

<p style="text-align: center;">中 華 民 國 比 較 病 理 學 會 第十六次比較病理學研討會(人畜共通傳染病-中樞神經系統感染專題) 病 歷 摘 要</p>
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時 間：中華民國八十八年六月六日（星期日）上午 8:00~下午 3:30
地 點：新光吳火獅紀念醫院
地 址：台北市士林區文昌路 95 號
主辦單位：新光吳火獅紀念醫院 佛教慈濟綜合醫院 國立臺灣大學獸醫學系
臺灣養豬科學研究所 中華民國比較病理學會

CP Case 133 花蓮佛教慈濟綜合醫院 (202)

A 35-year-old man suffered from headache, fever ($>38.5^{\circ}\text{C}$) and chillness for more than 3 days. He visited MGH ER at 23:28 on June 19, 1998. CBC revealed WBC 9,280, Hb 14.7, platelet 236,000, and neutrophil 64.8%, lymphocyte 26.7%, monocyte 8.1%, eosinophil 0.2%, basophil 0.2%. Chest X-ray showed normal appearance, symptom treatment was performed then he went home. Unfortunately, apnea, cyanosis, general weakness and heart arrest attacked at AM 6:30 June 21, 1998. He was sent to our ER quickly. After CPR 30 minutes, he expired. Forensic autopsy was performed on June 22.

CP Case 134 國立中興大學 (CO97-5935B)

A hog farm raises about 15,000 pigs, which includes 40 boars and 1,300 sows. Ten litters of 3~4 week-old piglets, showed nervous signs sporadically in February of this year. The morbidity and mortality in each litter were 100%.

CP Case 135 國科會國家實驗動物繁殖及研究中心&台灣養豬科學研究所 (P98-52-3a)

The piglet, about 2~3 week-old, showed nervous sign. The morbidity was 1~2%, Streptococcal infection and pseudorabies were suspected. These piglets had been treated with lincomycin, 20% of affected piglets showed obvious improvement. The owner sent three piglets to PRIT for pathological diagnosis. The sow had been immunized with pseudorabies, FMD, JE, TGE, and HC vaccines.

Nipah Virus Infection

馬來西亞流行的致命性新病毒腦炎

許清曉

台灣省立花蓮醫院

1998秋到1999年春約半年間，馬來西亞發生了從未見到的由豬隻傳染的致命性新病毒腦炎大流行，引起全世界、尤其是亞洲各國衛生單位的注意，紛紛派員考察、瞭解、並研討預防措施。

一、疫情經過

1998年秋始，馬來西亞首都吉隆坡北部Ipoh市附近養豬場人員陸續因病毒性腦炎死亡。根據台灣大學獸醫系朱瑞民教授三月中旬應馬來西亞禽畜聯合總會邀請前往調查時會中所聽寫之記錄，每週死亡人數（大約）依次為：1，1，4，1，1，2，1，5，10，1（1999年），1，3，1，2，4，16，9等。後來發生在吉隆坡南部Sembilan省、Bukit Pelandok，更在第三地區Sikamat發生。Ipoh附近養豬農已棄豬逃亡，而無新病例。[第四地區，最南部的Seelong有豬被發現有抗體（？）]死亡人數三月下旬以來達每天一、兩名，四月初更增加到三至五名，四月底則因撤離疫區政策而無新病例。衛生當局起初以為是以豬為儲主的日本腦炎（Japanese encephalitis，JE。是以*Culex*蚊為傳染媒介的一種flavivirus感染。每300~1,000名受感染者中只一人發病，病患主要是小孩，約1/2死亡，存活者中約1/2有後遺症，帶病毒之豬隻不會死亡但會有死胎、流產），十二月開始在疫區四周兩公里範圍內噴灑殺蚊劑（fogging），並對其中居民施打JE疫苗。

但流行並未減緩，並有數點不能以JE說明之現象：病患幾乎都是成人，受感染之豬有死亡者，並且有些腦炎患者血清檢驗顯示已對JE有免疫。三月初University of Malaya 之病毒學家Dr. Chua，在Nipah地區從病人脊髓液分離出一種病毒，送往美國CDC查驗結果証明有和Hendra virus類似的病毒，正式命名為Nipah virus（原暫稱Hendra-like virus，馬來西亞華人報紙譯名力百病毒）。衛生部馬上要求疫區養豬農撤離養豬場。治療上，三月下旬開始使用ribavirin, iv，共給七天。三月二十五日已有182例viral encephalitis（42例證實有JE），其中63例（有18例JE）已死亡。78名仍然住院。到四月五日住院病人數為221人，84人死亡；212病人中170得Nipah virus感染。四月底已無新住院病人，最後統計共有257人感染入院，100人死亡，186人已證實有JE &/or Nipah virus感染。

二、Hendra Virus

此病毒首發現於1994年Australia 之Hendra 市。約20匹馬及兩個訓馬師受感染，12匹

馬及一人死亡。1995年在另一市有一人受感染。1999年仍有馬匹受感染。馬會發生肺炎，三病人分別得到流行性感冒似症狀（存活）、腦炎（13個月後再發死亡）、及肺炎（死亡）。病毒是大型（38~600 nm）單股RNA 病毒，屬Paramyxoviridae（副黏液病毒科）下獨立的新屬別。它有18,234 bp，可製造數種蛋白質，電子顯微鏡下可看到包膜（envelope）上特有的雙鬚（double-fringed）突出物。它會侵犯血管內皮細胞形成融合細胞（syncytial cell formation），因為有包膜而易被肥皂、清潔劑、消毒劑殺死，在環境中活不久。澳洲專家對污染組織用autoclave、廁所用lysol、房間則用formaldehyde燻煙消毒。其儲主為flying fox（fruit bat，狐蝠），在其胎盤（placenta）及胎兒（fetus）中。它不生病、其尿液中也無病毒。可感染貓、天竺鼠、兔、蝙蝠等。但狗、小白鼠、老鼠、及雞則不受感染。包括豬的其他農場動物無感染或流行現象 [劉振軒、楊平政、朱瑞民、蔡敬屏等：亨德拉及類亨德拉病毒感染]。使動物感染之途徑不明，已知不是經空氣傳染（air-borne infection）。診斷要看動物發燒、呼吸困難、行為異常、四肢不協調，而以病毒分離最為可靠。病毒分離須要在 biosafety level 4 containment之設備內執行。用Vero cell細胞培養基培養三天就可看出其生長，出現融合細胞。如五天subculture兩次無viral growth 就是無病毒。其他細胞培養基，如 MBDK、BHK、RK13、LLK-MK2、MRC5 上也會生長。馬之唾液、尿液中有病毒。以immunohistochemistry及PCR可看出腎中有virus antigen，而肺的病變最厲害。

三、Nipah Virus Infection of Pigs

和Hendra virus有16%的核酸序列差異。也是paramyxovirus之一。約200~300 nm大小。也有包膜。可以和 anti-Hendra virus 抗體有交叉反應。豬受Nipah virus感染後之潛伏期不明。發病時會發燒、不安、呼吸困難、劇烈咳嗽（one mile cough syndrome）、最後有含血口沫、肌肉顫抖（muscle tremor）、僵直性痙攣（tetanic spasm）、昏迷。可在三天內死亡，死亡率為5%，平時越健康的越容易死亡。解剖變化為肺炎，但不如馬之Hendra virus pneumonia時嚴重；另外淋巴腺會腫大，而腦則正常。

四、Nipah Virus Infection of Human

因為馬來西亞學術單位仍無正式疫情、病情的調查報告，因此以下訊息來自著者在馬來西亞考察期間各方詢問及其後網路搜尋所得，因而有如下的問題：

- （一）臨床資料以豬農發生腦炎死亡者為主，有 bias。
- （二）原先只能重複檢驗 IgM anti-JEV 以診斷 JE，JE 之潛伏期為 4~14 天，而抗體需要七天才會出現，因此有時仍無法確定病人沒有 JE；四月才有有 Nipah virus infection 之檢驗法。
- （三）臨場觀察詢問的時間太短，無法取得更多詳情。
- （四）農場動物之病或死，到最近才開始有病毒檢驗。
- （五）四月以來的消息皆來自網路，而其來源則為記者報導，常缺乏重要技術上的訊息。

1. 感染源及其特徵? (動物、植物、環境?)

- 豬已被確認為感染原，因為腦炎都發生在養豬場人員。不碰豬、不吃豬肉的回教徒馬來人都沒發生腦炎。有症狀的豬應該就是感染原，不過也說不定無症狀的被感染的豬，或在豬感染後的潛伏期該豬就已具有感染性。
- 農場之貓、狗、老鼠、馬、牛、羊、鵝有死亡之現象。但皆無獸醫診斷。最近已發現兩隻死亡之流浪狗有Nipah virus感染，顯然是吃了死豬肉或和病豬接觸而受到感染。問題是這些狗死亡時離疫區有多遠。附近約800隻流浪狗已被捕殺。

2. 傳染途徑? (接觸? 飛沫? 空氣? 昆蟲媒介? 物體媒介?)

- 死亡病患六十三名中六十名為養豬場工作者，直接和豬接觸，三名為運送豬隻貨車的駕駛員，負責關緊門檻、沖洗豬及貨車，可能和豬的體液有間接的接觸。有一位75歲養豬場老人，不工作，但晚間會經過豬欄旁可能有泥濘的通道出去廁所小便，未做JE vaccination，得到腦炎，昏迷、插管。另一位35歲女性病患住離養豬場1.5公里處，丈夫也不是養豬業者，不知是否JE。
- 已知醫護人員只戴口罩、一般丟棄式latex gloves、穿無袖之plastic apron，但迄今尚無人得腦炎。由以上事實可見接觸是傳染途徑，而經空氣及人對人傳染之機率極低。
- 其他種動物是否可能再度引起其他地點疾病的流行，或原流行地區疫情的持續，則有待後續的調查。

3. 潛伏期? (關係檢疫留置觀察的期間)

- 豬發病到人生病的時間是7~14日。不過豬在潛伏期就可能已有感染性，因此人的潛伏期可能更長。

4. 和豬隻接觸者的發病率?

- 一家養豬業者有14人養約八千隻豬，其中4~5名負責搬運死豬，業者之哥哥也搬運死豬。只哥哥得病。其他養豬場有五人工作，三人得病死亡；一人工作病死；夫妻兩人工作妻子死亡。就是說不一定每一個和病(?)豬接觸者都會受感染、或發病。¹

5. 臨床症狀?

