
中 華 民 國 比 較 病 理 學 會
九十六年度會員大會暨第三十九次比較病理學研討
會

新式病理學診斷技術之應用



主辦單位：中華民國比較病理學會

財團法人羅東博愛醫院

財團法人台灣動物科技研究所

時 間：中華民國九十六年三月十七日（星期六）

地點：宜蘭縣羅東鎮南昌街 83 號 (<http://www.pohai.org.tw/>)

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議 程 表

時間：上午 08：40~下午 17：30

地點：羅東博愛醫院 (五樓大禮堂)

時 間	議 程	
08:40~09:00	報 到	主持人
09:00~09:10	主席致詞	呂福江 理事長 羅東博愛醫院
09:10~10:00	【專題演講】 Imprint cytology --- A valuable diagnostic method for fresh specimens	羅東博愛醫院病理科 施洽雯 主任 呂福江 理事 長
10:00~10:15	Coffee Break	
10:15~11:05	【專題演講】 電顯在新興傳染病診斷上之應 用	國立中興大學 陳三多 教授 施洽雯 主任
11:05~11:55	【專題演講】 原位雜交及非生物素性染色應 用於犬瘟熱病毒感染診斷	國家實驗動物中心 梁鍾鼎 研究員
11:55~12:15	會 員 大 會	
12:15~13:30	午 餐 (中華民國比較病理學會理監事會議)	
13:30~13:55	病例討論 Case 264	羅東博愛醫院 病理科 陳朱德 醫師 許永祥 主任
13:55~14:20	病例討論 Case 265	國立台灣大學獸醫學研究所 林俊明 獸醫師
14:20~14:45	病例討論 Case 266	財團法人天主教耕莘醫院病理 科 江蓉華 主任
14:45~15:10	病例討論 Case 267	國立屏東科技大學獸醫學系 張聰洲 教授 劉振軒 教授
15:10~15:35	病例討論 Case 268	花蓮慈濟醫院病理檢驗科 李明勳 醫師
15:35~16:00	病例討論 Case 269	國立中興大學獸醫病理學研究 所 廖俊旺 博士
16:00~16:25	病例討論 Case 270	財團法人天主教耕莘醫院病理 科 呂福江 主任 張文發 祕書 長
16:25~16:50	病例討論 Case 271	國立台灣大學獸醫學研究所 許哲銘 獸醫師
16:50~17:15	病例討論 Case 272	羅東聖母醫院 病理科

17:15~17:30

祝志平 主任
綜 合 討 論

中華民國比較病理學會章程

第一章 總則

- 第一條 本會定名為中華民國比較病理學會，英文名稱為 **Chinese Society of Comparative Pathology (CSCP)** (以下簡稱本會)
- 第二條 本會依內政部人民團體法設立，為非營利目的之社會團體，以結合人類醫學與動物醫學資源，提倡比較病理學之研究與發展，交換研究教學心得，聯絡會員友誼及促進國際間比較醫學之交流為宗旨。
- 第三條 本會以全國行政區域為組織區域，會址設於主管機關所在地區，並得報經主管機關核准設主分支機構。前項分支機構組織簡則由理事會擬訂，報請主管機關核准後行之。會址及分支機構之地址於設置及變更時應報請主管機關核備。
- 第四條 本會之任務如左：
- 一、 提倡比較病理學之研究與發展。
 - 二、 舉辦學術演講會、研討會及相關訓練課程。
 - 三、 建立國內比較醫學相關資料庫。
 - 四、 發行比較病理學相關刊物。
 - 五、 促進國內、外比較醫學之交流。
 - 六、 其他有關比較病理學術發展之事項。
- 第五條 本會之主管機關為內政部。目的事業主管機關依章程所訂之宗旨與任務，主要為行政院衛生署及農業委員會，其目的事業應受各該事業主管機關之指導與監督。

第二章 會員

- 第六條 本會會員申請資格如下：
- 一、 一般會員：贊同本會宗旨，年滿二十歲，具有國內外大專院校(或同等學歷)生命科學及其它相關科系畢業資格或高職畢業從事生命科學相關工作滿兩年者。
 - 二、 學生會員：贊同本會宗旨，在國內、外大專院校生命科學或其它相關科系肄業者 (檢附學生身份證明)。
 - 三、 贊助會員：贊助本會工作之團體或個人。
 - 四、 榮譽會員：凡對比較病理學術或會務之推展有特殊貢獻，經理事會提名並經會員大會通過者。
- 前項一、二、三項會員申請時應填具入會申請書，經一般會員二人之推

