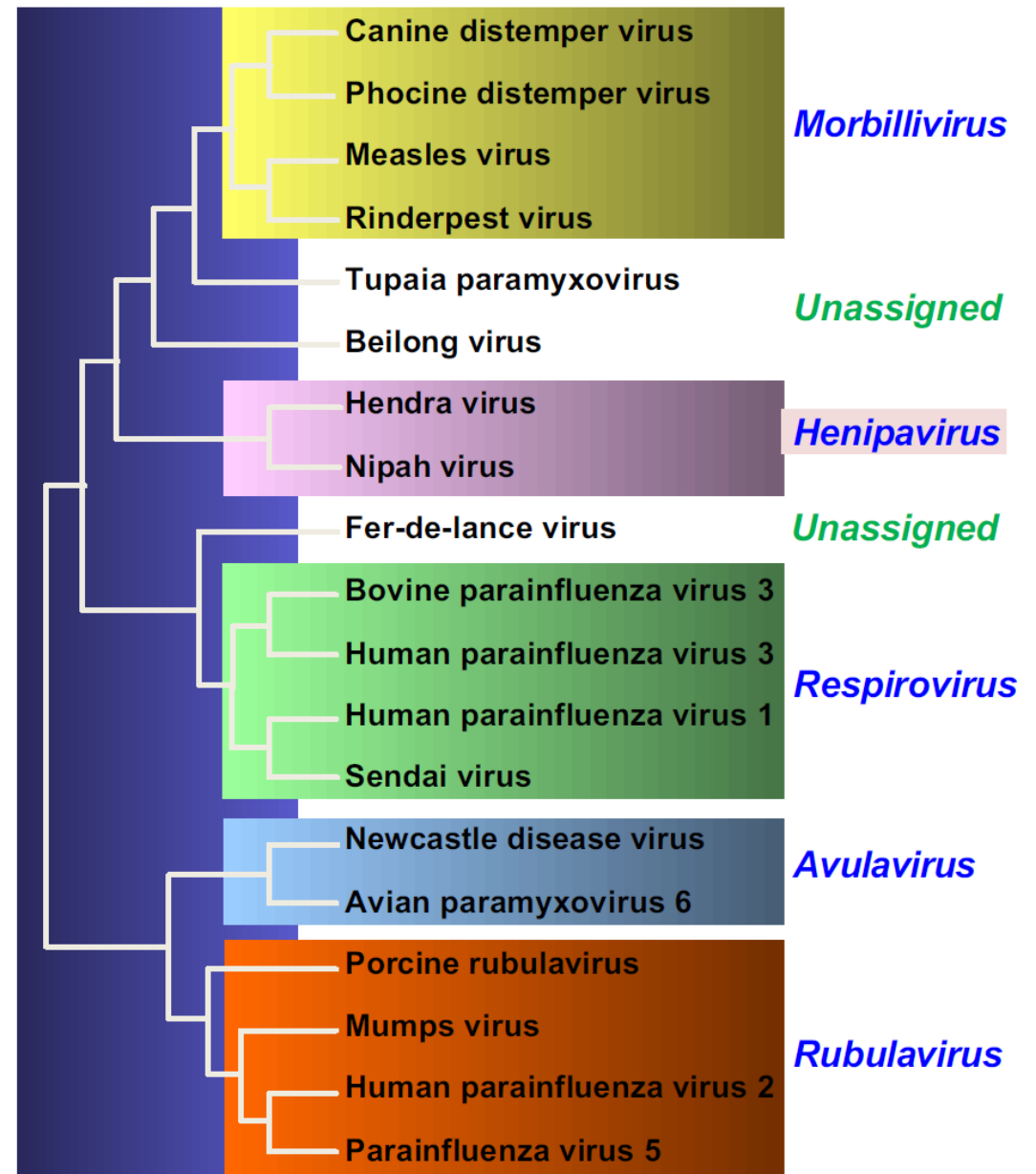
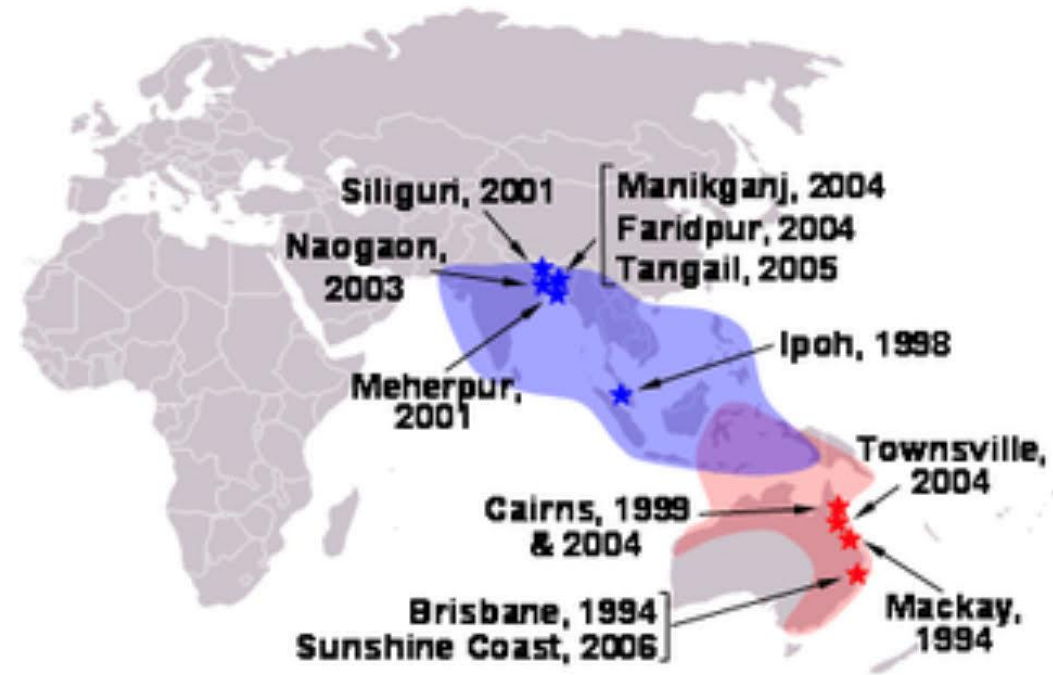


FIGURE 6.2 Phylogenetic relationship of selected viruses in the subfamily *Paramyxoviridae*. The phylogenetic tree was based on protein sequences of nucleocapsid (N) proteins of viruses representing the five existing genera and several unclassified viruses.

Henipavirus 發生地區



Locations of henipavirus outbreaks (red stars–Hendra virus; blue stars–Nipah virus) and distribution of henipavirus flying fox reservoirs (red shading–Hendra virus; blue shading–Nipah virus)

天然宿主：果蝠

- Fruit bats of the family *Pteropodidae* – particularly species belonging to the *Pteropus* genus.
- Geographic distribution of *Henipaviruses* overlaps with that of *Pteropus* category. This hypothesis was reinforced with the evidence of *Henipavirus* infection in *Pteropus* bats from **Australia, Bangladesh, Cambodia, China, India, Indonesia, Madagascar, Malaysia, Papua New Guinea, Thailand and Timor-Leste (東帝汶)**
- African fruit bats of the genus *Eidolon*, family *Pteropodidae*, were found positive for antibodies against Nipah and Hendra viruses.

<https://youtu.be/tbx6fqYdNWc>



Figure 1 Geographical locations of up to date reported Hendra virus (blue) and Nipah virus (pink) outbreaks.





Note: The black line running across the image approximates the Wallace line where the ecozone of Asia starts to transition into the ecozone of Australia.

臨床症狀
Nipah virus infection 1min 20
sec.WMV

潛伏期

- 豬為7至14天，但可能短至4天。
- 實驗性感染的貓在6-8天出現臨床症狀。
- 實驗性感染雪貂6-10天出現症狀。

Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies – a comprehensive review

Raj Kumar Singh^a, Kuldeep Dhama^b , Sandip Chakraborty^c, Ruchi Tiwari^d, Senthilkumar Natesan^e, Rekha Khandia^f , Ashok Munjal^f , Kranti Suresh Vora^g, Shyma K. Latheef^h, Kumaragurubaran Karthik^h , Yashpal Singh Malikⁱ, Rajendra Singh^b, Wanpen Chaicumpa^j and Devendra T. Mourya^k

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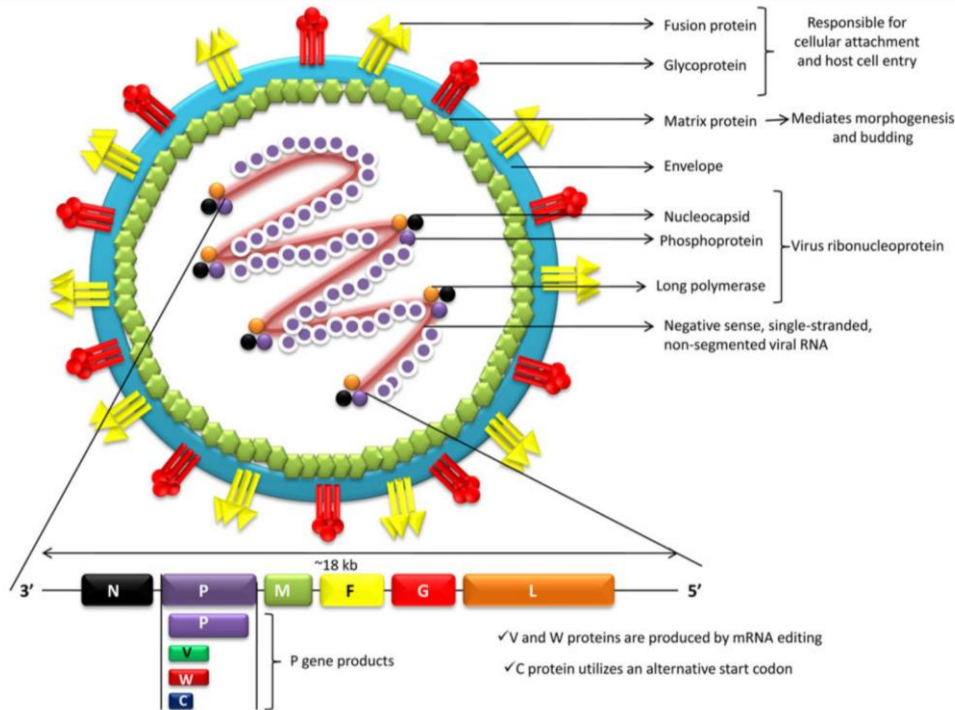


Figure 1. Structure of Nipah virus.

- Henipaviruses (HNV) are the only Paramyxoviruses classified as biosafety level 4 (BSL4) pathogens.
- HNV use ephrin-B2 and ephrin-B3, highly conserved proteins, as viral entry receptors.