- 先有兩三天的低燒，然後燒到 40°C、頭痛、意識混亂、抽搐、昏迷而插入 endotracheal tube、最後休克死亡。過程可短到 4~5 天。不一定每一腦炎病患或昏迷的病人都死亡。38 名正在住院的病人中，16 名仍有氣管插管、15 名仍然 drowsy、7 名改善中。
- 因為案例收集的 bias，只知有腦炎之發生。將來應執行追溯性調查，查詢所有養豬場人員在此流行期間發生的疾病。住院病患中有兩三名有輕度 interstitial pneumonia。有一名發燒後 ptosis of left eye、有一名 visual loss 而求診，有一名上

肢肌肉(?)無力。

- 很多病人有高血壓、高燒、面紅、流汗等可能是副交感神經被刺激的症狀。
- 18~20%病患有 diaphragmatic myoclonus (橫膈膜肌陣攣)，在 epigastrium 有明顯肌陣動，是由於 medulla oblongata 的病變所引起，在其他種腦炎少見。
- 病毒是主要侵犯腦神經組織。

6. 其他臨床特徵?

- 63名死亡病患之平均年齡為42歲。最年輕者為8歲女孩，她和小豬玩耍。其次為14歲。男女性別比為18:1。
- 消化道、關節、肝、腎、淋巴腺、耳、鼻、喉、皮膚都無特異現象。一般檢驗結果：尿檢、CBC、AST、ALT、BUN、Cr、electrolytes、無特殊變化。
- CSF有lymphocytic pleocytosis及蛋白質增加。Brain CT之90%正常。

7. 如何診斷?

- 抗原抗體檢驗目前利用anti-Hendra virus antibody 和 Nipah virus 會交叉反應之事實。病毒分離需BSL 4設備。

8. 治療、死亡率?

- JE病患之死亡率為36%；Nipah virus encephalitis者為36%；有兩者共同感染者為52%。
- Ribavirin之治療效果：已知越早期用藥治癒的可能性越大。馬來西亞衛生部已公告養豬戶凡是有發燒者皆應接受ribavirin治療。

9. 發病到死亡之時間?

- Nipah encephalitis致死之時間可短到為四、五天。

10. 後遺症?

- 存活者可能有神經後遺症。有意識混亂者、有locked-in syndrome者，輕重不一。

11. 是否有再發或再度感染者? (免疫力)

- 仍待觀察。

五、疫情處理及預防

(一) 流行病需要有系統地辦理[衛生署陳國東]:

1. 要有一個中心單位主持epidemiologic surveillance，全責收集資料；
2. 要有case investigation；
3. 要研討治療及預防的方法；
4. 要訓練醫護及公衛流行病學人員；
5. 要教育民眾；
6. 要統一發佈媒體新聞等。

- (二) 醫療方面，由各次專科醫師成立特別醫療團，輪流到各醫院，加強臨床診療之能力及資料之收集。
- (三) 旅遊到馬來西亞，要避免到疫區或和各種動物接觸。
- (四) 對台灣之影響可能不大。不必恐慌。但必須持續：
 - 1. 對進口及國內豬隻的檢疫，防止走私豬隻、豬肉、及其他動物、飼料入境。
 - 2. 醫療防疫單位對任何不明原因疾病警覺性之提昇。
 - 3. 通報系統之加強。
 - 4. 對民眾經大眾媒體之教育。
 - 5. 醫界須對人畜共通傳染病（zoonotic infectious diseases）更提高警覺。

六、需注意的新消息

- (一) 豬被傳染後的潛伏期、感染期？（輕症的病豬似乎不少，可能不受注意，可能存在市售冰凍豬肉中，以後屠宰業者是否都必需用防護配備？）
- (二) 豬被感染後免疫力的出現及其持續性如何？有無慢性帶原者？
- (三) 人被傳染後之潛伏期？（影響可能受感染者的檢疫期間長短）
- (四) Nipah virus特異的檢驗試劑何時研發市售？
- (五) 有何種其他動物可能受感染？狗？貓？老鼠？鳥類？這些動物是否會感染人類？其潛伏期及死亡率？
- (六) 病毒在細胞外、環境中、動物屍體及人屍體內之存活期間？（死豬掩埋場何時可以回去而不懼病毒感染？市售豬肉可能有潛伏期病毒存在，冰凍後會如何？病人屍體解剖時如何防護？）
- (七) 對各種清潔劑、消毒劑的敏感性？（有病死豬或其他污染物時如何消毒？）
- (八) 台灣走私攜帶奇禽異獸、小寵物、或動物飼料入境者是否會減少？
- (九) 醫療界及一般民眾是否對人畜共通疾病（zoonoses）有更高的警覺性？

七、Nipah virus 感染疑似病患之處理

(一) 採檢對象：

曾在流行地區出入並接觸豬隻或其他可疑動物，並有高燒、頭痛、嘔吐、眩暈、痙攣、意識混亂、昏迷、或麻痺等臨床症狀者。

[注意：1. 醫師發現此病患，應將其移至傳染病隔離病房，並通知地方衛生局。

2. 採檢體的醫護人員需要使用可滅菌焚燬之器材，並採取嚴格的自我保護措施，穿戴護目鏡、口罩、手套和丟棄式保護衣物。]

(二) 檢體種類：

- 1. 生前檢體：血液、咽喉擦拭液、尿液、腦脊髓液。
- 2. 解剖檢體：腦、肺、脾、腎等器官。

(三) 採檢方法：

1. 以採檢器（各檢驗站都有）採咽喉擦拭液。
2. 用注射器採血並離心，在無菌下取血清3 mL注入血清瓶中，栓緊瓶蓋。
3. 解剖檢體各取3立方公分，放入無菌容器中，栓緊瓶蓋。

(四) 檢體輸送：以上檢體取得後，應迅速放入低溫（4~8°C）輸送箱（向各衛生局取用），並在24小時內送到預防醫學研究所病毒組。

(五)（疑問？：TEL：02-2785-6710，或參考防疫檢體採檢手冊）。

Factsheet of Hendra and Nipah Virus

朱瑞民

國立台灣大學獸醫學系

一、Hendra virus

(一)自然感染狀況：

1. 在 Queensland 東北角海岸 Mackay 附近的馬場，1994 年在 7 月底，一母馬在放牧吃草時出現呼吸症狀，於 8/1 死亡。另一匹公馬於 8/11 生病，隔日死亡。獸醫與畜主解剖並未做出任何特殊診斷。在 1995 年 10 月畜主因 Hendra virus 感染死亡後，再檢查（PCR），證實此兩匹馬死于 Hendra virus。
2. 1994. Sept. 在 Brisbane 郊區小鎮 Hendra 離 Mackay 約 1000 公里，有 13~14 horses 感染死亡。為 9/7 引進 Brisbane 附近 Cannon Hill 賽車場用場之母馬發病所引起，此母馬於二天內死亡，9/27 有 12~13 頭死亡，7 頭生病痊癒，另 9 頭無病。1 人死亡，死于 acute respiratory disease，此係為訓練師。一人為 stable hand，僅出現頭痛及較輕微呼吸症狀，6 星期後痊癒。
3. 第三個病歷在 Jan. 1999，馬於 Cairns 死于此病。
4. 此病毒屬於 Paramyxoviridae 中的一個新的 subfamily。
5. 自然界除馬及（豬）外 fruit bats (Pteropus) 會受到感染，後者為 natural reservoir host（陽性率約 9%）。
6. 自然情況下可能因接觸污染的尿而傳播，抗體量與病情有關，抗體高血管病變嚴重。自然情況下馬於臨床症狀出現前 4 天血清仍為陰性。可能馬接觸貓而感染，可能由感染動物的尿而傳播到其他哺乳類，在 Hendra 爆發時受感染而恢復的馬，有二匹出現神經症狀。

7.臨床症狀:

(1)動物：

1994 年 9 月，孕馬生病，2 天後死亡，21 匹馬生病，14 匹死亡，症狀為：

Depression, loss of appetite, fever, ataxia, tachycardia, tachypnoea, dyspnoea, copious frothy nasal discharge, marked subpleural edema, lung ventral consolidation, interstitial pneumonia, focal necrotizing alveolitis, edema, syncytial cell formation affecting vascular endothelium.

(2)人：

- ① Stable hand: 40 歲，smoking, flu-like symptoms: myalgia, headaches, lethargy 及 vertigo，無呼吸症狀，未住院，6wks 後痊癒。

- ② Trainer：49 歲，heavy smoker，與馬排出物緊密接觸（協助病馬）、噁心、嘔吐。
- ③ 1995 Oct. 21 發生於一位 farmer（in Mackay, Brisbane），他在 1994 年 8 月份做死馬解剖，後來 1995 年診斷為 Hendra virus。此人出現 acute progressive encephalitis (Oct. 2 to Oct 19: SN Titer 自 1:16 到 5792，PCR HeV(+) from CSF，10/19 日死亡。此農夫在解剖病馬數天後生病，喉嚨痛，頭痛，嘔吐及頸僵硬，CSF 含 PMN，無細菌及病毒，然後痊癒。15 個月後（Oct.1995）再發，出現明顯神經症狀，抽搐，昏迷等，25 天後死亡。
- ④ 血清調查：
- (a) 附近馬匹（3,101），貓（64）及其他 14 種動物（包括豬），共 3,541 血清樣品及另一實驗的 4,731 馬及 564 貓的樣品，HeV 均為陰性。
 - (b) Fly fox（fruit bat）9%（20/224）帶中和抗體，13 種野生動物中僅 bat 為陽性，包括四種 species（spectacled，black，littlered 及 grey-headed）。
 - (c) 附近人的血清陰性（157）。
 - (d) 調查 46 種動物 5,264 個血清樣品均為陰性。

(二)人工接種：

1. Hendra virus 目前已知會感染：貓、guinea pig、humans 及 horses 出現臨床病症。Bat、rabbit 感染、不發病。在呼吸道無病毒。
2. 接種的 bat 與馬在一起 3wk，馬不受感染。bat 以皮下接種的抗體力價較高，但無法自內臟器官、尿及糞便分離出病毒。
3. 接種馬（3/4）會感染造成 interstitial pneumonia 及 vascular degeneration，在血管內皮細胞出現 syncytial cells, mild lymphocytic meningitis。病毒不存在鼻腔及糞。馬接觸的貓無病，未分離出病毒、血清亦為陰性。與 bat 接觸之馬無病（血清亦陰性），接種馬腎臟病毒量高、尿及糞便無病毒，結膜及氣管內亦無病毒。與馬接觸的貓無病毒亦無病。貓接種後臨床症狀輕微（上呼吸道），病毒大量于腎中、尿中。發現貓感染馬（1/3），接種貓之糞便、鼻腔及氣管無病毒（與感染馬接觸過 46 天後的馬出現類似臨床症狀，但未見任何其他資料）。
4. 人工接種，一匹馬有神經症狀及腦膜炎，2 匹有 meningoencephalitis。bat 不會傳染 bat，horse 不會傳染 horse(?)，cat 會傳染 cat，也會致死。
5. Aerosol, urine, feces 不含病毒。Bat 之間（3wk 內）也不易互相感染，aerosol 也不會感染馬，自馬呼吸道分離不出此病毒，因此空氣感染的機會不大。
6. 尿道分泌 HeV 的機會較大，在腎臟的病毒濃度高，在貓無法在結膜、鼻腔及口腔中分離出病毒，馬唾液含量高，糞便機會不大。

(三)其他：

須消毒徹底，用肥皂及一般消毒藥水即可。歸類為 Level 4 security- 即須最嚴格的 security procedures。

(四)診斷方法：

1. ELISA for NA (SN)
2. 病毒分離 (Vero cell passage)
3. IFA
4. PCR

二、Nipah virus

(一)現況：

1. 目前已發現陽性豬遍佈西馬幾個州，包括 Perak、Negeri sembilan、Selangor、Melaka、Kalantan 及 Johr。至 5 月 20 日止，尚陸續發現陽性豬。如診斷正確則代表此病已廣泛散佈於馬國。
2. 目前的政策是陽性動物場採撲殺政策，因目前的診斷方法僅限於血清學檢查，故陽性豬豬場內動物的撲殺已逐漸遭受農民反抗。
3. 撲滅動物（官方）數字已近百萬隻豬。
4. 會受感染動物包括：豬、羊、馬、狗、及 Bat。澳洲 Geelong E 進行實驗室正進行豬的接種實驗。
5. 5 月 2 日為目前最後一個人的病例，5 月 17 日增加一位人的死亡，共 258 懷疑病例。101 位死亡，出院 135 位。
6. 診斷方法：與 Hendra 同。

Nipah virus

(取自 OIE 馬國報告)

1. Symptoma in human

- (1) Mild to severe clinical signs.
- (2) Fever and headaches of varying severity.
- (3) Few showed drowsiness and disorientation, later slipping into coma, requiring artificial ventilation.
- (4) Most of the comatosed cases ended in fatality.
- (5) Full course of the disease is still unknown.
- (6) Incubation period postulated to be from 1 to 3 weeks.
- (7) Milder cases showed serological reactivity without apparent clinical symptoms.