- 薦，經理事會通過，並繳納會費。學生會員身份改變成一般會員時，得再補繳一般會員入會費之差額後，即成為一般會員，榮譽會員免繳入會費與常年會費。
- 第七條 一般會員有表決權、選舉權、被選舉與罷免權，每一會員為一權。贊助會員、學生會員與榮譽會員無前項權利。
- 第八條 會員有遵守本會章程、決議及繳納會費之義務。
- 第九條 會員有違反法令、章程或不遵守會員大會決議時，得經理事會決議，予以警告或停權處分，其危害團體情節重大者，得經會員大會決議予以除名。
- 第十條 會員喪失會員資格或經會員大會決議除名者，即為出會。
- 第十一條 會員得以書面敘明理由向本會聲明退會。但入會費與當年所應繳納的常年會費不得申請退費。

第三章 組織及職員

- 第十二條 本會以會員大會為最高權力機構。
- 第十三條 會員大會之職權如下：
- 一、 訂定與變更章程。
 - 二、 選舉及罷免理事、監事。
 - 三、 議決入會費、常年會費、事業費及會員捐款之方式。
 - 四、 議決年度工作計畫、報告、預算及決算。
 - 五、 議決會員之除名處置。
 - 六、 議決財產之處分。
 - 七、 議決本會之解散。
 - 八、 議決與會員權利義務有關之其他重大事項。
- 前項第八款重大事項之範圍由理事會訂定之。
- 第十四條 本會置理事十五人，監事五人，由會員選舉之，分別成立理事會、監事會。
- 選舉前項理事、監事時，依計票情形得同時選出候補理事五人，候補監事一人，遇理事或監事出缺時，分別依序遞補之。
- 本屆理事會得提出下屆理事及監事候選人參考名單。
- 第十五條 理事會之職權如下：
- 一、 審定會員之資格。
 - 二、 選舉及罷免常務理事及理事長。
 - 三、 議決理事、常務理事及理事長之辭職。
 - 四、 聘免工作人員。
 - 五、 擬訂年度工作計畫、報告、預算及決算。
 - 六、 其他應執行事項。
- 第十六條 理監事置常務理事五人，由理事互選之，並由理事就常務理

- 事中選舉一人為理事長。
理事長對內綜理監督會議，對外代表本會，並擔任會員大會、理事會主席。
理事長因事不能執行職務時，應指定常務理事一人代理之，未指定或不能指定時，由常務理事互推一人代理之。
理事長或常務理事出缺時，應於一個月內補選之。
- 第十七條 監事會之職權如左：
一、監察理事會工作之執行。
二、審核年度決算。
三、選舉及罷免常務監事。
四、議決監事及常務監事之辭職。
五、其他應監察事項。
- 第十八條 監事會置常務監事一人，由監事互選之，監察日常會務，並擔任監事會主席。
常務監事因事不能執行職務時，應指定監事一人代理之，未指定或不能指定時，由監事互推一人代理之。監事會主席（常務監事）出缺時，應於一個月內補選之。
- 第十九條 理事、監事均為無給職，任期三年，連選得連任。理事長之連任以一次為限。
- 第二十條 理事、監事有下列情事之一者，應即解任：
一、喪失會員資格。
二、因故辭職經理事會或監事會決議通過者。
三、被罷免或撤免者。
四、受停權處分期間逾任期二分之一者。
- 第二十一條 本會置祕書長一人，承理事長之命處理本會事務，令置其他工作人員若干人，由理事長提名經理事會通過後聘免之，並報主管機關備查。但祕書長之解聘應先報主管機關核備。
前項工作人員不得由選任之職員（理監事）擔任。
工作人員權責及分層負責事項由理事會令另定之。
- 第二十二條 本會得設各種委員會、小組或其它內部作業組織，其組織簡則由理事會擬定，報經主機關核備後施行，變更時亦同。
- 第二十三條 本會得由理事會聘請無給顧問若干人，其聘期與理事、監事之任期同。