臨床症狀



Swine Available observations of clinical signs in swine would suggest a respiratory and neurologic foundation; clinical manifestations associated with age groups (OIE)

Suckling pigs and piglets (< 1 month old)

- Laboured breathing and muscle tremors with limb weakness
- Mortality in piglets can be high (40%)

Young swine (1 to 6 months old)

- Begins as an acute fever with respiratory signs; laboured breathing, nasal discharge and loud nonproductive cough (“barking pig syndrome” and “one-mile cough”)
- Accompanying neurologic signs: muscular fasciculation, myoclonus, limb weakness, and spastic paresis; in some cases, lateral recumbency with paddling and tetanic spasms
- Disease presentation can be mild to fulminant with high morbidity and low mortality (< 5%)

Older animals (> 6 months old)

- Acute febrile condition with marked neurologic signs
- Central nervous system: nystagmus, bruxism, head pressing, aggressive behaviour, tetanic spasms and seizures
- Respiratory signs: open-mouthed breathing, nasal discharge and sialorrhea (possibly due to pharyngeal paralysis)
- Morbidity in confined animals approaches 100%
- Fulminant death in this age group with few signs has been reported; mortality still tends to be low
- First trimester abortions have also been reported

- Swine can act as amplifying hosts and shed this virus in respiratory secretions and saliva.
- Experimental infections: shedding may start as early as 2 days after infection and persist for up to 3 weeks.

人臨床症狀

- 感染平均年齡42歲，男女性別比為18：1，先有2-3天的低燒，然後發燒到40°C，有頭痛、頸部僵硬、暈眩、肌肉無力、抽搐，昏睡，意識不清並昏迷，最後休克死亡，病程約4-5天。
- 少數有呼吸症狀，包括有間質性肺炎，此外消化道、關節、肝臟、腎臟、淋巴結、耳、鼻、喉及皮膚均無特異現象。
- 許多病人有高血壓、高燒、面紅及流汗等疑似副交感神經被刺激的症狀。18-20% 病人的橫膈膜肌陣攣（diaphragmatic myoclonus）。
- 立百病毒對於人類危害性大，感染者致死率約為38%（豬隻則小於5%），而感染日本腦炎病毒致死率約為36%，若兩者混合感染則致死率為52%。
- 並無醫護人員因為照顧立百病毒病人而遭受感染的案例。



其他物種

- Limited clinical information exists for other species
- In dogs, distemper-like syndrome observed with pyrexia, depression, dyspnoea and conjunctivitis with purulent ocular-nasal discharge
- Nipah affected cats were observed on farms during outbreaks in Malaysia and some of these resulted in death; acute febrile disease with respiratory complications was observed experimentally in cats
- Fruit bats show no serious signs of infection

動物的發病率和死亡率

- Malaysia: 9-17% of *Pteropus vampyrus* and 21-27% of *P. hypomelanus* had antibodies to this virus; the frequency and timing of virus shedding in bats is unknown.
- Before eradication, seropositive pigs were approximately 5.6%. On one farm, more than 95% of all sows and 90% of the piglets had antibodies to this virus. The morbidity rate is estimated 70-100%, but the mortality rate is low (e.g., 1-5% in 1-6 month old pigs) except in piglets. Mortality in the latter age group was approximately 40% in Malaysia.
- Seroprevalence rates of 15%- 55% in dogs, 4%-6% in cats, and 1.5% in goats in the outbreak area. Five horses out of more than 3200 were positive by serology, and viral antigens were found in a single horse that died with signs of meningitis.
- Four cats and one dog died soon after eating tissues from sick horses during 2014 outbreak in Philippines. Antibodies to Nipah virus were detected in dogs but not cats in the area.

貓與許多疾病都有關係

Rabies: acquired rabies from wildlife (bats, racoon, and skunks)

Feline spongiform encephalopathy

COVID-19

H5N1

Nipah virus infection

Hendra virus infection

SARS-CoV-2迄今感染動物物種 (2021/9/30)

Mink

Cat

Dog

White
tailed deer

5. Lion
6. Tiger
7. Ferret
8. Gorilla
9. Snow leopard
10. Cougar
11. Otter
12. Beaver

2010-2019年美國狂犬病監控 (Blanton JD et al, JAVMA)

• 註: 美國每年約有1.6萬~3.9萬人接受狂犬病暴露後預防治療。

年度	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
地區	48州及波多黎各	49州及波多黎各	49州及波多黎各	49州及波多黎各、加拿大、墨西哥	50州及波多黎各	50州及波多黎各	50州及波多黎各	52個地區	54個地區	53個地區
動物感染	6,154	6,031	6,163	5,868	6,033	5508	4910	4454	4951	4690
92%來自野生動物(1980年以後野生動物佔90%以上)	1. 浣熊: 2,246 2. 臭鼬: 1,448 3. 蝙蝠: 1,430 4. 狐狸: 429 5. 貓: 303 6. 牛: 71 7. 犬: 69	1. 浣熊: 1,981 2. 臭鼬: 1,627 3. 蝙蝠: 1,380 4. 狐狸: 427 5. 貓: 303 6. 牛: 65 7. 犬: 70	1. 浣熊: 1,953 2. 臭鼬: 1,539 3. 蝙蝠: 1,680 4. 狐狸: 340 5. 貓: 257 6. 牛: 115 7. 犬: 84	1. 浣熊: 1,898 2. 臭鼬: 1,447 3. 蝙蝠: 1,598 4. 狐狸: 344 5. 貓: 247 6. 牛: 86 7. 犬: 89	1. 浣熊: 1,822 2. 蝙蝠: 1,756 3. 臭鼬: 1,588 4. 狐狸: 311 5. 貓: 272 6. 牛: 78 7. 犬: 59	1. 蝙蝠: 1,704 2. 浣熊: 1619 3. 臭鼬: 1365 4. 狐狸: 325 5. 貓: 244 6. 牛: 85 7. 犬: 62	1. 蝙蝠: 1646 2. 浣熊: 1403 3. 臭鼬: 1031 4. 狐狸: 313 5. 貓: 257 6. 牛: 70 7. 犬: 58	1. 蝙蝠: 1433 2. 浣熊: 1275 3. 臭鼬: 939 4. 狐狸: 314 5. 貓: 276 6. 犬: 62 7. 牛: 36	1. 蝙蝠: 1635 2. 浣熊: 1499 3. 臭鼬: 1004 4. 狐狸: 357 5. 貓: 241 6. 犬: 63 7. 牛: 33	1. 浣熊: 1545 2. 蝙蝠: 1387 3. 臭鼬: 915 4. 狐狸: 361 5. 貓: 245 6. 犬: 66
人感染	2例，皆與蝙蝠接觸有關(1例在墨西哥感染，1例感染處不詳)	6例，其中2例與蝙蝠接觸，3例在國外被犬感染，1例疑與貓有關	1例，與蝙蝠接觸有關	3例，其中1例為腎臟移植感染，1例為瓜地馬拉非法移民被捕，	1例，與蝙蝠接觸有關	3例，其中1例國外遭犬咬，1例接觸蝙蝠，另1例遭貓咬	沒有人感染病例	2例死亡	3例死亡	沒有人病例

Transmissible spongiform encephalopathies (TSE)

Animals	Humans
Scrapie (綿羊搔癢症) 1700s	Creutzfeldt-Jakob disease (CJD) (庫賈氏病) 1921
Transmissible mink encephalopathy (傳播性貂腦病, TME) 1947	Gerstamann-Sträussler-Scheinker disease (GSSD) 1936
Chronic wasting disease (慢性消耗性病, CWD) 1967	Kuru (庫魯病) 1957
Bovine spongiform encephalopathy (牛海綿狀腦病, BSE) 1986	Fatal familial insomnia (致死性家族性失眠症, FFI) 1986
Zoo spongiform encephalopathy (動物園海綿狀腦病) 1988	New variant CJD (新型庫賈氏病, vCJD) 1994
Feline spongiform encephalopathy (貓海綿狀腦病) 1990	
Prion Disease in Dromedary Camels (單峰駱駝普里昂病) 2018	

Numbers of BSE reported in worldwide and CJD (including vCJD) in UK

Number of reported cases of bovine spongiform encephalopathy (BSE) in farmed cattle worldwide* (excluding the United Kingdom)

Country/Year	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16		
Austria	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2	2	1	0	0	2	0	0	0	0	0	0		
Belgium	0	0	0	0	0	0	0	0	1	6	3	9	46	38	15	11	2	2	0	0	0	0	0	0	0	0	0	0 ^c		
Brazil	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 ⁿ	0	1 ^p	0	0 ^c		
Canada	0	0	0	0	1 ^b	0	0	0	0	0	0	0	0	0	2 ^a	1	1	5	3	4	1	1	1	0	0	0	1	0 ^c		
Czech Republic	0	0	0	0	0	0	0	0	0	0	0	0	2	2	4	7	8	3	2	0	2	0	0	0	0	0	0	0 ^c		
Denmark	0	0	0	1 ^b	0	0	0	0	0	0	0	0	1	6	3	2	1	1	0	0	0	1	0	0	0	0	0	0 ^c		
Finland	0	0	0	0	0	0	0	0	0	0	0	0	1 ^a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 ^c		
France	0	0	5	0	1	4	3	12	6	18	31 ^a	162 ^d	274 ^e	239 ^f	137 ^g	54 ^h	31	8	9	8	10	5	3	1	2 ^o	3 ^p	0	1 ^c		
Germany	0	0	0	1 ^b	0	3 ^b	0	0	2 ^b	0	0	7	125	106	54	65	32	16	4	2	2	0	0	0	0	0	2 ^p	0	0 ^c	
Greece	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Ireland	15 ^a	14 ^a	17 ^a	18 ^a	16	19 ^a	16 ^a	73	80	83	91	149 ^d	246 ^e	333 ^f	183 ^g	126 ^h	69 ^j	41 ^k	25 ^k	23 ^l	9	2	3	3	1	0	1	0 ^c		
Israel	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0 ^c		
Italy	0	0	0	0	0	2 ^b	0	0	0	0	0	0	48	38 ^a	29	7	8	7	2	1	2	0	0	0	0	0	0	0 ^c		
Japan	0	0	0	0	0	0	0	0	0	0	0	0	3 ^e	2	4 ^g	5	7	10	3	1	1	0	0	0	0	0	0	0 ^c		
Liechtenstein	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Luxembourg	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0		
Netherlands	0	0	0	0	0	0	0	2	2	2	2	20	24	19	6	3	2	2	1	0	2	1 ^m	0	0	0	0	0	0 ^c		
Norway	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 ^q	0 ^c	
Poland	0	0	0	0	0	0	0	0	0	0	0	0	0	4 ^f	5	11	19	10	9	5	4	2	1 ^m	3	1	0	0	0		
Portugal	0	1 ^b	1 ^b	1 ^b	3 ^b	12	15	31	30	127	159	149 ^a	110	86	133	92 ^a	46	33	14	18	8	6	5	2	0	1	0	0 ^c		
Romania	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2 ^p	0	0
Slovakia	0	0	0	0	0	0	0	0	0	0	0	0	5	6	2	7	3	0	1	0	0	1	0	0	0	0	0	0	0 ^c	
Slovenia	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2 ^a	1	1	1	0	0	0	0	0	0	0	0	1 ^q	0 ^c	
Spain	0	0	0	0	0	0	0	0	0	0	0	2	82	127	167	137	98	68	36	25	18	13	6	n	0	2 ^p	1 ^q	1 ^c		
Sweden	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	
Switzerland	0	2	2021/9/30	45	38	14	50	33 ^d	42	24	21 ^g	3	3 ⁱ	5	0	0	0	0	0	0	0	2 ^m	1 ⁿ	0	0	0	0	0 ^c		
United Kingdom																														