2. Disease in pigs

Generally mortality is low but case morbidity is high.

Spread of disease: between and within pig farms has not been established.

(1) Clinical signs

a) Weaners and porkers

Mild to severe coughing, with varying reports of mortality and morbidity.

b) Sows and boars

Disease more pronounced, moderate to severe respiratory disorder characterized by dyspnea, convulsion and death.

In boars disease may be acute, death after several hours. Thick mucopurulent discharge and pneumonia in less severe forms.

c) Piglet, gits and sows

Convulsions and other neurological signs.

(2) Necropsy:

a) Varying degress of consolidation of the lungs, primarily the disphragmatic lobes prominently thickened interlobular septa.

b) Cut surface showed exudate of varying consistencies in the bronchi.

c) Kidneys showed congestion both on the surface and in the cortex.

d) Brain appeared normal except in 1 case with petechial hemorrhage.

e) Other visceral organs appeared normal.

3. Disease in other animals

Dogs, cats, horses and goats were found serologically positive in the infected areas.

Dog: lesions observed at necropsy of sick dogs were similar to sick pigs pigs. Kidneys showed severe hemorrhages and congestion. Exudates in the trachea and bronchi.

4. Mode of transmission

Transmission studies in animals are being carried out at the Australian Animal Health Laboratory (AAHL). CSIRO, Australin.

(1) Oral inoculation

- a) Incubation period for clinical signs was 14-16 days.
 - b) Clinical signs and gross pathology were mild.
 - c) Virus isolation work is in progress.
- (2) Parenteral inoculation
- 2 inoculated pigs developed a more severe disease, 1 showing CNS disease and the other a respiratory tract disease. Signs developed within 7-10 days of challenge.
- (3) In-contact pigs
- a) Exposure occurred quickly, possibly at the time of challenge.
Neutralizing antibodies were detected at day 14.
 - b) Virus multiplication in the tonsils and respiratory epithelium, together with contaminated cellular debris in the lumen of air passages in the lung, suggests that the virus may be at least transmitted by pharyngeal and bronchial secretions.
 - c) Other results are pending.

5. Diagnosis

- (1) Virus isolation
- Tissue samples of the lung, kidney, spleen, heart and brain from necropsied animals were collected for virological examinations. Samples were sent to the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia.
- Molecular studies done on the virus isolate show 21% difference in the nucleotide sequence and 11% in the amino acid sequence to the Hendra virus.
- (2) Serological tests
- Two laboratories namely the Veterinary Research Institute (VRI), Ipoh and the Task Force Laboratory at Department of Medical Microbiology, University Malaya were identified to carry out serological tests for the veterinary and human sera respectively. Samples were tested using the IgG and IgM capture ELISA with at the above laboratories and serum neutralization tests at AAHL Geelong Australia.

6. Results of serological surveillance in animals during the outbreak period.

- (1) Pigs
- In a previously infected farm, more than 95% of sows were positive to Nipah virus antibodies. More than 90% of the piglets had antibodies assumed to be maternal antibodies. Antibody prevalence across all ages in an infected farm is currently being studied.
- (2) Horses
- Two out of 47 polo horses from a farm in an infected area found positive to Nipah virus antibodies were euthanized. All race horses in the country had been tested negative.
- (3) Dogs
- More than 50% of dogs captured in one of the infected area were positive to Nipah virus by IgG capture ELISA using Hendra antigen. Antibodies in dogs in other infected areas is being studied.

(4) Cats

One out of 23 cats in the affected area was seropositive.

(5) Bats

15 out of 99 flying foxes were found positive to the serum neutralization test against the Nipah virus.

(6) Rodents

To date, serum samples from rats trapped in infected areas were negative. Tests are in progress.

(7) Other animals

Sera were also collected from cattle, goats, sheep, squirrels, wildboars, wild birds, poultry and ostriches for testing later.

7. Control and eradication program

(1) Control Program for Nipah Disease Phase I

With the discovery of the new virus etiology, a program was developed for immediate eradication of the disease by mass culling of pigs. From 28 February to 26 April 1999, a total of 901,918 pigs were culled in 4 infected areas 1 in State of Perak, 1 in Selangor and 2 in Negeri Sembilan.

(2) Control Program for Nipah Disease Phase II

A surveillance program was developed to search for previously infected farms by determining the presence of pigs with antibodies to the Nipah virus. All farms outside the previously designated high risk areas will be screened by randomly taking a statistically significant sample size of sows for detection of Nipah virus antibodies. Farms with 2 consecutive negative tests performed within an interval of 3 weeks will be given a "Provisionally-Free" status. However, farms found positive during the first or second tests will be culled.

To date, 235 farms were tested and out of which 9 were found positive, these involving 23,736 animals and 11,458 pigs in 1 of the positive farm have been culled. In this program a total of 824 farms will be tested with 1.6 million SPP (standing pig population), will be tested.

Epidemiology of Japanese Encephalitis Viral Infection in Taiwan

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Japanese encephalitis (JE) is a major public health problem in Asia. Taiwan has had about 100~300 reported JE cases and about 10~20% of them were confirmed cases each year. In mainland China, JE is an important summer encephalitis resulting deaths and disabilities.

Both Nakayama and Beijing killed mouse brain vaccines have been widely used to immunize Taiwan children. Our measurements of neutralization antibodies (Nt Ab) against both two vaccine strains and two Taiwan wild type JE viruses among 320 serum samples collected from Taiwan children found that Beijing vaccine elicited better homologous and heterologous humoral immunity than Nakayama vaccine. CC-27 strain isolated from *Culex* mosquitoes in Chaochow of Pingtung in 1983 had neutralization antigenic variation from CH-1392 isolated from the same mosquito species in Changhwa in 1990. We recommended that the best strain for JE vaccine depends on level of Nt Ab induced, the molecular epidemiology and antigenic variation of the JEV in each local area (Ku et al., J. Med. Virol. 44:122-131, 1994).

Because 14.2% of confirmed JE cases in 1996 had been vaccinated on schedule, we conducted a nested case-control study including JE vaccinees in Taipei and confirmed JE cases in 1995 and 1996 in Taiwan to evaluate qualitative and quantitative difference between antibody profiles induced by JE vaccinees versus viral infection. We found that threshold titer of HI and Nt Abs in naturally infected persons were much higher than vaccinees. Besides, anti-NS₁, anti-NS₁', anti-NS₃ and anti-MAbs were specific in naturally infected individuals whereas only anti-E appeared in vaccinees and increased its intensity after increasing the numbers of dose (Wu et al., Thesis at NTU, 1997).

JE virus is still very active after mass immunization started among children since 1968 in Taiwan. Chiou et al (1999) used ELISA-IgM and PRNT to search for JEV high activity areas. The preliminary results found residents living in Hopin Li of Yuanlin Township without pig farm and rice field had the highest JEV IgM positive rate (7.76%, 9/116) and the residents in Lunya Li of Yuanlin Township with pig farms and rice fields had lower IgM positive rate (3.39%, 2/59). The seroincidence rate of JEV was highest in grade one elementary school children (19.6%). Therefore, JE virus was very active in Changhwa even in those areas without pig farms nor rice fields. Future research needs to investigate the reservoir host, other vectors, molecular and antigenic changes of JE viruses in different hosts in Taiwan.

CURRENT STATUS AND RESEARCH DEVELOPMENT OF JAPANESE ENCEPHALITIS VACCINES

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Abstract. Three Japanese encephalitis (JE) vaccines are in use: inactivated mouse brain-derived; inactivated primary hamster kidney cell-based; and live attenuated, SA-14-14-2 vaccines. The latter two are used exclusively in China. Purified mouse brain vaccine, has been used in Japan for 30 years, whether based on Nakayama strain along or including Beijing strain, has an efficacy of 91% in Asian field trials. However, three doses appear to be necessary to produce a protective immune response in persons from regions where flaviviral infections are uncommon. In addition, there is much concern about genetic variability and virulence characteristics of JE strains from different locations in Asia, and the incidence of hypersensitivity in secondary immunization around 15%. Efforts have been done to improve the disadvantages of current JE vaccine in Taiwan: 1) a highly attenuated mutant (RP-2ms) was successfully generated from a Taiwan local JE isolate. Single RP-2ms immunization induced both humoral and cellular immune responses, then completely protected mice from lethal challenge with virulent JEV. Change of organ-tropism and responsible amino-acid substitution of RP-2ms were characterized. 2) Immunization of DNA vaccine expression JEV nonstructural protein NS1 alone has been demonstrated sufficient to elicit protective immunity in mice.

動物日本腦炎病毒感染

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疾病特性

一 定義

日本腦炎是一種藉節肢動物傳播的病毒性疾病，主要侵犯人類的神經系統，而較少發生在馬。本病亦會導致母豬流、死產及感染豬產生腦炎與睪丸炎。此外，其他動物如牛、綿羊、山羊、兔子、老鼠、鴿子、犬、鴨、雞及蜥蜴，對本病亦有感受性。

二 症因

本病毒為黃病毒科 (Flaviviridae) 【以前稱披衣病毒科(Togaviridae)】中，黃病毒屬 (Flavivirus) 病毒，亦為 B 群節肢病毒 (group B arboviruses)，抗原性類似 St. Louis encephalitis virus。直徑約 40nm，為 RNA 病毒，對脂溶劑及蛋白溶解劑敏感。可以用中和試驗、補體結合試驗、HI、免疫螢光及酵素結合免疫吸附測定 (enzyme-linked immunosorbent assay; ELISA) 等血清學方法來鑑定感染與否。

三 病史

在日本，人類腦炎早在 1871 年即已被認知。自 1924 年起，日本腦炎出現流行性型，在日本造成 4,000 人的死亡。本病的流行病學在第二次世界大戰後，為美軍的醫學專家們廣泛的研究，在控制疫情上，同時併用疫苗與殺蟲劑，本病才從日本逐漸被控制，然而在印度、尼泊爾、中國大陸、泰北，人與馬感染的病例又逐漸增加。本病目前在亞洲仍是人類頭號病毒性腦炎，每年 30~50,000 病例被報告。

本病病毒的分離與鑑定，最早由 Fujita (1933) 及 Taniguchi 等人 (1936) 所完成。台灣自 1955 年起，開始有病例記錄。自此台灣幾乎每年都有人的病例發生。

症狀

一 臨床特徵

- (一) 馬感染後的症狀，先是發燒、運動障礙、木僵及磨牙。嚴重病例有失明、昏迷及死亡。雖然症狀似西方馬腦脊髓炎 (western equine encephalomyelitis) 及東方馬腦脊髓炎 (eastern equine encephalomyelitis)，但死亡率很低。在馬，不顯性或無症狀感染很常見。

(二) 豬的症狀主要是懷孕末期母豬產出死胎或木乃伊化胎，即使活產豬也常在出生不久後即死亡，或死亡前出現震顫及抽搐。實驗或自然感染公豬，導致精子數目減少及活力降低而造成不孕，並有睪丸水腫、充血及副睪變硬及性慾減低。病毒可藉精液傳播給種母豬。大部分公豬病例之病害只是暫時性而會恢復正常，少數嚴重病例才會造成永久性不孕。

(三) 人可能輕微感染，除了發燒及頭痛外，而沒有明顯症狀。嚴重感染時，可能突然發生，包括頭痛、高燒、頸部僵硬、木僵、失去方向感、昏迷、震顫、偶而抽搐（尤其嬰兒）及痙攣性（但是很少弛緩性）麻痺。死亡率 0.3% ~60%。懷孕婦女曾有流產之報告。本省流行期為四月到十月，六月為高峰期。

二 潛伏期

馬感染的潛伏期約 8~10 天。人感染的潛伏期約 5~15 天。懷孕母豬感染本病到生出不正常胎兒的時間未明，一般相信在早期感染比晚期感染易產生異常胎兒。

三、致病機轉

在自然情況下，豬經由蚊子之叮咬而感染後，會有持續 2~4 天的病毒血症，然後在 1~4 週內有循環抗體的形成。在懷孕母豬，日本腦炎病毒便是在病毒血症時期，經由血行通過胎盤而感染胎兒。如以靜脈注射人工感染懷孕母豬，最早在感染後第 7 天便可自胎兒分離到病毒。在某些情況下，病毒似乎無法通過胎盤，這表示如要成功的通過胎盤，可能要視母豬感染時的懷孕日數而定，或者與所用的病毒株有關。如在母豬懷孕期間前 1/3 時期感染，病毒穿過胎盤之感染及致病作用都較顯著。自然感染而致胎兒死亡及木乃伊化，通常發生在母豬懷孕第 40~60 天時。如果在懷孕 85 天以後感染，就很少會發生胎兒死亡。胎兒的死亡與病毒不受控制的增殖以及胎兒在感染時尚未達到具免疫力時期有關。據報告，豬胎兒在子宮內就已成能形成對日本腦炎病毒的抗體，但是胎兒在懷孕多久才能對日本腦炎具有免疫力則尚不清楚。不過胎兒對其他病毒如豬小病毒（parvovirus）具免疫力的平均時期是在懷孕第 70 天時，發現日本腦炎病毒如果在此時期以後通過胎盤對胎兒並無致病作用。所以日本腦炎病毒對胎體的致病過程可能與豬小病毒相似。豬小病毒必須在胎兒達到具免疫力的時期以前侵犯胎體，經由對個別胎兒的致病作用，才會造成胚胎早期死亡、木乃伊化、延遲死亡及死產等不同的結果。

病理變化

一 肉眼病變

馬的肉眼病變類似於東方馬腦脊髓炎及西方馬腦脊髓炎病毒感染，而且無特徵性病變可做為病原診斷。

出生後的豬在感染日本腦炎病毒後並無可見之剖檢病變。但是在懷孕時期感染本病的懷孕母豬，會產下木乃伊化黑仔，有時亦可見感染的胎兒有水腦症、小腦發育不全及脊髓鞘生成不良（hypomyelination）。在部分水腦仔豬大腦皮質會變的極薄。在死產及虛弱的新生小豬，可以看到的解剖病變，除有水腦外，並可見皮下水腫、胸腔積水、腹水、漿膜面有出血點、淋巴結充血、肝及脾有壞死病灶、脊髓膜或腦膜充血。

二 組織病變

馬的組織病理變化類似東方腦脊髓炎與西方腦脊髓炎的神經病理變化。水腫，噬神經細胞作用（neuronophagia），圍管現象及星形膠細胞增生（astrocytosis）常見，沒有包涵體產生。

感染仔豬或死產胎兒所見的病變只限於中樞神經系統，其他組織很少有產生病變的報告。腦的病變以淋巴球及漿細胞之圍繞血管浸潤為特徵的非化膿性腦炎，包括神經細胞退化，局部之神經膠質細胞結節（glial nodules）及室管膜炎等。

有關日本腦炎的公豬睪丸病理變化的記載並不多。在自然感染病例，於鞘膜腔可見大量的粘液，副睪邊緣及鞘膜之臟層有纖維性增厚。此種睪丸在顯微鏡檢下可見水腫及炎症的變化，在副睪的間質組織及鞘膜有炎症細胞浸潤，在睪丸的間質組織亦有顯著的細胞浸潤及出血。在生精上皮（seminiferous epithelium）亦常見到退行性變化。

診斷

一 野外診斷

馬的暫時診斷可基於神經症狀伴隨發燒，尤其在流行期間。馬來西亞賽馬場的馬罹患日本腦炎常只有表現發燒及短暫的無精打采。在熱帶地區，本病出現在夏末與初秋之間。在豬，疑似診斷是基於一胎中有較高比率的死產、木乃伊胎及衰弱豬被產出，但絕不能據此而下診斷。

二 實驗室診斷

血清陽轉（seroconversion）可以證實動物遭感染。常用的中和試驗、補體結合試驗（CF）、HI 及酵素結合免疫吸附測定（enzyme-linked immunosorbent assay; ELISA）可以顯示急性期到死亡或恢復，血清力價的上升。

罹患腦炎的馬，血清中產生日本腦炎特定 IgM，可以證明感染。

由於另一種無病原性黃病毒（Flavivirus）感染及流行地區許多無症狀但有血清陽轉的馬，並不能只是藉血清陽轉及 IgM 產生來診斷本病。

進一步確診馬日本腦炎，可以靠檢查腦脊髓液及腦組織。證實脊髓液中存在 IgM 可以表示中樞神經系統感染。雖然顯微鏡下腦病變有一些診斷價值，但確診需要基於由腦分

離與鑑定病毒。適用於節肢病毒的分離技術亦可應用於分離日本腦炎病毒。哺乳小白鼠對日本腦炎病毒非常敏感，尤其由腦內接種病材。病毒分離可藉由接種脊椎動物組織、蚊子或蚊子組織培養。在動物死亡後立即由腦分離病毒，成功比率很高。

確診豬胎兒罹患日本腦炎，主要是由具腦炎症狀的胎兒腦組織分離病毒。由產出異常胎兒母豬的抗體升高來診斷感染日本腦炎，並非可靠方法，因為血清陽轉可能發生在感染初期。

三 鑑別診斷：

本病在馬必須與其他病毒性腦炎區別。在亞洲，日本腦炎常是被考慮為節肢病毒引起馬的主要腦炎。因為有許多輕微或無症狀的感染，因此必需靠實驗室診斷。

各種型式的中毒性腦炎必需列入鑑別診斷。在亞洲熱帶地區，在盛夏季節性馬發生日本腦炎可以幫助做為區別診斷。

豬日本腦炎必需與血球凝集性（hemagglutinating）DNA 病毒感染區別，後者在日本與日本腦炎的疾病表現有相似之處。DNA 病毒的感染於女豬發生於懷孕期中後期。

預後

馬罹患日本腦炎，在日本的死亡率約 5%。在東南亞，真正死亡率可能少於日本。成年豬感染的死亡率幾乎為零。沒有抗體的懷孕母豬感染，可能產下死胎、弱仔或產後即表現腦炎症狀。

流行病學

日本腦炎廣泛存在於亞洲熱帶與溫帶地區，但在這些地區之外的感染情況並不明。在自然界，病毒存在於稻田繁殖 *Culex tritaeniorhynchus*、*annulus*、*fuscocephala*、*gelidus* 及 *vishnui* 的蚊子。這些蚊子叮咬已感染日本腦炎病毒的野鳥及豬血液，再將病毒利用叮咬機會，傳染給人類或動物。

由流行病學觀點來看，人與馬是日本腦炎病毒感染的最終宿主（dead-end hosts）。病毒血症在人類與馬類都很低量，因此並不能提供媒介蚊子飽食含足夠感染病毒量的血液，亦即人與人之間不會藉接觸或接吻而傳播。然而在實驗情況下，有學者證實馬與馬之間傳播可以靠 *Culex tritaeniorhynchus* 完成。

在日本與台灣，豬是本病的感受性動物及自然界感染的增幅者（ampliers），這項事實尤其發生在懷孕母豬生產時期及同時傳播本病的蚊子開始活躍時。正常出生的小豬在移行抗體消失後，即對節肢動物媒介的感染非常敏感。日本腦炎在豬呈無症狀感染，但病毒在血中的量卻高到足以讓 *Culex tritaeniorhynchus* 在吸食血後，經過潛伏期，蚊子即可將病

毒傳播給具感受性的脊椎動物。

在日本，蒼鷺（herons）及白鷺（egrets）擔任散佈日本腦炎給人類及其他脊椎動物的角色，並且也可能將病毒自鄉下帶到都市。*Culex tritaeniorhynchus* 很容易吸蒼鷺與白鷺的血，而且也可以飛離地面到較高處去吸取鳥巢中幼鳥的血液。

在溫帶亞洲區，蚊子攜帶的病毒在晚春出現叮咬馬與豬後，在八月及九月，人感染的疾病即接著出現。在亞洲熱帶及亞熱帶地區，上述疾病與季節性的關係較不明顯。

基本上，日本腦炎不管發生在任何地區，在流行病學上，*Culex* 蚊子與鳥類是常見的影響因子。在亞洲，因為豬的數量，亦是重要的影響因素。

控制

控制本病的方法包括消滅媒介蚊蟲、阻止鳥與豬成為感染圈的增幅者及免疫人與馬。在東南亞，保持清潔、不蓄積髒水、減少 *Culex tritaeniorhynchus* 的聚集及併用殺蟲劑，在控制昆蟲的媒介上獲得一些成功的例子。減少鳥類的保毒宿主似乎並非可行的方法。人感染後並無特殊療法，只能靠加護支持療法。