Number of cases of bovine spongiform encephalopathy (BSE) reported in the United Kingdom (1)

	Alderney	Great Britain	Guernsey (3)	Isle of Man (2)	Jersey	Northern Ireland	Total United Kingdom
1987 and before (4)	0	442	4	0	0	0	446
1988 (4)	0	2 469	34	6	1	4	2 514
1989	0	7 137	52	6	4	29	7 228
1990	0	14 181	83	22	8	113	14 407
1991	0	25 032	75	67	15	170	25 359
1992	0	36 682	92	109	23	374	37 280
1993	0	34 370	115	111	35	459	35 090
1994	2	23 945	69	55	22	345	24 438
1995	0	14 302	44	33	10	173	14 562
1996	0	8 016	36	11	12	74	8 149
1997	0	4 312	44	9	5	23	4 393
1998	0	3 179	25	5	8	18	3 235
1999	0	2 274	11	3	6	7	2 301
2000	0	1 355	13	0	0	75	1 443
2001	0	1,113	2	0	0	87	1,202
2002	0	1,044	1	0	1	98	1,144
2003	0	549	0	0	0	62	611
2004	0	309	0	0	0	34	343
2005	0	203	0	0	0	22	225
2006	0	104	0	0	0	10	114
2007	0	53	0	0	0	14	67
2008	0	33	0	0	0	4	37
2009	0	9	0	0	0	3	12
2010	0	11	0	0	0	0	11
2011	0	5	0	0	0	2	7
2012	0	2	0	0	0	1	3
2013	0	3	0	0	0	0	3
2014	0	1	0	0	0	0	1
2015 (5)	0	2	0	0	0	0	2
2016	0	0	0	0	0	0	0

CREUTZFELDT-JAKOB DISEASE IN THE UK (By Calendar Year)

REFERRALS OF SUSPECT CJD		DEATHS OF DEFINITE AND PROBABLE CJD					
Year	Referrals	Year	Sporadic ¹	Iatrogenic	Genetic ²	vCJD	Total Deaths
1990	[53] ⁺	1990	28	5	0	-	33
1991	75	1991	31	1	4	-	36
1992	96	1992	45	2	6	-	53
1993	79	1993	36	4	7	-	47
1994	119	1994	53	1	9	-	63
1995	87	1995	35	4	5	3	47
1996	132	1996	40	4	6	10	60
1997	163	1997	59	6	7	10	82
1998	155	1998	64	3	5	18	90
1999	170	1999	62	6	2	15	85
2000	178	2000	48	1	3	28	80
2001	179	2001	58	4	6	20	88
2002	164	2002	73	0	5	17	95
2003	162	2003	79	5	6	18	108
2004	114	2004	50	2	6	9	67
2005	124	2005	67	4	13	5	89
2006	112	2006	68	1	9	5	83
2007	119	2007	63	2	11	5	81
2008	150	2008	84	5	6	2	97
2009	153	2009	78	2	8	3	91
2010	150	2010	85	3	6	3	97
2011	158	2011	91	4	14	5	114
2012	127	2012	93	5	11	0	109
2013	152	2013	108	2	10	1	121
2014	130	2014	100	3	13	0	116
2015	140	2015	105	0	4	0	109
2016	148	2016	118	1	6	1	126
2017	159	2017	122	0	12	0	134
2018	167	2018	137	2	12	0	151
2019	146	2019	127	1	7	0	135
2020	168	2020	128	1	6	0	135
2021	22	2021	12	0	1	0	13
Total Referrals	4251	Total Deaths	2347	84	226	178	2835

¹ Referral figure for 1990 is from 1 May onwards

² As at 1st March 2021

Summary of vCJD cases

Deaths

Deaths from definite vCJD (confirmed):	123
Deaths from probable vCJD (without neuropathological confirmation):	55
Deaths from probable vCJD (neuropathological confirmation pending):	0
Number of deaths from definite or probable vCJD (as above):	178

Alive

Number of definite/probable vCJD cases still alive:	0
Total number of definite or probable vCJD (dead and alive):	178

¹ There are in addition a total of 18 cases of vPSP (death in 1997(1 case), 2004(1), 2006(1), 2008(3), 2010(1), 2012(4), 2013(1), 2016(3), 2017(1), 2018(1), 2019(1)) not included in the above figures.

² includes all genetic prion disease, including GSS.

Source: NCJDRSU website www.cid.ed.ac.uk - updated 01/03/2021



- Mild or subclinical presentation common; clinical cases manifest acute neurologic condition
- Begins as influenza-like illness: high fever, headache, muscular pain, and weakness.
- Drowsiness, dizziness, convulsions and/ or coma accompanied by nausea and vomiting.
- Respiratory signs less common
- Seriously affected patients can develop septicaemia, GI bleeding, and renal impairment
- Recovered patients may experience encephalitic relapse up to years later and subclinically infected individuals may show central nervous signs up to 4 years later
- **The case fatality rate is estimated at 40% to 75%.**
- Humans can shed Nipah virus in respiratory secretions, saliva, and urine, and contact with respiratory secretions

Morbidity and Mortality in Humans

- Human cases in Southeast Asia, with more than 500 cases identified as of 2016.
- Outbreaks in Bangladesh are seasonal and occur mainly between December and May.
 - Drinking raw date palm sap, person-to-person transmission and climbing tree
- Some human infections may be asymptomatic or mild.
- In the Malaysian outbreak, the subclinical infection rate was estimated to be 8-15%.
- The case fatality rate is much higher in Bangladesh and India than Malaysia, but whether this is due to strain variability or to differences in healthcare is uncertain.
- One study reported a higher mortality rate in people with diabetes. Among surviving patients, an estimated 19-32% have residual neurological deficits.

病變

Pathogenesis of Nipah virus infection

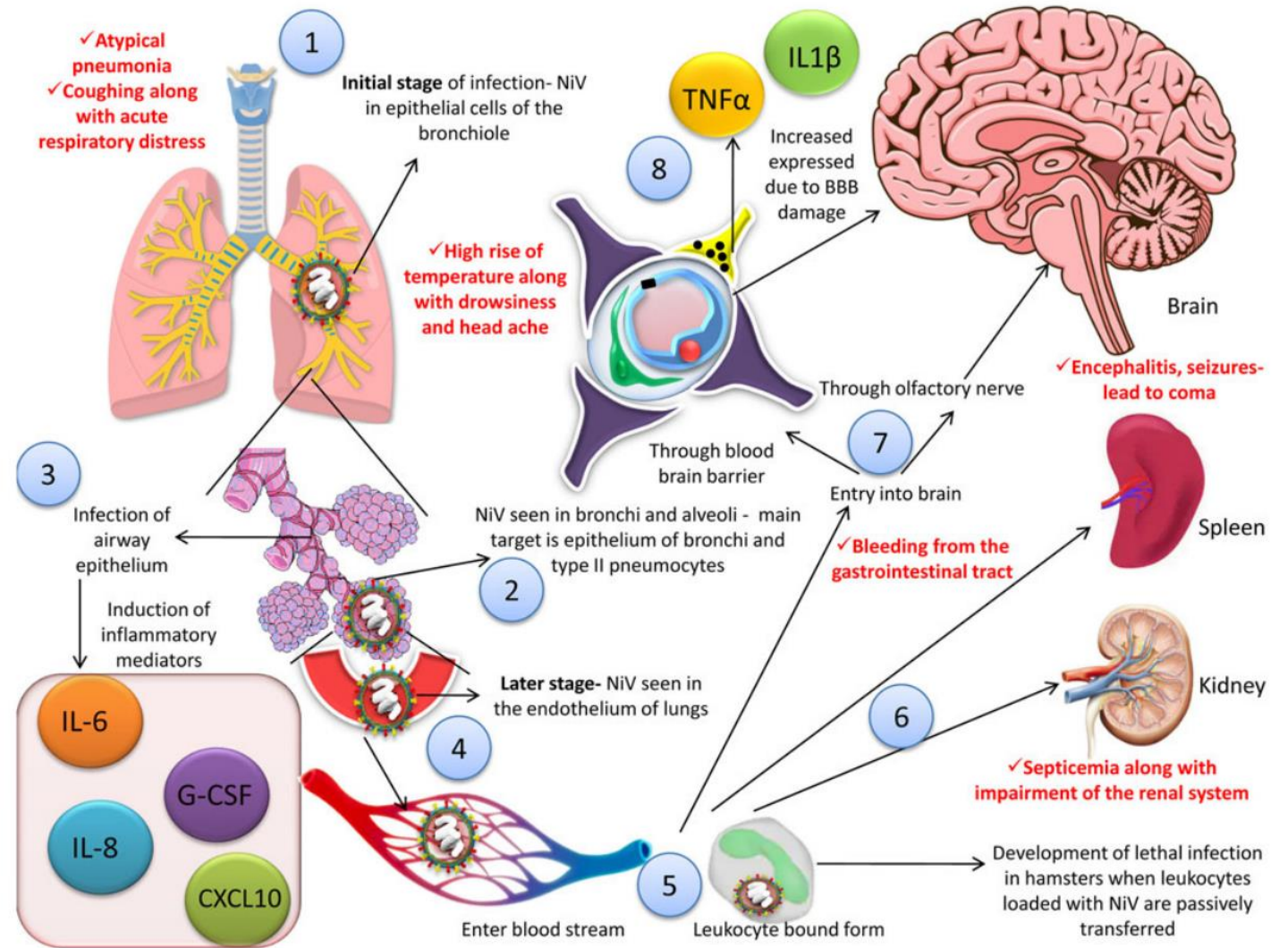


Figure 4. Pathogenesis of NiV. 1. NiV can be seen in the epithelial cells of the bronchiole in the initial stage of infection. 2. NiV antigen can be detected in bronchi and alveoli. 3. Inflammatory mediators are activated as a result of infection to the airway epithelium. 4. Virus is disseminated to the endothelial cells of the lungs in the later stage of the disease. 5, 6. Virus enter the blood stream followed by dissemination, either freely or in host leukocyte bound form, reach brain, spleen and kidneys. 7. Two pathways are involved in the process of viral entry into the central nervous system (CNS), *via* hematogenous route and anterogradely *via* olfactory nerve nerves. 8. The blood brain barrier (BBB) is disrupted and IL-1 β along with tumor necrosis factor (TNF)- α are expressed due to infection of the CNS by the virus which ultimately leads to development of neurological signs. Red font shows the symptoms in human.