減少家畜的損失及降低自然界的感染，最令人看好的方法就是廣泛實施豬的疫苗注射。日本及台灣使用減毒疫苗。免疫女豬不僅可以保護動物免受感染，同時又可以減低其成為自然界增幅者的角色。留種豬必須免疫，才能抵抗懷孕期間的感染而產下正常仔豬。

雖然控制豬的日本腦炎可以減少自然界的散佈，但是其他感染原仍然對人與馬有潛在威脅。中國大陸，以大頰鼠腎組織培養製造的減毒疫苗，廣泛使用於馬，這種疫苗可減少約 85% 疾病的發生。在日本與韓國，以小白鼠腦製成的不活化疫苗，被允許使用於人類。自 1960 年代，中國大陸以大頰鼠腎組織培養的不活化疫苗用於免疫兒童。

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Comparative Pathology Case 133

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Clinical history: A 35-year-old man suffered from headache, fever ($>38.5^{\circ}\text{C}$) and chillness for more than 3 days. He visited MGH ER at 23:28 on June 19, 1998. CBC revealed WBC 9,280, Hb 14.7, platelet 236,000, and neutrophil 64.8%, lymphocyte 26.7%, monocyte 8.1%, eosinophil 0.2%, basophil 0.2%. Chest X-ray showed normal appearance, symptom treatment was performed then he went home. Unfortunately, apnea, cyanosis, general weakness and heart arrest attacked at AM 6:30 June 21, 1998. He was sent to our ER quickly. After CPR 30 minutes, he expired. Forensic autopsy was performed on June 22.

Diagnosis: 1. Japanese encephalitis
2. Neurogenic pulmonary edema

Gross findings: The brain is moderately congested and swollen. On cut, mottled dusky discoloration of the thalamus and brain stem is prominent. Marked heavy lungs (R't 800gm and L't 750gm) are also seen. On cut, marked hemorrhage and edema are present.

Histopathological findings: Histology reveals leptomeningeal, perivascular and parenchymal infiltration, predominantly by lymphocytes and microglia or macrophages. Affected gray matter regions contain perivascular cuffs of mononuclear inflammatory cells, especially lymphocytes and microglial nodule formation, often surrounding degenerating neuronal cell bodies (neuronophagia). The lungs show marked hemorrhagic edema.

Immunohistochemistry stain: Monoclonal mouse anti-human JE antibody is used to immunohistochemistry stain. Positive immunostainings of JE viral antigens are present in the neuron, dendritic processes, axonal processes and necrotic area.

Discussion: Japanese encephalitis is caused by a Flavivirus that produces serious epidemics that affect more people in large areas of the world than any other Togavirus. This virus is maintained in extrahuman reservoirs such as wild and domestic birds that develop sustained viremia. Man is an incidental host and plays no role in its transmission. The disease has a seasonal incidence, although in tropical regions where mosquitoes are active throughout the year,

it can occur in any season. The most important vector is rural mosquito, *Culex tritaeniorhynchus*, which prefers to bite large domestic animals but also feeds on birds and man.

Japanese encephalitis occurs more frequently in children than in adults. Mortality ranges from 10 to 40%. Encephalitis usually takes two to four days before it becomes full-blown. The presenting symptoms are headache, fever, shaking chills, nuchal rigidity, vomiting and nausea.

During the acute stage, congestion, edema, and small hemorrhages are found in the brain. Microscopic lesions include neural degeneration and necrosis, neuronophagia, microglial proliferation forming glial nodules, and perivascular inflammation. These changes occur in gray matter and predominantly affect diencephalic, mesencephalic and brain stem structures. Destruction of cerebellar purkinje cells may be prominent. Extranuclear tissue change includes hyperplasia of germinal centers of lymph nodes, enlargement of malpighian bodies in spleen, interstitial myocarditis and interstitial pneumonia.

In one study of fatal human cases, JE viral antigen is localized to neurons, with no evidence for glial cell infection. The highest concentration of infected neurons is in thalamus and brain stem, the same as our case. Among inflammatory cells recruited into perivascular infiltrates, help T cells predominated, but a minority are T – suppressor/cytotoxic lymphocytes. Macrophages predominated among cells recruited into the brain parenchyma.

The cause of death in our case is pulmonary edema. The infection and destruction of neurons in the brain stem can explain the pulmonary edema.

Diagnosis criteria: 1. Classic virus encephalitis, especially involved thalamus and brain stem
2. Immunohistochemistry stain shows positive of JE virus antigen in neuron.

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Comparative Pathology Case 134

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Clinical history: A hog farm raises about 15,000 pigs, which includes 40 boars and 1,300 sows. 10 litter piglets, 3-4 weeks old, showed nervous signs sporadically in February of this year. The morbidity and mortality were 100% in each litter. The vaccination program was performed as follow: Hog cholera vaccination was administrated at 3 and 6 weeks old and every 2 years to sows. The sows also vaccinated with atrophic rhinitis bacterin and pseudorabies vaccine at 3 and 4, 8 weeks before parturition respectively. The sick piglets appeared severe ataxia, convulsion, peddling and died suddenly.

Diagnosis: Swine salmonellosis with meningitis

Gross findings: Many pin-point white foci were observed in the liver. Meninge was hyperemic.

Histopathological findings: Focal necrosis and many paratyphoid nodules were revealed in the liver parenchyma. Meninge was infiltrated by a lot of leukocytes, above all, the lymphocytes and macrophages.

Immunofluorescence test: The frozen sections of tonsil, liver and brain were labeled with anti-Hog cholera or pseudorabies antisera that were conjugated with fluorescence isothiocyanate. All the sections showed negative result to both viruses.

Bacterial isolation: Bacteria were isolated from the brain. Some colonies grew in the XLD agar after 24 hours cultivation in 37°C. The pinkish colony contained a black center and was verified into the negative bacillus by Gram stain. *Salmonella* spp. was identified by GFB-12E code system.

Differential diagnosis: All the following diseases will cause nervous signs in piglets.

1. Streptococcosis
2. Salmonellosis
3. Pseudorabies
4. Hog cholera

Diagnostic criteria: Liver focal necrosis, paratyphoid nodules, lymphocytic meningitis

Discussion: Swine Salmonella was firstly isolated in 1885, which mainly caused enteritis and septicemia, however, meningitis, pneumonia, encephalitis and caseous lymphadenitis were also reported⁽¹⁾. Some reports mentioned that a few cases presented nervous signs, which were similar to Hog cholera or pseudorabies. This disease always occurred in the 8-16 weeks old pigs but rare in suckling or adult pigs⁽²⁾.

The septicemic Salmonellosis can cause systemic signs and lesions, and its pathogen is *S. choleraesuis*. However, Lawson and Dow mentioned that the pathogen of piglet's meningitis was *S. dublin* or *S. enteritidis*.⁽²⁾

This case occurred in 3-4 weeks old suckling piglets. It is different from the usual case. The possible reasons were the piglets obtained too little maternal antibody from sow or the owner abused too many antibiotics for a long period, therefore the bacteria possessed resistance to those drugs.

The pathogenicity of septicemic Salmonellosis was initiated by its endotoxin that can activate the complements, induce endogenous blood coagulation and trigger inflammation, platelets coagulation and leukocytes chemotaxis. It always causes necrotic vasculitis and perivascular cuffing in the brain⁽³⁾.

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Comparative Pathology Case 135

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Clinical history: The piglet, about 2~3 week-old, showed nervous signs. The morbidity was 1~2%, Streptococcal infection and pseudorabies were suspected.

The piglets had been treated with lincomycin, 20% showed obvious improvement. The owner sent three piglets to PRIT for pathological diagnosis. The vaccination program of the sow were 2 times in pseudorabies, 1 in FMD, 2 in JE, 1 in TGE, 2 in HC.

Diagnosis: Meningoencephalitis, fibrinopurulent and lymphocytic, diffuse, subacute, moderate, cerebrum, cerebellum and brain stem, caused by *Streptococcus* spp. infection, swine.

Gross findings: Synovial fluid in the stifle joints of three piglets are fibrinopurulent and increased in volume. Increased amounts of fluid are also noted in pericardium and CSF. Mild congestion of the leptomeninges are noted.

Histopathological findings: Fibrin tags, edema, congestion, hyperemia, and cellular infiltrates on the leptomeninges of cerebrum, cerebellum and brain stem are easily noted. Numerous and diffuse neutrophils, macrophages and lymphocytes are plugging on the meninges and the sulci. Perivascular lymphocytic cell cuffings are also noted, chiefly in the cerebrum and the brain stem.

Isolation and identification:

1. Joint, pericardial fluid, brain: *Streptococcus* spp.
2. Antibiotics Sensitivity Test:
Brain: *Streptococcus* spp.

No	Gram positive Disc	Sensitivity	No	Gram positive Disc	Sensitivity	No	Gram positive Disc	Sensitivity
1	Oxacillin (Ox1)	+	1	Gentamicin (GM10)		1	Ampicillin (AP25)	+++
2	Methicillin (MT5)	+	2	Kanamycin (K30)		2	Amoxycillin (A20)	+++
3	Lincomycin (L2)	-	3	Streptomycin (S10)		3	Carbenicillin (PY100)	++
4	Novobiocin (No5)	-	4	Nalidixic Acid (NA30)		4	Penicillin (PG10)	++
5	Erythromycin (E15)	-	5	Colistin (Co10)		5	Cephalothin (KF30)	++
6	Bacitracin (BA10)	++	6	Cefamandole (CMD30)		6	Ceftiofur (EFT30)	+++
7	Spectinomycin (S200)	++	7	Cefotaxime (CTx30)		7	Tetracycline (T30)	+++
8	Tylosin (TY30)	-	8	Flumequine (Flu5)		8	Oxyteracycline (OT30)	-
			9			9	Doxycycline (DXT10C)	-
			10			10	Tiamulin + Tetracycline	+
						11	Lincospectin (L30)	-
						12	Chloramphenicol (C30)	+
						13	Chloramphenicol (C50)	+
						14	Thiamphenicol (TPC20C)	+
						15	Cotrimoxazole (TS50C)	-
						16	Furazolidone (Fu30)	-
						17	Furazolidone (Fu50)	-
						18	Nitrofurantoin (NI)	-
						19	Florocl (FF100)	+++

3. Virus isolation: blood, lymph node and spleen- PRRS negative

4. IFA: HC negative

Electromicroscopic findings: EM negative stain examination: Intestinal contents- TGE virus negative

Discussion: *Streptococcus suis* is a Gram-positive, hemolytic, facultatively anaerobic coccus. Strains of *S. suis* are divided into 35 serotypes according to their capsular antigen (type 1 to 34, and type 1/2). The syndrome in swine caused by *S. suis* include arthritis, meningitis, pneumonia, septicemia, endocarditis, encephalitis, polyserositis, abortion and abscess. The economic loss to the swine industry from *S. suis* infection is estimated at over 300 million dollars in USA.

The prevalence of and the morbidity and mortality from *S. suis* vary among herds. Morbidity ranges from 1% to more than 50%, although it rarely exceeds 5%. Mortality is 0~20%, dependant on prompt and appropriate treatment.

The disease usually peaks during weaning (about 6 weeks of age) and mixing of pigs. Pigs harbouring *S. suis* Type II may become carriers without showing clinical signs. The highest carrier rates occur in pigs between 4 and 10 weeks of age. *S. suis* Type II may persist in the tonsils of carrier pigs for over 1 years.

The sow is a probable source of infection. Gilts and sows may harbor *S. suis* in the uterus or vagina. Piglets born to sows with uterine or vaginal *S. suis* infections may become infected at birth, before or soon after birth.

The carrier rates in herds vary from 0 to 100%, however, the carrier rate is not a good indicator of clinical disease within a herd. Crowding, poor ventilation, sudden weather change, mixing, moving, vaccination and concurrent disease are all stresses that predispose pigs to *S. suis* Type II infection. Vectors of *S. suis* can play a role in disease transmission. Houseflies can carry *S. suis* Type II for 5 days. *S. suis* Type II is an important contaminant of faeces, dust and water. *S.*

suis Type II can be inactivated easily with 5% bleach at 1:799 dilution.

In the acute form, clinical signs may include fever (up to 42°C), depression, anorexia, and lassitude, followed by one or more of the following: ataxia, incoordination, tremors, opisthotonus, blindness, loss of hearing, paddling, paralysis, dyspnea, convulsions, nystagmus, arthritis, lameness, erythema, and/or abortion.

S. suis type I is most often associated with disease in 10 to 14-day-old piglets. Type II is the serotype most often associated with disease, primarily affects weanlings, but also associated with fading piglets syndrome in neonates and meningitis outbreaks in finishing pigs weighing 330~350kg.

The most common gross lesions are congestion of the meninges, lymph nodes and lungs, and the most common histopathological lesion of acute *S. suis* meningitis is a diffuse neutrophilic infiltrate, other features include fibrin, edema and cellular infiltrates of the meninges, choroid plexus and ventricles. The leptomeningitis in these cases can be characterized as fibrinopurulent, lympholeukocytic, or rarely, lymphocytic.

Other lesions include purulent, fibrinous or fibrinopurulent arthritis, polyserositis, pericarditis, vegetative valvular endocarditis, and to a lesser extent hemorrhagic necrotizing myocarditis. Pulmonary lesions are variable, include interstitial fibrinous and fibrinohemorrhagic pneumonia, suppurative bronchopneumonia with or without perivascular, peribronchial and peribronchiolar cuffings of lymphocytes.

It is generally accepted that *S. suis* enters the palatine tonsils. The major site of replication, and exits via the lymphatics or efferent blood supply. Mononuclear phagocytes may engulf bacteria and carry *S. suis* to the CNS, joint or serosal cavities.

Virulent *S. suis* Type II isolates possess a 136 kDa muramidase-released protein (MRP) and a 110 kDa extracellular protein factor (EF) which have been showed to be necessary for full expression of virulence, EF-positive strain (EF+) produced the typical meningoencephalitis, polyserositis, and polyarthritis in pigs, but negative strain (EF-) produced only a mild disease. Isolates that did not produce either of these proteins (MRP- EF-) failed to cause any clinical signs of disease. Because the 136 kDa and 110 kDa proteins are absent in avirulent strain, they are thought to be virulent markers. Other virulence factors include 44 kDa proteins, 52 kDa IgG-binding protein, thiol-activated hemolysins, surface components, such as fimbriae, adhesins and capsules, trihexosylceramide (GbO₃), sialic acid as well as superoxide dismutase (SOD).

Concurrent infection with pseudorabies virus, porcine reproductive and respiratory syndrome virus (PRRS), *Pasteurella multocida*, *E. coli*, *Actinobacillus pleuropneumoniae* and *Actinomyces pyogenes* produced more severe clinical signs than either agent alone.

In human, *S. suis* Type II can cause meningitis and/or septicemia followed by deafness or diplopia. Ataxia and deafness occur in 50~75% of patients with purulent meningitis and persist in half of these cases. *S. suis* Type II has also been isolated from human causes of arthritis, acute gastroenteritis, endocarditis, endophthalmitis, and may cause death. The organisms probably gained entry via small wounds or through inhalation, and the people at greatest risk are pig breeders, abattoir workers. They are estimated to be 1500 times more likely to streptococcal

meningitis than people not associated with pigs or their meat.

The identification of *S. suis* can use biochemical, serological, molecular and other systems. However, biochemical characteristics are so variable that identification is often difficult and may require a combination of biochemical reactions followed by confirmational serotyping. *S. suis* isolates are verified by serotyping based on polysaccharide capsular antigens using one or more of the following techniques: a slide agglutination test, a capsular seaction, a capillary precipitation or a co-agglutination test. Other methods include multilocus enzyme electrophoresis (MEE) IFA, ELISA, selective media, restriction fragment length of chromosomal DNA.

Medication of feed with antibiotics at therapeutic levels may suppress clinical disease while it is being done but does not eliminate carriers.

Injectable ampicillin or penicillin, penicillin or tiamulin in drinking water or feed has been beneficial in decreasing the incidence of *S. suis* type II infection. Cefuroxime (2ug/ml) was effective in killing more than 99% of *S. suis* type II. Resistance of *S. suis* to tetracyclines, benzylpenicillin, clindamycin, tilmicosin, norfloxacin, streptomycin, kanamycin and erythromycin has been reported.

Commerical vaccines are variable. However, because of the larger number of capsular types, overall success with commerical vaccines may be elusive until the specific virulence factors contributing to the pathogenicity of the organisms are better understood.

The risk of disease can be minimized by maintaining proper ventilation, avoiding overcrowding and stress, minimizing mixing and moving, incorporating pest control measures, cleaning and drying the housing areas adequately, and using disinfectants between housing groups.

Diagnostic criteria:

1. Disease usually peaks during weaning (6 weeks) and mixing.
2. Stress predispose pigs to *S. suis* infection.
3. Clinical signs include fever, and CNS signs.
4. Gross lesions include congestion of the meninges, lymph nodes and lung, fibrino purulent arthritis, vegetative valvular endocarditis, polyserositis.
5. Histopathological lesions include suppurative meningoencephalitis, arthritis, endocarditis and pneumonia.
6. Bacteria isolation and serotyping.
7. Virulent factor-MRP, EF.
8. Higher carrier rates in pigs (4~10 weeks) and possible source of infection from gilt and sows (uterus, vagina), tail cutting, teeth remove as well as castration in piglets.

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<p style="text-align: center;">中華民國比較病理學會 第一次至第十五次比較病理學研討會病例一覽表</p>
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第一次比較病理學研討會病例（83年10月30日於台灣養豬科學研究所舉行）：

動物別	診斷	提供單位
1. Dog	Myxoma	美國紐約動物醫學中心
2. Ferret	Chordoma	美國紐約動物醫學中心
3. Human	Ependymoblastoma	長庚紀念醫院
4. Goat	Cryptosporidiosis	台灣養豬科學研究所
5. <i>Lemur fulvus</i>	Amoebiasis	台灣養豬科學研究所
6. Monkey	Tuberculosis	台灣大學獸醫學系
7. Human	Tuberculosis	省立新竹醫院

第二次比較病理學研討會病例（84年4月9日於台北病理中心舉行）：

8. Pigeon	Synovial sarcoma	美國紐約動物醫學中心
9. Cat	Perinephric pseudocyst	台灣大學獸醫學系
10. Human	Choledochocyst	長庚紀念醫院
11. Rat	Bile duct ligation	中興大學獸醫學系
12. Human	<i>H. pylori</i> -induced gastritis	台北病理中心
13. Human	Pseudomembranous colitis	省立新竹醫院
14. Dog	Dirofilariasis	台灣省家畜衛生試驗所
15. Human	Pulmonary dirofilariasis	台北榮民總醫院
16. Squirrel	Toxoplasmosis	台灣養豬科學研究所
17. Pig	Toxoplasmosis	屏東技術學院獸醫學系

第三次比較病理學研討會病例（84年8月27日於國立台灣大學舉行）：

18. Human	Malignant lymphoma	長庚紀念醫院
19. Wistar rat	Malignant lymphoma	國家實驗動物繁殖及研究中心
20. Human	Sparganosis	台北榮民總醫院
21. Chickens	Newcastle disease	國立台灣大學獸醫學系
22. Goldfish	Herpesvirus infection	國立台灣大學獸醫學系
23. Human	Chromomycosis	台北病理中心
24. Human	Metastatic thyroid carcinoma	省立新竹醫院
25. Human	Chordoma	新光吳火獅紀念醫院
26. Pig	Swine salmonellosis	國立中興大學獸醫學系
27. Pig	Vegetative valvular endocarditis	台灣養豬科學研究所

第四次比較病理學研討會病例（84 年 11 月 19 日於新光吳火獅紀念醫院舉行）：

28. Human	Nocardiosis	台灣省立新竹醫院
29. Largemouth bass	Nocardiosis	屏東縣家畜疾病防治所
30. Dog	Demyelinating canine distemper encephalitis	台灣養豬科學研究所
31. Malayan sun bears	Adenovirus infection	國立台灣大學獸醫學系
32. Human	Actinomycosis	台灣省立豐原醫院
33. Human	Tuberculosis	苗栗頭份為恭紀念醫院
34. Dog	Interstitial cell tumor	國立中興大學獸醫學系
35. Human	Carcinoid tumor	長庚紀念醫院
36. Siamese cat	Hepatic carcinoid	美國紐約動物醫學中心
37. Human	Myositis ossificans	台北醫學院

第五次比較病理學研討會（85 年 2 月 4 日於台北市立仁愛醫院舉行）：

中華民國比較病理學會成立大會暨專題演講

第六次比較病理學研討會（85 年 6 月 9 日於台中榮民總醫院舉行）：

38. Ferret	Pheochromocytoma	美國紐約動物醫學中心
39. Human	Extra adrenal pheochromocytoma	新光吳火獅紀念醫院
40. Rat	Mammary gland fibroadenoma	國家實驗動物繁殖及研究中心
41. Human	Fibroadenoma	省立豐原醫院
42. Pointer bitch	Canine benign mixed type mammary gland tumor	國立中興大學獸醫學系
43. Human	Phyllodes tumor	台中榮民總醫院
44. Dog	Canine oral papilloma	國立台灣大學獸醫學系
45. Human	Squamous cell papilloma	中國醫藥學院