宿主

- Primary reservoir for Nipah virus are fruit bats of the genus *Pteropus*.
- Domestic swine are extremely susceptible to infection; act as amplifying host.
- Infections have also been reported in other animal species.

其他感染動物

- Goats, dogs, cats, sheep and horses.
- Nipah virus seems to have affected horses in the Philippines in 2014.
- Seropositive cattle, pigs and goats in Bangladesh; these antibodies did not neutralize Nipah virus, and could have been caused by related henipaviruses
- Experimental infections established in pigs, cats, ferrets, nonhuman primates, guinea pigs, golden hamsters (*Mesocricetus auratus*) and mice.

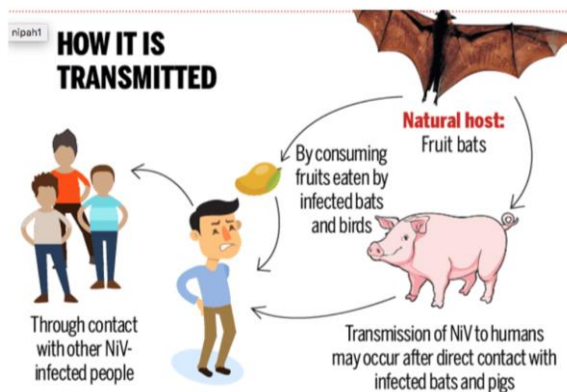
傳染途徑



(FAO)



(IndiaMART)



- Exposure to sick pigs (direct contact and aerosol) and flying fox (family Pteropodidae)
- Raw date palm sap (棗椰樹汁) contaminated by an infected bat.
- Person-to-person spread.
- Scavenging animals may transport virus into pigs
- Movement of animals
- Vertical transmission across the placenta, by iatrogenic means and in semen has been suggested but not confirmed in swine
- In Philippines, eaten undercooked meat from sick horses or participated in slaughter

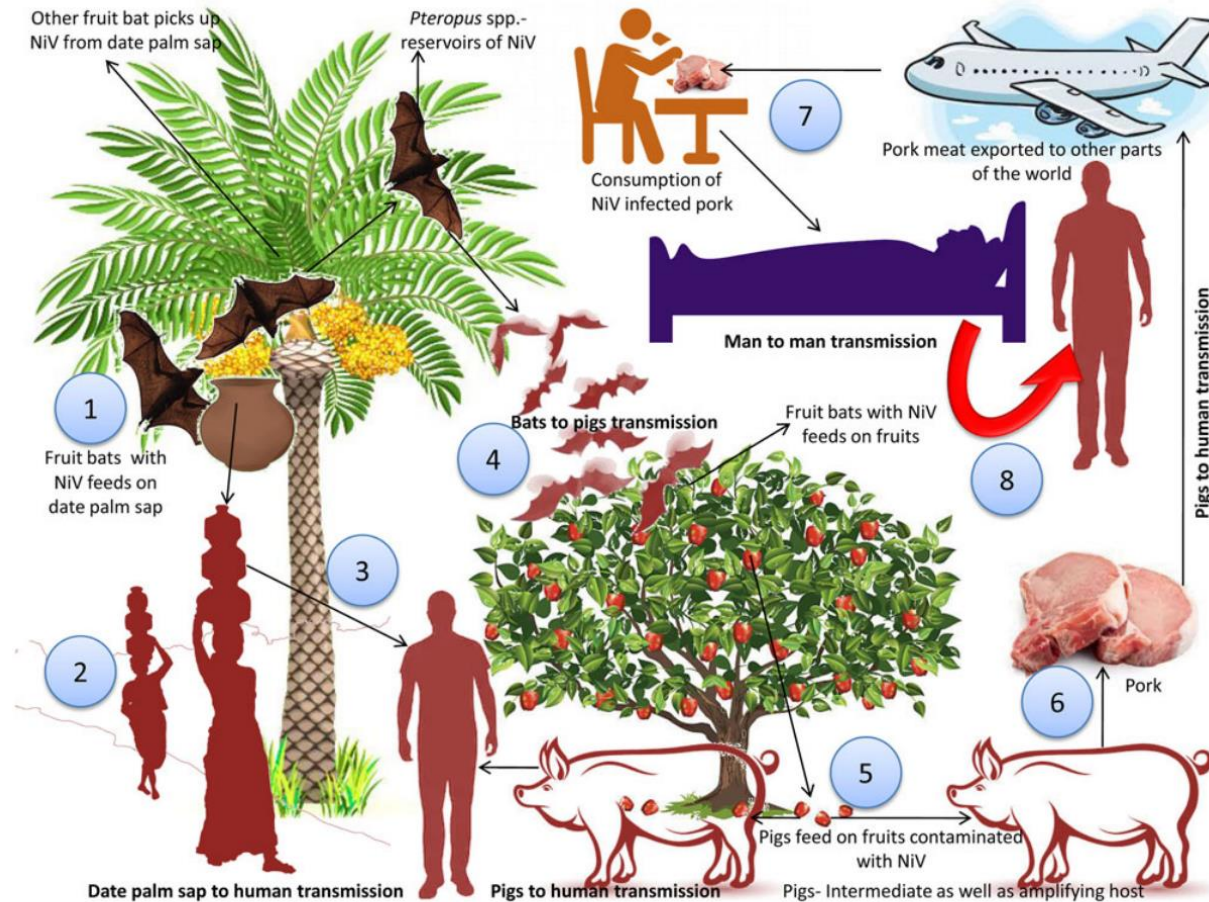


Figure 2. Transmission of the Nipah virus. 1. Fruit bats acts as natural reservoir of Nipah viruses. Fruit bats with NiV feeds on date palm sap. Virus can survive in solutions that are rich in sugar, viz., fruit pulp. 2. Virus transmitted to human through the consumption of date palm sap. 3. Fruit bats of *Pteropus* spp. which are NiV reservoirs visited such fruit trees and got opportunity to naturally spill the drop containing virus in the farm to contaminate the farm soil and fruits. 4. Contaminated fruits are consumed by pigs and other animals. Pigs act as intermediate as well as amplifying host. Combination of close surroundings of fruiting trees, fruits-like date palm, fruit bats, pigs and human altogether form the basis of emergence and spread of new deadly zoonotic virus infection like Nipah. 5. Pork meat infected with NiV are exported to other parts. 6. Consumption of infected pork can act as a source of infection to human. 7. Close contact with NiV affected human can lead to spread of NiV to other persons.

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病毒分佈

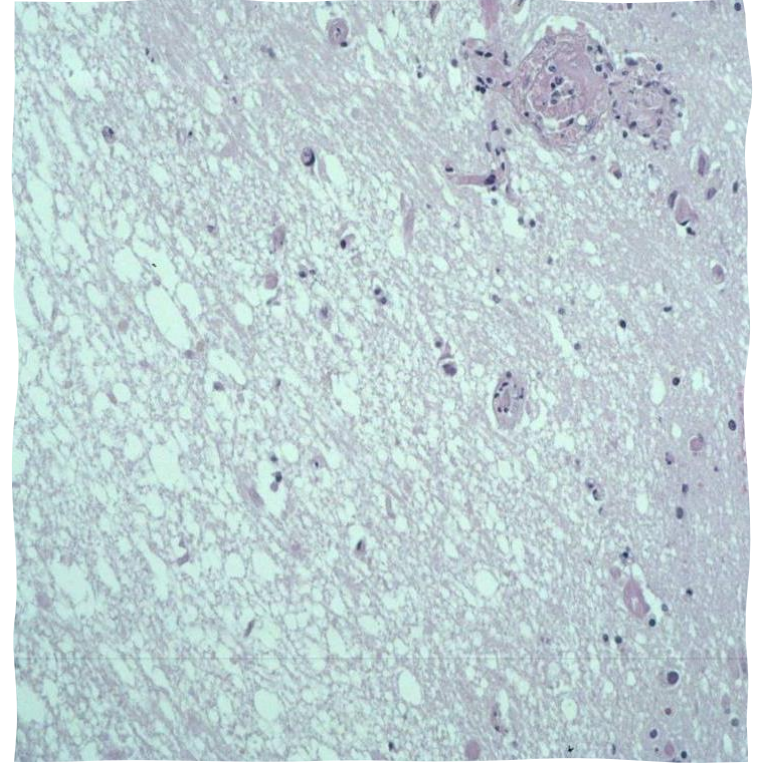
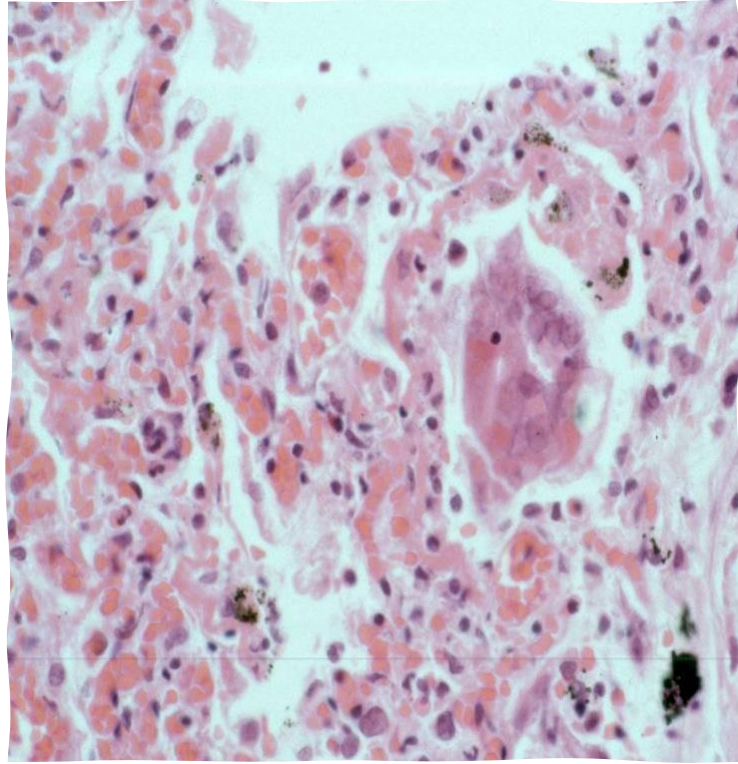
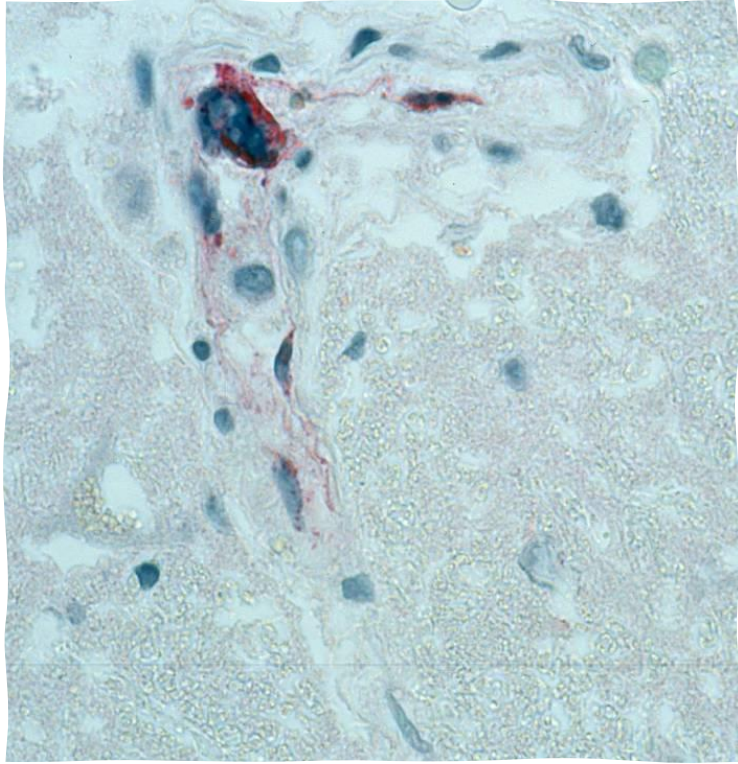
- In urine , saliva and uterine fluids of wild pteropid bats; experimentally isolated from urine, kidney and uterus of infected bats
- Contaminated drinking water and access to aborted bat foetuses or other fluids/tissues of parturition
- Pigs shed Nipah virus in respiratory secretions and saliva; urine of infected swine should also be considered a risk
- Sources of infective material for humans include swine respiratory secretions or via fruit or juice contaminated by bat secretions

診斷

.

A series of 32 fatal cases of Nipah infection, which comprised all of the cases autopsied from late 1998 to mid1999, was drawn from five hospitals in Malaysia.

- Systemic vasculitis with extensive thrombosis and parenchymal necrosis, particularly in the central nervous system.
- Endothelial cell damage, necrosis, and syncytial giant cell formation were seen in affected vessels.
- Viral inclusions were seen by light and electron microscopy.
- IHC showed widespread presence of Nipah virus antigens in endothelial and smooth muscle cells of blood vessels.
- Abundant viral antigens in various parenchymal cells, particularly in neurons.
- Infection of endothelial cells and neurons as well as vasculitis and thrombosis seem to be critical to the pathogenesis



Pathology of Nipah virus infection in humans

Emergence of Canine Distemper Virus Strains With Modified Molecular Signature and Enhanced Neuronal Tropism Leading to High Mortality in Wild Carnivores

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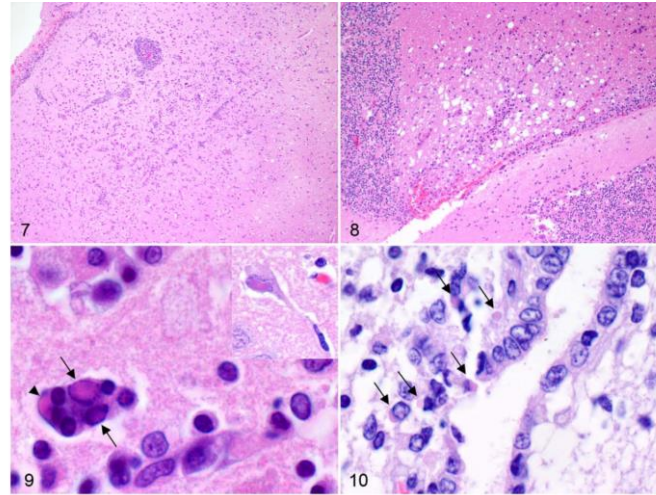
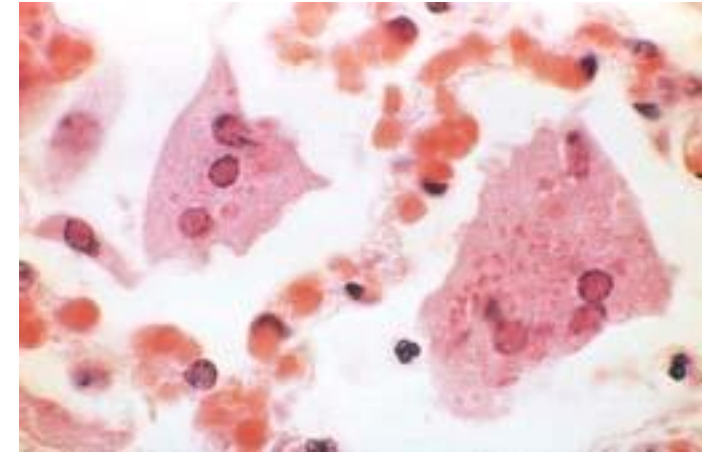


Figure 7. Brain; red fox. Multifocal perivascular cuffs and diffuse gliosis within the neuropil and meningeal infiltration. HE. **Figure 8.** Cerebellum; red fox. Locally extensive vacuolation of the white matter (demyelination) with gliosis. HE. **Figure 9.** Brain; red fox. Syncytial cells with intranuclear (arrow) and intracytoplasmic (black arrowhead) inclusions. Inset: neuron with an intranuclear inclusion. HE. **Figure 10.** Brain; Eurasian badger. Necrosis of the ependymal epithelium with intracytoplasmic inclusions (arrows) in ependymal cells and subependymal cells consistent either with macrophages or glial cells. There is locally extensive vacuolization of the subependymal tissue. HE.



巨細胞或融合細胞出現於麻疹及犬瘟熱病毒感染

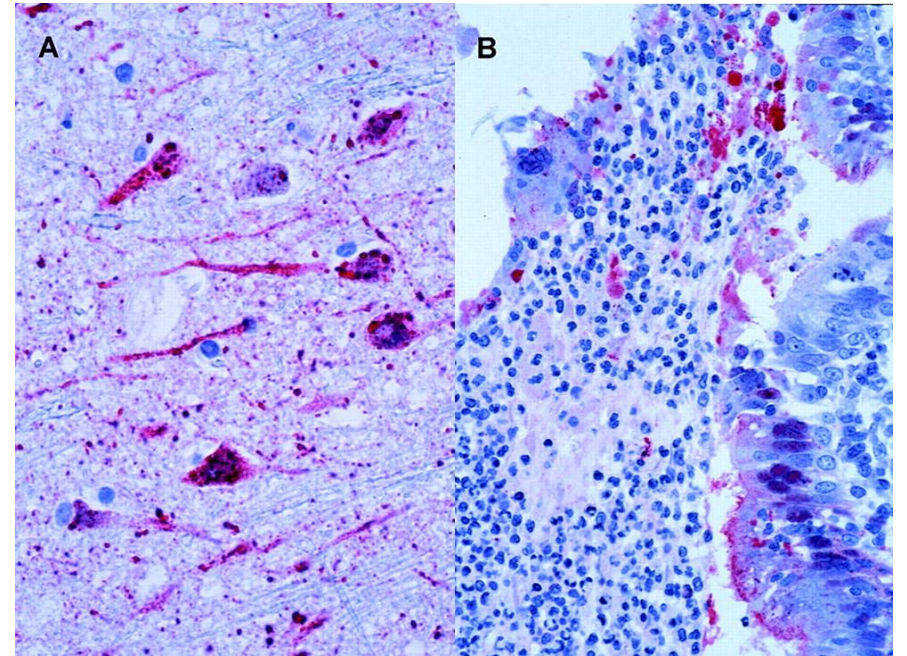
病變

- 肉眼病變：大多數豬感染主要以肺臟為主，包括輕微至嚴重實質化，肺氣腫及點狀至斑狀的出血。肺小葉間隔在切面上常呈擴張。氣管及支氣管偶有帶血或不帶血之氣泡樣液體。
- 組織病理：主要病變為巨細胞或融合細胞的間質性肺炎，其偶有廣泛出血，及有融合細胞於肺血管內皮細胞上。其他病灶包括纖維性壞死性血管炎，伴有單核球浸潤及血栓形成的病變。少部分的豬隻有非化膿性腦膜炎及有顯著的神經膠質細胞增生。

豬病變

- Lesions in the lungs, brain or both organs .
- Lung : mild to severe pulmonary consolidation with petechial or ecchymotic haemorrhages and distended interlobular septa.
- Trachea and bronchi may be filled with frothy exudate varying from clear to blood-tinged .
- Meningeal oedema with congestion.
- Epithelia of all respiratory pathways are affected with presence of syncytial cells in vascular endothelium.
- A mononuclear vasculitis with fibrinoid necrosis and thrombosis .
- Principal histologic changes in the brain are perivascular cuffs and gliosis.

2021/9/30



Detection of Nipah virus antigens in human brain (A) and pig lung (B)

犬病變

- Necropsy reported only for two animals.
- In one dog, diffuse red-pink mottling and consolidation in the lungs, with exudates in the bronchi and trachea. The visceral pleura were yellowish cream and opaque.
- Irregular reddening in the renal capsules and cortices. nonsuppurative meningitis, signs of cerebral and hepatic vascular degeneration, and necrosis and inflammation of the adrenal gland.
- Similar lesions were reported in the other dog, although there was severe autolysis.

實驗感染貓的病變

- Hydrothorax, consolidation and edema in the lungs, edema of the pulmonary lymph nodes and froth in the bronchi.
- Meningitis in some cats. More subtle lesions in earlier stages included numerous small hemorrhagic nodules in the lungs, scattered hemorrhagic nodules on the visceral pleura, and, in one cat, edema of the bladder serosa with dilation of the serosal lymphatic vessels.
- Generalized vasculitis was seen in one naturally infected cat in Malaysia, particularly in the brain, kidney, liver and, to a lesser extent, the lung.
- Nonsuppurative meningitis was reported in an infected horse in Malaysia.