第七次比較病理學研討會（85 年 11 月 10 日於國立屏東技術學院獸醫系舉行）：

46. Cat	Feline dirofilariasis	美國紐約動物醫學中心
47. Human	Lung: metastatic carcinoma associated with cryptococcal infection. Liver: metastatic carcinoma. Adrenal gland, right: carcinoma (primary)	三軍總醫院
48. Wild rodents	Adiaspiromycosis	國立台灣大學獸醫學系
49. Human	Echinococcosis	台北榮民總醫院
50. Piglet	Porcine cytomegalovirus infection	台灣省家畜衛生試驗所
51. Human	Pneumocystis carinii pneumonia	台北病理中心
52. Goslings	Aspergillosis	屏東縣家畜疾病防治所

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| 53. Human | Intracavitary aspergilloma and cavitary tuberculosis, lung. | 羅東聖母醫院 |
| 54. Human | Fibrocalcified pulmonary TB mixed actinomycosis and aspergillosis lung infection with abscess DM, NIDDM. | 林口長庚紀念醫院 |
| 55. Broilers | Infectious laryngo-tracheitis (Herpesvirus infection) | 國立屏東技術學院獸醫學系 |

第八次比較病理學研討會（86年3月2日於台中榮民總醫院第一會議廳舉行）：

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|--------------|--|------------|
| 56. Human | Gastrointestinal stromal tumor | 台中榮民總醫院 |
| 57. Chicken | Cecal coccidiosis | 國立中興大學獸醫學系 |
| 58. Human | Tuberculous enteritis with perforation | 佛教慈濟綜合醫院 |
| 59. Dog | Colonic adenocarcinoma | 美國紐約動物醫學中心 |
| 60. Human | Intestinal capillariasis | 台北馬偕醫院 |
| 61. Goose | Spirochetosis | 國立嘉義農專獸醫科 |
| 62. Human | Submucosal leiomyoma of stomach | 頭份為恭紀念醫院 |
| 63. Porcine | Proliferative enteritis (<i>Lawsonia Intracellularis</i> infection) | 屏東縣家畜疾病防治所 |
| 64. Human | 1. Adenocarcinoma of sigmoid colon
2. Old schistosomiasis of rectum | 省立新竹醫院 |
| 65. Carprine | Cryptosporidiosis | 台灣養豬科學研究所 |

第九次比較病理學研討會（86年7月20日於新光吳火獅紀念醫院B1大會議室舉行）：

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| 66. Chapman's zebra | Echinococcosis | 國立台灣大學獸醫學系 |
| 67. Human | Hepatic ascariasis and cholelithiasis | 彰化基督教醫院 |
| 68. Human | Liver abscess (<i>Klebsillae pneumoniae</i>) | 台北醫學院 |
| 69. Pig | Pseudorabies (Herpesvirus infection) | 台灣養豬科學研究所 |
| 70. Human | Acute Q fever hepatitis | 佛教慈濟綜合醫院 |
| 71. Human | Myelolipoma | 台北耕莘醫院 |
| 72. Mouse | Reticulum cell sarcoma | 國家實驗動物繁殖及研究中心 |
| 73. Human | Hepatocellular carcinoma | 新光吳火獅紀念醫院 |
| 74. Wistar strain rats | Hepatocellular carcinoma induced by aflatoxin B1 | 台灣省農業藥物毒物試驗所 |
| 75. Rabbits | Acute yellow phosphorus intoxication | 國立中興大學獸醫學系 |

第十次比較病理學研討會（86年11月2日於三軍總醫院研究大樓一樓視聽教室舉行）：

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| 76. Cat | Polycystic kidney bilateral and renal failure | 美國紐約動物醫學中心 |
| 77. Human | 1.Xanthogranulomatous inflammation with nephrolithiasis, kidney, right.
2.Ureteral stone, right. | 羅東聖母醫院 |

78. Chicken	Marek's disease in native chicken	屏東縣家畜疾病防治所
79. Human	Emphysematous pyelonephritis	彰化基督教醫院
80. SHR rat	1.Glomerular sclerosis and hyalinosis, segmental, focal, chronic, moderate 2.Benign hypertension	國防醫學院 & 國家實驗動物繁殖及研究中心
81. Human	Angiomyolipoma	羅東博愛醫院
82. Human	Inverted papilloma of prostatic urethra	省立新竹醫院
83. SD rats	Phagolysosome-overload nephropathy	國家實驗動物繁殖及研究中心
84. Human	Nephrogenic adenoma	國泰醫院
85. Dog	Renal amyloidosis	台灣養豬科學研究所
86. Human	Multiple myeloma with systemic amyloidosis	佛教慈濟綜合醫院
87. Human	Squamous cell carcinoma of renal pelvis and calyces with extension to the ureter	台北病理中心
88. Human	Fibroepithelial polyp of the ureter	台北耕莘醫院
89. Goose	1.Severe visceral gout due to kidney damaged 2.Infectious serositis	國立中興大學獸醫學系
90. Human	Clear cell sarcoma of kidney	台北醫學院
91. orange-rumped agoutis	Hypervitaminosis D	國立台灣大學獸醫學系

第十一次比較病理學研討會（87年3月1日於佛教慈濟綜合醫院舉行）：

92. Pig	Foot-and-mouth disease (FMD)	屏東縣家畜疾病防治所
93. Dog	Mammary gland adenocarcinoma, complex type, with chondromucinous differentiation	國立台灣大學獸醫學系
94. Human	1.Breast, left, modified radical mastectomy, showing papillary carcinoma, invasive 2.Nipple, left, modified radical mastectomy, papillary carcinoma, invasive 3.Lymph node, axillary, left, lymphadenectomy, papillary carcinoma, metastatic	羅東聖母醫院
95. Dog	Transmissible venereal tumor	國立中興大學獸醫學系
96. Human	Malignant lymphoma, large cell type, diffuse, B-cell phenotype	彰化基督教醫院
97. Tiger	Carcinosarcomas	台灣養豬科學研究所
98. Human	Mucinous carcinoma with intraductal carcinoma	省立豐原醫院
99. Mouse	Mammary gland adenocarcinoma, type B, with pulmonary metastasis, BALB/cBYJ mouse	國家實驗動物繁殖及研究中心

100. Human	Malignant fibrous histiocytoma and paraffinoma	中國醫藥學院
101. Pig	Swine pox	國立屏東科技大學獸醫學系
102. Human	Pleomorphic adenoma (benign mixed tumor)	佛教慈濟綜合醫院

第十二次比較病理學研討會（87年4月19日於臺灣養豬科學研究所舉行）：心臟血管專題演講

第十三次比較病理學研討會（87年6月14日於台北市立動物園舉行）：

103. Human	Atypical central neurocytoma	新光吳火獅紀念醫院
104. SD rat	Cardiac schwannoma	國家實驗動物繁殖及研究中心
105. Human	1. Mucormycosis 2. Diabetes mellitus	花蓮佛教慈濟綜合醫院
106. Dog	Parasitic meningoencephalitis, caused by <i>Toxocara canis</i> larvae migration	臺灣養豬科學研究所
107. Human	1. Primary cerebral malignant lymphoma 2. Acquired immune deficiency syndrome	台北市立仁愛醫院
108. Lamb	Listeric encephalitis	屏東縣家畜疾病防治所
109. Human	Desmoplastic infantile ganglioglioma	高雄醫學院
110. Piglet	Pseudorabies	國立屏東科技大學
111. Human	Schwannoma	三軍總醫院
112. Chicken	Avian encephalomyelitis	國立中興大學
113. Human	Tuberculous meningitis	羅東聖母醫院
114. Dog	Osteosarcoma	美國紐約動物醫學中心

第十四次比較病理學研討會（87年11月15日於國立中興大學舉行）：

115. Dog	Mixed germ-cell stromal tumor, mixed Sertoli cell and seminoma-like cell tumor	美國紐約動物醫學中心
116. Human	Krukenberg's Tumor	台北病理中心
117. Human	Primary insular carcinoid tumor arising from cystic teratoma of ovary.	花蓮慈濟綜合醫院
118. Dog	Cystic endometrial hyperplasia	臺灣養豬科學研究所
119. Human	Polypoid adenomyoma	大甲李綜合醫院
120. Human	Gonadal stromal tumor	耕莘醫院
121. Dog	Cystic subsurface epithelial structure (SES)	國科會實驗動物中心
122. Human	Gestational choriocarcinoma	彰化基督教醫院
123. Horse	Ovarian granulosa cell tumor	國立中興大學

第十五次比較病理學研討會（88年4月11日於國立臺灣大學農學院附設動物醫院舉行）：

124. Dog	Superficial necrolytic dermatitis	美國紐約動物醫學中心
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125. Human	Solitary congenital self-healing histiocytosis	羅東博愛醫院
126. Mouse	Alopecia areata	國家實驗動物繁殖及研究中心
127. Human	Eumycotic mycetoma	花蓮佛教慈濟綜合醫院
128. Goat	Contagious pustular dermatitis	屏東縣&台東縣家畜疾病防治所
129. Human	Kaposi's sarcoma	華濟醫院
130. Chicken	Fowl pox and Marek's disease	國立中興大學獸醫學系
131. Human	Basal cell carcinoma (BCC)	羅東聖母醫院
132. Dog	Transmissible venereal tumor	國立臺灣大學獸醫學系

中華民國比較病理學會
第一次至第十五次比較病理學研討會病例分類一覽表

分 類	病例 編號	診 斷	動物別	提 供 單 位
腫 瘤	1	Myxoma	Dog	美國紐約動物醫學中心
	2	Chordoma	Ferret	美國紐約動物醫學中心
	3	Ependymoblastoma	Human	長庚紀念醫院
	8	Synovial sarcoma	Pigeon	美國紐約動物醫學中心
	18	Malignant lymphoma	Human	長庚紀念醫院
	19	Malignant lymphoma	Wistar rat	國家實驗動物繁殖及研究中心
	24	Metastatic thyroid carcinoma	Human	省立新竹醫院
	25	Chordoma	Human	新光吳火獅紀念醫院
	34	Interstitial cell tumor	Dog	國立中興大學獸醫學系
	35	Carcinoid tumor	Human	長庚紀念醫院
	36	Hepatic carcinoid	Siamese cat	美國紐約動物醫學中心
	38	Pheochromocytoma	Ferret	美國紐約動物醫學中心
	39	Extra adrenal pheochromocytoma	Human	新光吳火獅紀念醫院
	40	Mammary gland fibroadenoma	Rat	國家實驗動物繁殖及研究中心
	41	Fibroadenoma	Human	省立豐原醫院
	42	Canine benign mixed type mammary gland tumor	Pointer bitch	國立中興大學獸醫學系
	43	Phyllodes tumor	Human	台中榮民總醫院
	44	Canine oral papilloma	Dog	國立台灣大學獸醫學系
	45	Squamous cell papilloma	Human	中國醫藥學院
	47	Lung: metastatic carcinoma associated with cryptococcal infection. Liver: metastatic carcinoma. Adrenal gland, right: carcinoma (primary)	Human	三軍總醫院
	56	Gastrointestinal stromal tumor	Human	台中榮民總醫院
	59	Colonic adenocarcinoma	Dog	美國紐約動物醫學中心
	62	Submucosal leiomyoma of stomach	Human	頭份為恭紀念醫院
	64	1. Adenocarcinoma of sigmoid colon 2. Old schistosomiasis of rectum	Human	省立新竹醫院