All field investigations should take necessary precautions to prevent infection

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 and 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

實驗室診斷

- Nipah is classified as a **biosafety level 4 (BSL4)** agent and special precautions must be undertaken in the collection, submission and processing of samples.
- See Chapter 1.1.1 of the OIE Terrestrial Manual, Collection and shipment of diagnostic specimens.

Identification of the agent: Virus isolation and characterisation

- Isolation in cultured cells : African green monkey kidney (Vero) and rabbit kidney (RK-13) cells; CPE usually develops within 3 days but two 5-day passages are recommended before judging the attempt unsuccessful
- Methods of identification :Immunostaining of fixed cells
- Virus neutralization: Plaque reduction: virus ; Immune plaque assay
- Nucleic acid based recognition methods: RT-PCR
- Henipavirus antigen detection in fixed tissue – immunohistochemistry
 - Brain at various levels, lung, mediastinal lymph nodes, spleen, kidney, uterus, placenta and foetal tissues
- [Russia](#), [September](#) 15 (Sputnik) - [Russia](#)'s research center Vector has created a test system for detecting the dangerous Nipah virus.

Serological tests

Virus neutralisation tests: accepted as the reference standard

Enzyme-linked immunosorbent assay (ELISA)

- Indirect ELISA for detection of IgG
- Capture ELISA for detection of IgM
- Modified ELISA developed based on relative reactivity of sera with NiV antigen
- Due to false-positives related to specificity of ELISA, all suspect-positive ELISA confirmed by VNT

消毒

存活及消毒

87

- Survive for up to 3 days in some fruit juices or mango fruit, and for at least 7 days in artificial date palm sap (13% sucrose and 0.21% BSA in water, pH 7.0) held at 22 °C.
- A half-life of 18 hours in the urine of fruit bats.
- Inactivated by soaps, detergents and many disinfectants. Routine cleaning and disinfection with **sodium hypochlorite** or commercially available disinfectants is expected to be effective.
- Completely inactivated by heating at 100 °C for more than 15 minutes.

治療與預防

預防和控制 (OIE)

Sanitary prophylaxis

- Strict biosecurity with avoiding contact with fruit bats and their secretions
- Active surveillance program with detection and culling of seropositive swine
- Effective quarantines and control of animal movements
- All materials and equipment should be cleaned and disinfected
- Control of any access to swine by wild or domestic animals

Medical prophylaxis

- No treatment or vaccine available for either people or animals.
- The 2018 annual review of the WHO R&D Blueprint list of priority diseases indicates that there is an urgent need for accelerated research and development for the Nipah virus.

疫苗

- In July 2021, researchers at the Jenner Institute, Oxford University and the National Institutes of Health, United States, reported that the ChadOx1 vaccine vector, when customised to the Nipah virus, fully protected African green monkeys.

Great News: This vaccine is effective against Nipah virus

By [Laxman Chaurasiya](#) 📅 Sep 08 2021 09:23 AM ⚙️ News



Public health educational messages should focus on:

- Reducing the risk of bat-to-human transmission.
Reducing the risk of animal-to-human transmission.
- Reducing the risk of human-to-human transmission.



法規及因應

法規及演習

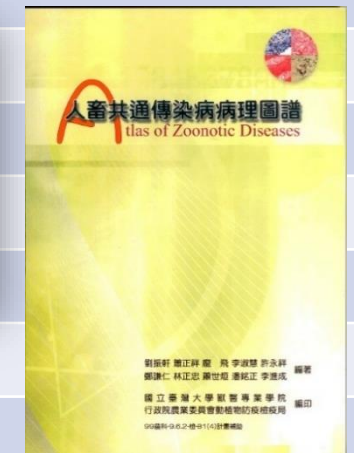
疾病管制署：Nipah virus infection 疾病管制署列入「重點監視項目」

防檢局：立百病毒腦炎 (Nipah virus encephalitis) 列入乙類動物傳染病

- [九十年年度立百病毒緊急防疫模擬演習劇本第四稿.doc](#)
- [立百病毒之實驗室生物安全指引.pdf](#)
- [立百病毒感染症通報說明.pdf](#)

獸醫病理/比較病理與人畜共通傳染病發展里程碑

1976	美國Cornell University John M. King教授及Animal Medical Center劉錫光教授指導獸醫診斷病理學、獸醫組織病理討論會 (CSVP)、美國Armed Forces Institute of Pathology (AFIP) 切片討論會
1984	野生動物疾病監控及病理討論會
1985	實驗動物疾病監控及病理討論會、外科病理檢查
1986	魚蝦病歸獸醫掌管
1994	中華民國比較病理學會成立
1997	中華民國獸醫病理學會成立
1998	興大設立獸醫病理生物學研究所
2003	防檢局支持出版「動物冠狀病毒疾病」
2005	獸醫病理專科獸醫師認證
2004	防檢局支持出版「簡明人畜共通傳染病」
2006	疾管署支持出版「人畜共通傳染病臨床指引」第一版
2008	主編「世界動物衛生組織及甲乙丙類通報動物傳染病」二冊
2009	疾管署支持出版「人畜共通傳染病臨床指引」第二版 (獲疾管署出版佳作獎)
2010	防檢局支持舉辦「人畜共通傳染病病理講習班」
2011	台大設立分子暨比較病理生物學研究所
2013/30	台大建立研究生兼病理住院獸醫師訓練制度、台大建立動物法醫學



獸醫行政、診斷及研發

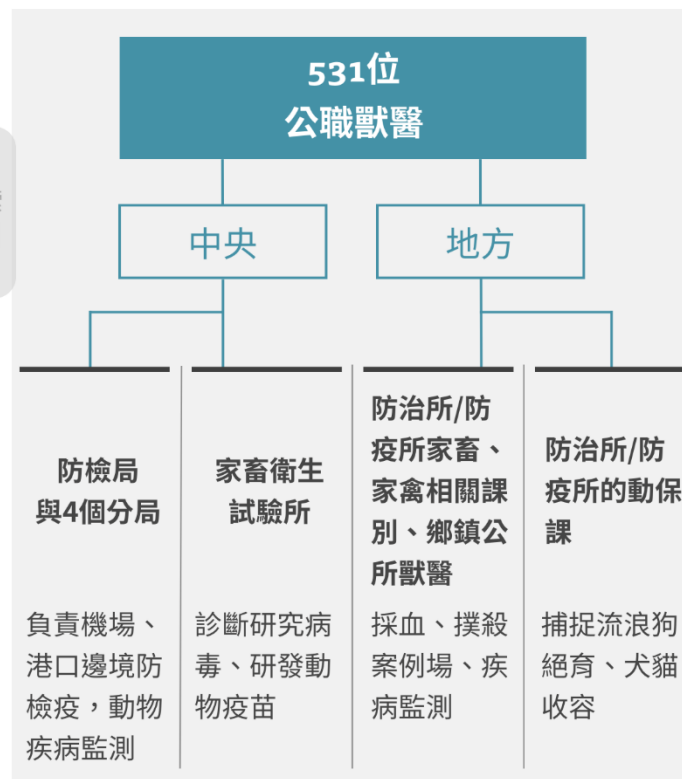


農委會動植物防疫檢疫局



- 農科院動物科技研究所前身台灣養豬科學研究所

公職獸醫分類與負責業務



資料來源：農委會動植物防疫檢疫局

資料整理：林慧貞

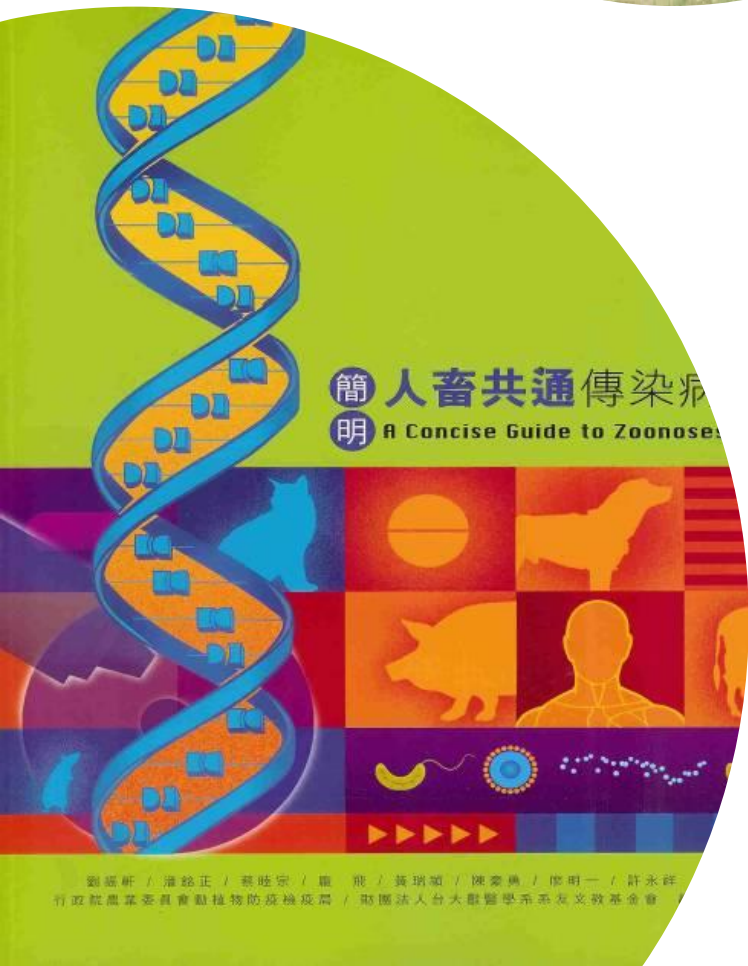
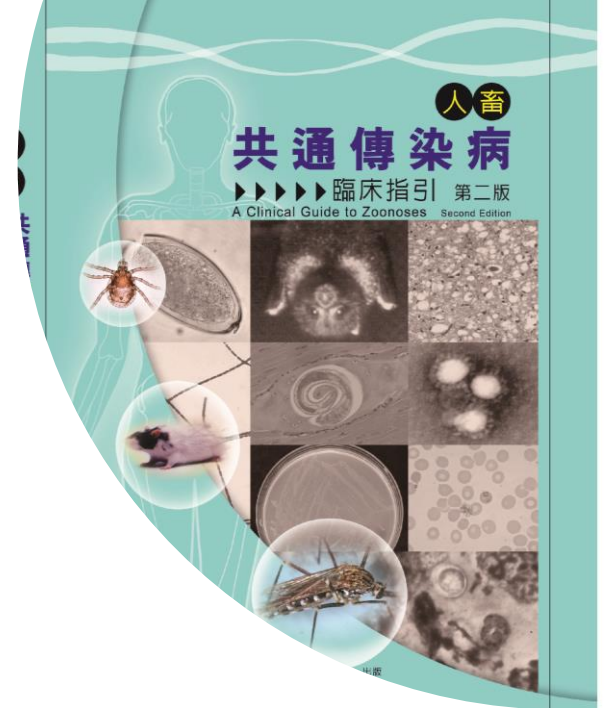
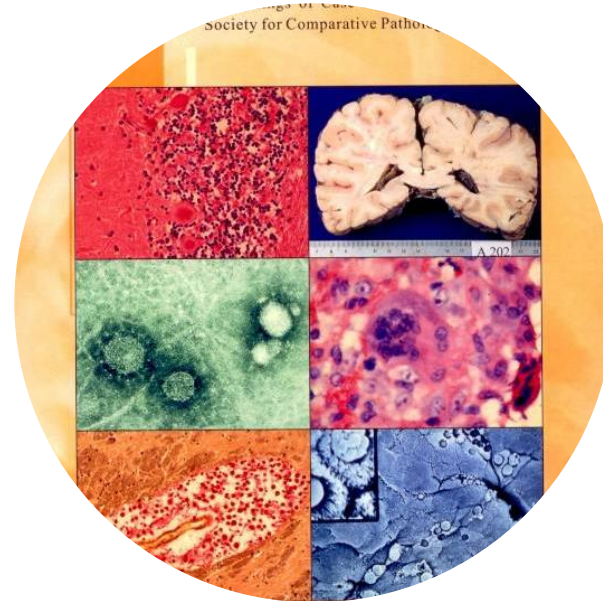
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農委會家畜衛生試驗所

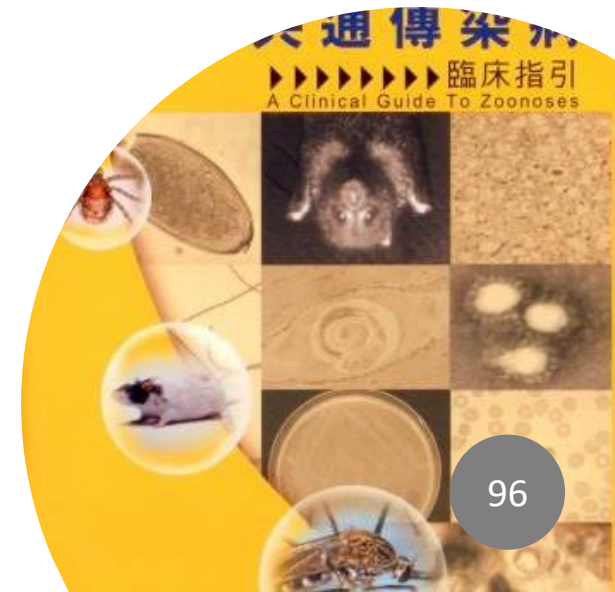


各縣市動物防疫機關及公所獸醫師



比較病理學會 (1994-),
 至2021年已經27年, 每年舉行三次
 研討會, 累積80次, 討論病例達559
 例。

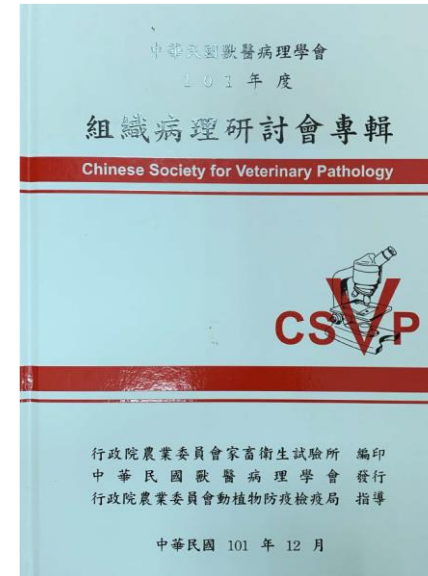
2021/9/30



獸醫組織病理討論會 (1976-)

- 1997年成立獸醫病理學會CSVP
- 一年8次會議至2021/7已舉行382次會議，共討論3109個病例。
- 專題演講。前有病理小講堂。
- 切片掃描電子化。
- 全台各地輪流提供各種動物病例。
- 年度組織病理研討會專輯。
- 繼續教育學分。

2021/9/30



第300次CSVP組織病理研討會於中興大學2010/9/3

美國 Armed Forces Institute of Pathology (AFIP) (Joint Pathology Conference, JPC) 切片討論會

- 始於台灣養豬科學研究所 (2001年改制為動物科技研究所)及台糖公司畜產研究所，每週一次4個病例讀片討論會。
- 目前移至台大舉行。
- 40多年來對訓練獸醫病理人材貢獻卓著。



野生動物疾病監控及病理討論會 (1984-)

- 劉錫光教授因擔任美國紐約Bronx zoo顧問，極力促成臺北市立動物園及六福村動物園合作。
- 台大師生每週兩次赴臺北市立動物園解剖所有死亡動物，協助監控及防治野生動物疾病。
[NTU2005-846\(Zoo_臺灣狐蝠\).pdf](#)
- 每年一次臨床及病理討論會
- 發表論文。

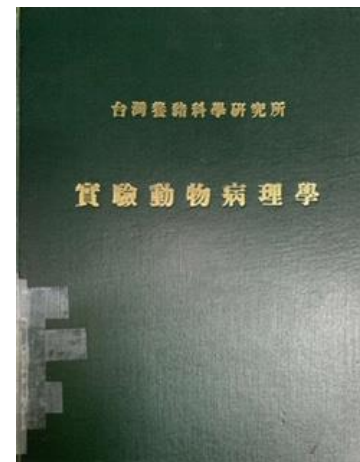


實驗動物疾病監控及病理討論會 (1985-)