分 類	病例 編號	診 斷	動物別	提 供 單 位
	71.	Myelolipoma	Human	台北耕莘醫院
	72.	Reticulum cell sarcoma	Mouse	國家實驗動物繁殖及研究中心
	73.	Hepatocellular carcinoma	Human	新光吳火獅紀念醫院
	74.	Hepatocellular carcinoma induced by aflatoxin B1	Wistar strain rats	台灣省農業藥物毒物試驗所
	81.	Angiomyolipoma	Human	羅東博愛醫院
	82.	Inverted papilloma of prostatic urethra	Human	省立新竹醫院
	84.	Nephrogenic adenoma	Human	國泰醫院
	86.	Multiple myeloma with systemic amyloidosis	Human	佛教慈濟綜合醫院
	87.	Squamous cell carcinoma of renal pelvis and calyces with extension to the ureter	Human	台北病理中心
	88.	Fibroepithelial polyp of the ureter	Human	台北耕莘醫院
	90.	Clear cell sarcoma of kidney	Human	台北醫學院
	93.	Mammary gland adenocarcinoma, complex type , with chondromucinous differentiation	Dog	國立台灣大學獸醫學系
	94.	1.Breast, left, modified radical mastectomy, showing papillary carcinoma, invasive 2.Nipple, left, modified radical mastectomy, papillary carcinoma, invasive 3.Lymph node, axillary, left, lymphadenectomy, papillary carcinoma, metastatic	Human	羅東聖母醫院
	95.	Transmissible venereal tumor	Dog	國立中興大學獸醫學系
	96.	Malignant lymphoma, large cell type, diffuse, B-cell phenotype	Human	彰化基督教醫院
	97.	Carcinosarcomas	Tiger	台灣養豬科學研究所
	98.	Mucinous carcinoma with intraductal carcinoma	Human	省立豐原醫院
	99.	Mammary gland adenocarcinoma, type B, with pulmonary metastasis, BALB/cBYJ mouse	Mouse	國家實驗動物繁殖及研究中心
	100.	Malignant fibrous histiocytoma and paraffinoma	Human	中國醫藥學院

分 類	病例 編號	診 斷	動物別	提 供 單 位
	102.	Pleomorphic adenoma (benign mixed tumor)	Human	佛教慈濟綜合醫院
	103	Atypical central neurocytoma	Human	新光吳火獅紀念醫院
	104	Cardiac schwannoma	SD rat	國家實驗動物繁殖及研究中心
	109	Desmoplastic infantile ganglioglioma	Human	高雄醫學院
	107	1.Primary cerebral malignant lymphoma 2. Acquired immune deficiency syndrome	Human	台北市立仁愛醫院
	111	Schwannoma	Human	三軍總醫院
	114	Osteosarcoma	Dog	美國紐約動物醫學中心
	115	Mixed germ-cell stromal tumor, mixed sertoli cell and seminoma-like cell tumor	Dog	美國紐約動物醫學中心
	116	Krukenberg's Tumor	Human	台北病理中心
	117	Primary insular carcinoid tumor arising from cystic teratoma of ovary.	Human	花蓮慈濟綜合醫院
	119	Polypoid adenomyoma	Human	大甲李綜合醫院
	120	Gonadal stromal tumor	Human	耕莘醫院
	122	Gestational choriocarcinoma	Human	彰化基督教醫院
	123	Ovarian granulosa cell tumor	Horse	國立中興大學
	129.	Kaposi's sarcoma	Human	華濟醫院
細菌	131.	Basal cell carcinoma (BCC)	Human	羅東聖母醫院
	132.	Transmissible venereal tumor	Dog	國立臺灣大學獸醫學系
	6	Tuberculosis	Monkey	國立臺灣大學獸醫學系
	7	Tuberculosis	Human	省立新竹醫院
	12	<i>H. pylori</i> -induced gastritis	Human	台北病理中心
	13	Pseudomembranous colitis	Human	省立新竹醫院
	26	Swine salmonellosis	Pig	國立中興大學獸醫學系
	27	Vegetative valvular endocarditis	Pig	台灣養豬科學研究所
	28	Nocardiosis	Human	台灣省立新竹醫院
	29	Nocardiosis	Largemouth bass	屏東縣家畜疾病防治所
	32	Actinomycosis	Human	台灣省立豐原醫院
	33	Tuberculosis	Human	苗栗頭份為恭紀念醫院
	53	Intracavitary aspergilloma and cavitary tuberculosis, lung.	Human	羅東聖母醫院
	54	Fibrocalcified pulmonary TB, left Apex. Mixed actinomycosis and aspergillosis lung infection with abscess DM, NIDDM.	Human	林口長庚紀念醫院

分 類	病例 編號	診 斷	動物別	提 供 單 位
	58	Tuberculous enteritis with perforation	Human	佛教慈濟綜合醫院
	61	Spirochetosis	Goose	國立嘉義農專獸醫科
	63	Proliferative enteritis (<i>Lawsonia intracellularis</i> infection)	Porcine	屏東縣家畜疾病防治所
	68	Liver abscess (<i>Klebsillae pneumoniae</i>)	Human	台北醫學院
	77.	1.Xanthogranulomatous inflammation with nephrolithiasis, kidney, right. 2.Ureteral stone, right.	Human	羅東聖母醫院
	79.	Emphysematous pyelonephritis	Human	彰化基督教醫院
	89.	1.Severe visceral gout due to kidney damaged 2.Infectious serositis	Goose	國立中興大學獸醫學系
	108	Listeric encephalitis	Lamb	屏東縣家畜疾病防治所
	113	Tuberculous meningitis	Human	羅東聖母醫院
病 毒	21	Newcastle disease	Chickens	國立台灣大學獸醫學系
	22	Herpesvirus infection	Goldfish	國立台灣大學獸醫學系
	30	Demyelinating canine distemper encephalitis	Dog	台灣養豬科學研究所
	31	Adenovirus infection	Malayan sun bears	國立台灣大學獸醫學系
	50	Porcine cytomegalovirus infection	Piglet	台灣省家畜衛生試驗所
	55	Infectious laryngo-tracheitis (Herpesvirus infection)	Broilers	國立屏東技術學院獸醫學系
	69	Pseudorabies (Herpesvirus infection)	Pig	台灣養豬科學研究所
	78.	Marek's disease in native chicken	Chicken	屏東縣家畜疾病防治所
	92.	Foot- and- mouth disease (FMD)	Pig	屏東縣家畜疾病防治所
	101.	Swine pox	Pig	屏東科技大學獸醫學系
	110	Pseudorabies	Piglet	國立屏東科技大學
	112	Avian encephalomyelitis	Chicken	國立中興大學
	128.	Contagious pustular dermatitis	Goat	屏東縣&台東縣家畜疾病防治所
	130.	Fowl pox and Marek's disease	Chicken	國立中興大學獸醫學系
黴 菌	23	Chromomycosis	Human	台北病理中心
	47	Lung: metastatic carcinoma associated with cryptococcal infection. Liver: metastatic carcinoma. Adrenal gland, right: carcinoma (primary)	Human	三軍總醫院
	48	Adiaspiromycosis	Wild rodents	國立台灣大學獸醫學系
	52	Aspergillosis	Goslings	屏東縣家畜疾病防治所

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	53.	Intracavitary aspergilloma and cavitary tuberculosis, lung.	Human	羅東聖母醫院
	54.	Fibrocalcified pulmonary TB, left Apex. Mixed actinomycosis and aspergillosis lung infection with abscess DM, NIDDM.	Human	林口長庚紀念醫院
	105.	Mucormycosis Diabetes mellitus	Human	花蓮佛教慈濟綜合醫院
	127.	Eumycotic mycetoma	Human	花蓮佛教慈濟綜合醫院
寄生 蟲	14.	Dirofilariasis	Dog	台灣省家畜衛生試驗所
	15.	Pulmonary dirofilariasis	Human	台北榮民總醫院
	20.	Sparganosis	Human	台北榮民總醫院
	46.	Feline dirofilariasis	Cat	美國紐約動物醫學中心
	49.	Echinococcosis	Human	台北榮民總醫院
	60	Intestinal capillariasis	Human	台北馬偕醫院
	64	1. Adenocarcinoma of sigmoid colon 2. Old schistosomiasis of rectum	Human	省立新竹醫院
	66	Echinococcosis	Chapman's zebra	國立台灣大學獸醫學系
	67	Hepatic ascariasis and cholelithiasis	Human	彰化基督教醫院
	106	Parasitic meningoencephalitis, caused by <i>Toxocara canis</i> larvae migration	Dog	臺灣養豬科學研究所
原蟲	4	Cryptosporidiosis	Goat	臺灣養豬科學研究所
	15	Amoebiasis	<i>Lemur fulvus</i>	臺灣養豬科學研究所
	16	Toxoplasmosis	Squirrel	臺灣養豬科學研究所
	17	Toxoplasmosis	Pig	屏東技術學院獸醫學系
	51	<i>Pneumocystis carinii</i> pneumonia	Human	台北病理中心
	57	Cecal coccidiosis	Chicken	國立中興大學獸醫學系
	65	Cryptosporidiosis	Carprine	臺灣養豬科學研究所
立克 次體	70	Acute Q fever hepatitis	Human	佛教慈濟綜合醫院
其它	9	Perinephric pseudocyst	Cat	台灣大學獸醫學系
	10	Choledochocyst	Human	長庚紀念醫院
	11	Bile duct ligation	Rat	中興大學獸醫學系
	37	Myositis ossificans	Human	台北醫學院
	75	Acute yellow phosphorus intoxication	Rabbits	國立中興大學獸醫學系
	76.	Polycystic kidney bilateral and renal failure	Cat	美國紐約動物醫學中心
	80.	1. Glomerular sclerosis and hyalinosis, segmental, focal, chronic, moderate 2. Benign hypertension	SHR rat	國防醫學院 & 國家實驗動物繁殖及研究中心

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	83.	Phagolysosome-overload nephropathy	SD rats	實驗動物繁殖及研究
	85.	Renal amyloidosis	Dog	台灣養豬科學研究所
	89.	1. Severe visceral gout due to kidney damaged 2. Infectious serositis	Goose	國立中興大學獸醫學系
	91.	Hypervitaminosis D	Orange-rumped agoutis	國立台灣大學獸醫學系
	118	Cystic endometrical hyperplasia	Dog	臺灣養豬科學研究所
	121	Cystic subsurface epithelial structure (SES)	Dog	國科會實驗動物中心
	124.	Superficial necrolytic dermatitis	Dog	美國紐約動物醫學中心
	125.	Solitary congenital self-healing histiocytosis	Human	羅東博愛醫院
	126.	Alopecia areata	Mouse	實驗動物繁殖及研究中心