1985年Iowa State University修習實驗動物病理。

回台協助實驗動物中心監控疾病

1989年成立中華實驗動物學會





人畜共通傳染病病理圖譜
Atlas of Zoonotic Diseases

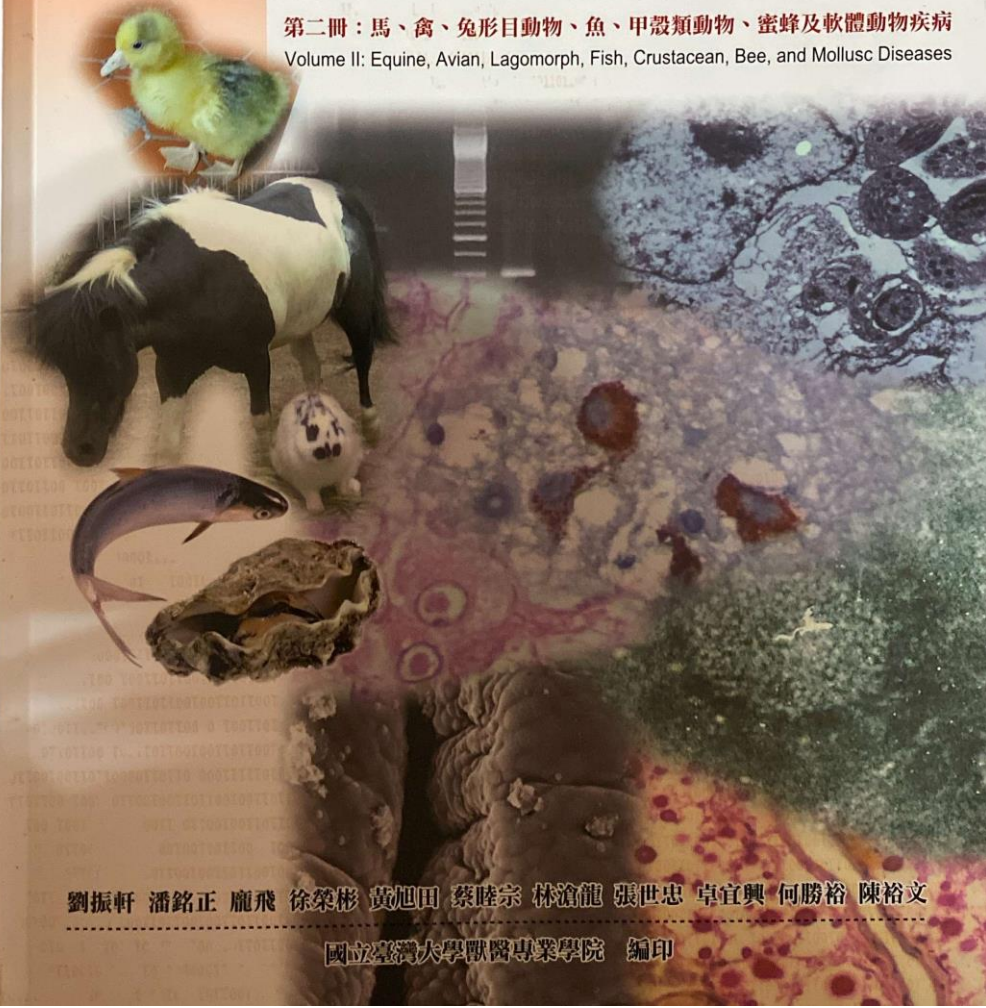


劉振軒 蕭正祥 龐飛 李淑慧 許永祥 鄭謙仁 林正忠 蕭世烜 潘銘正 李進成 編著
國立臺灣大學獸醫專業學院 行政院農業委員會動植物防疫檢疫局 編印

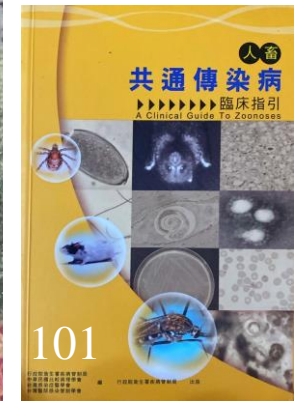
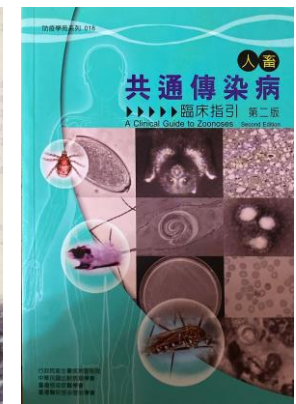
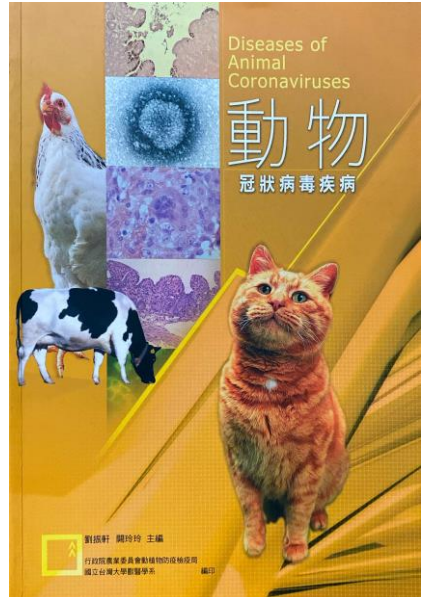
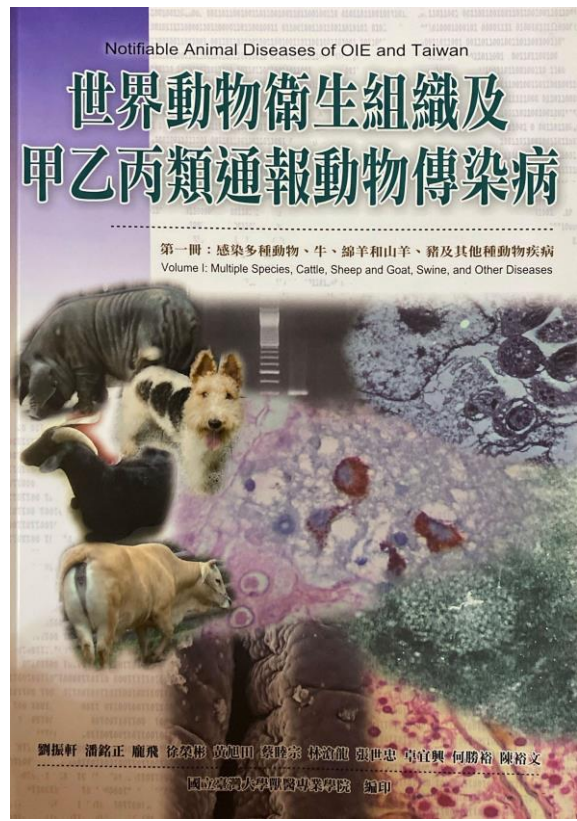
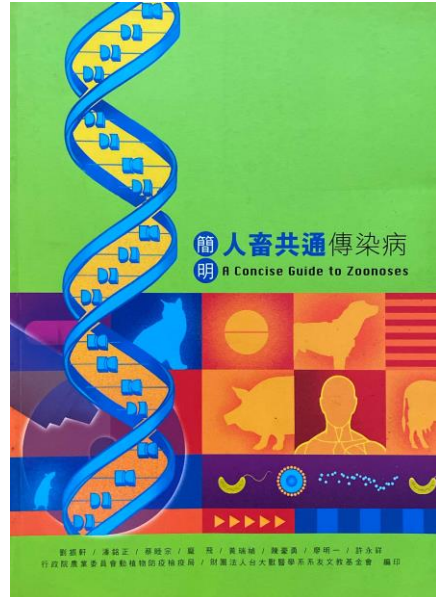
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2021/9/30

Notifiable Animal Diseases of OIE and Taiwan
世界動物衛生組織及
甲乙丙類通報動物傳染病

第二冊：馬、禽、兔形目動物、魚、甲殼類動物、蜜蜂及軟體動物疾病
Volume II: Equine, Avian, Lagomorph, Fish, Crustacean, Bee, and Mollusc Diseases

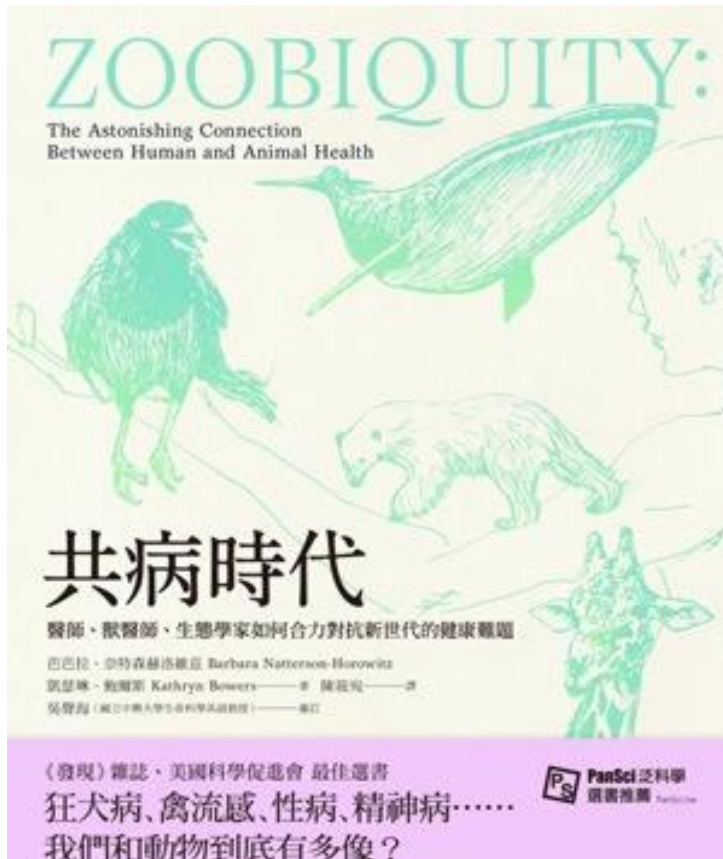


劉振軒 潘銘正 龐飛 徐榮彬 黃旭田 蔡睦宗 林滄龍 張世忠 卓宜興 何勝裕 陳裕文
國立臺灣大學獸醫專業學院 編印



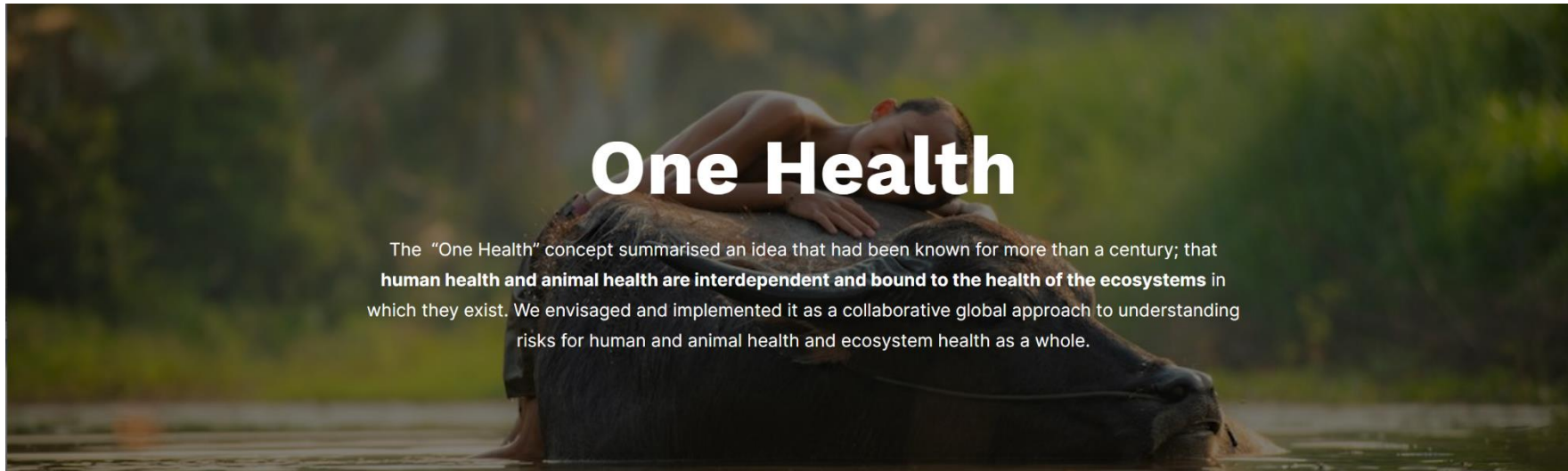
結語

醫學一體以保障一個地球上的 眾生健康與福利 (One medicine, one world and one health)



Rudolf Ludwig Karl Virchow was a German doctor, anthropologist, public health activist, pathologist, prehistorian, biologist and politician. He is referred to as the "Father of Pathology".

- 「在動物醫學與人類醫學之間並沒有界限-事實上也不應該有。雖然服務的對象不同，但是在彼此領域所獲得的經驗卻是建構了整個醫學的基礎。」
- *"Between animal and human medicine there is no dividing line – nor should there be. The object is different but the experience obtained constitutes the basis of all medicine." - Rudolf Virchow (1821-1902)¹*



One Health

The “One Health” concept summarised an idea that had been known for more than a century; that **human health and animal health are interdependent and bound to the health of the ecosystems** in which they exist. We envisaged and implemented it as a collaborative global approach to understanding risks for human and animal health and ecosystem health as a whole.

One Health

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建議

- 「相容並蓄，互通醫理。」-比較醫學人才培育。
- 「術業有專攻，聞道有先後。」，醫學及動物醫學緊密合作，共同聯防以阻止疫病入侵、擴散與撲滅。
- 善用既有資源及可信網路，以收「事半功倍」之效。
 - Google快訊 (Google Alerts)
- 超前佈署，有備無患：「勿恃其不來，恃吾有以待之。」-隨時掌控國內外疫情，急早因應準備。
- 建立症狀通報及快診系統。

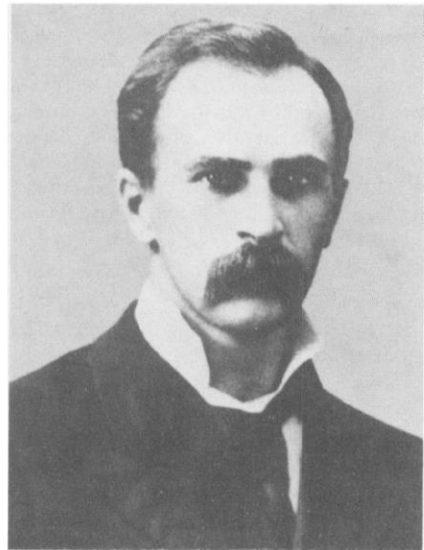


Fig. 4. William Osler, in 1881. (Courtesy of College of Physicians of Philadelphia).

parasitic bronchitis in dogs, was excellent, and dates 1877 (50). Having established the cause of a chronic cough condition in foxhounds at the Montreal by careful postmortem work, he named the disease on the basis of its etiology and to prevent the disease from succumb to the temptations of

the country it is rarely a condition of over 800 bodies have been found."

He also wrote of making "call on the shambles" to look for a veterinary student to look for students, Mr. A.W. Clement examined 270 hogs at the Montreal animals affected." (53).

Osler's most important veterinary standpoint, Albert W. Clement by him as a bright person. He assisting him on several papers published jointly. They worked parasites in the pork supply of hogs (54). Clement reported cysticercus infection in 76 of

In 1883, Osler and Clement bronchiectasis in a calf, on pyometra in a bitch (55-7) was assisting Osler in cases and small animals at Montreal. That same year Osler's experimental papers. They had conducted actual medical work.

謝謝！問題？