第四章 會議

- 第二十四條 會員大會分定期會議與臨時會議兩種，由理事長召集，召集時除緊急事故之臨時會議外應於十五日前以書面通知之。定期會

議每年召開一次，臨時會議於理事會過半數認為必要，或經會員五分之一以上之請，或監事會半數函請召集時召開之。

第二十五條 會員不能親自出席會員大會時，得以書面委託其他會員代理，每一會員以代理一人為限。

第二十六條 會員大會之決議，以出席人數過半之同意行之。但章程之訂定與變更、會員之除名、理事及監事之罷免、財產之處置、本會之解散及其他與會權利義務有關之重大事項應有出席人數三分之二以上同意。但本會如果辦理法人登記後，章程之變更應以出席人數四分之三以上之同或全體會員三分之二以上書面之同意行之。

第二十七條 理事會及監事會至少每六個月各舉行會議一次，必要時得召開聯席會議或臨時會議。

前項會議召集時除臨時會議外。應於七日以前以書面通知，會議之決議各以理事、監事過半數之出席，出席人較多數之同意行之。

第二十八條 理事應出席理事會議，監事應出席監事會議，不得委託出席；理事、監事連續二次無故缺席理事會、監事會者，視同辭職。

第五章 經費及會計

第二十九條 本會經費來源如下：

- 一、入會費：一般會員新台幣壹仟元，學生會員壹佰元，贊助會員伍仟元，於入會時繳納。
- 二、常年會費：一般會員新台幣五百元，學生會員壹佰元。
- 三、事業費。
- 四、會員捐款。
- 五、委託收益。
- 六、基金及其孳息。
- 七、其他收入。

第三十條 本會會計年度以國曆年為準，自每年一月一日起至十二月三十一日止。

第三十一條 本會每年於會計年度開始前二個月由理事會編造年度工作計劃、收支預算表、員工待遇表，提會員大會通過（會員大會因故未能如期召開者，先提理監事聯席會議通過），於會計年度開始前報主管機關核備，並於會計年度終了後二個月內由理事會編造年度工作報告、收支決算表、現金出納表、資產負債表、財產目錄及基金收支表，送監事會審核後，造具審核意見書送還理事會，提會員大會通過，於三月底前報主管機關核備（會員大會未能如期召開者，需先報主管機關備查）。

第三十二條 本會解散後，剩餘財產歸屬所在地之地方自治團體或主管機關指定之機關團體所有。

第三十三條 本章程未規定事項，悉依有關法令規定辦理。

第三十四條 本章程經大會通過，報經主管機關核備後施行，變更時亦同。

第三十五條 本章程經本會民國八十五年二月四日第一屆第一次會員大會通過，並報經內政部 85 年 3 月 14 日台(85)內社字第 8507009 號函准予備查。

病 例 摘 要

Case 264： 羅東博愛醫院病理科 LP07-315A or LP07-315B

A 80-year-old woman visited our OPD for the problem of protruding neck mass. There is a bulging out reddish mass at anterior aspect of neck with fragile looking, sized about 2.0 cm in diameter. It was found that the tumor enlarged rapidly in recent weeks. Neck CT scan was arranged and It shows a solid cutaneous mass at ant neck, sized about 1.5 X 1.9 cm. No cervical lymphadenopathy was found. Wide total excision was done smoothly. Clinically, there is no lung or liver metastasis noted.

Case 265： 國立台灣大學獸醫學研究所 T5

Five pigs from a conventional farm located in Chiayi were euthanized for sampling. These pigs were observed to have loss of appetite, progressive wasting and worsening respiratory distress. The clinician performed the necropsy and submitted lung samples for pathological examination.

Case 266： 財團法人天主教耕莘醫院病理科 260426

A 72-year-old woman complained of intermittent poor appetite, upper abdominal pain and insomnia for 1 to 2 weeks. She also noted tea color urine. Her eyeballs and skin have turned to yellow recently. Body weight has lost about 15 Kg (110to 95 kg) within 2 months. CT showed a hilar mass of liver with proximal CBD and bilateral distal IHDs compression. Exp. laparotomy was performed. A 115 gm brownish gray and friable tissue with necrosis was removed from omentum.

Case 267： 國立屏東科技大學獸醫學系 AR04-034-05a

Soft turtles, less than one year old. There were lack of apparent clinical signs, but the turtles have been frequently captured due to long- time staying on the feeding boards.

Case 268： 花蓮慈濟醫院病理檢驗科 S2007-0872A5

A 67 year old female patient, admitted due to bilateral renal stones, was found to have a tumor at the pelvis of right kidney during ureteroscopic examination. CT scan showed a hypodense lesion at the lower pole of right kidney with enlarged para-aortic lymph nodes. Needle biopsy proved malignancy. She received radical

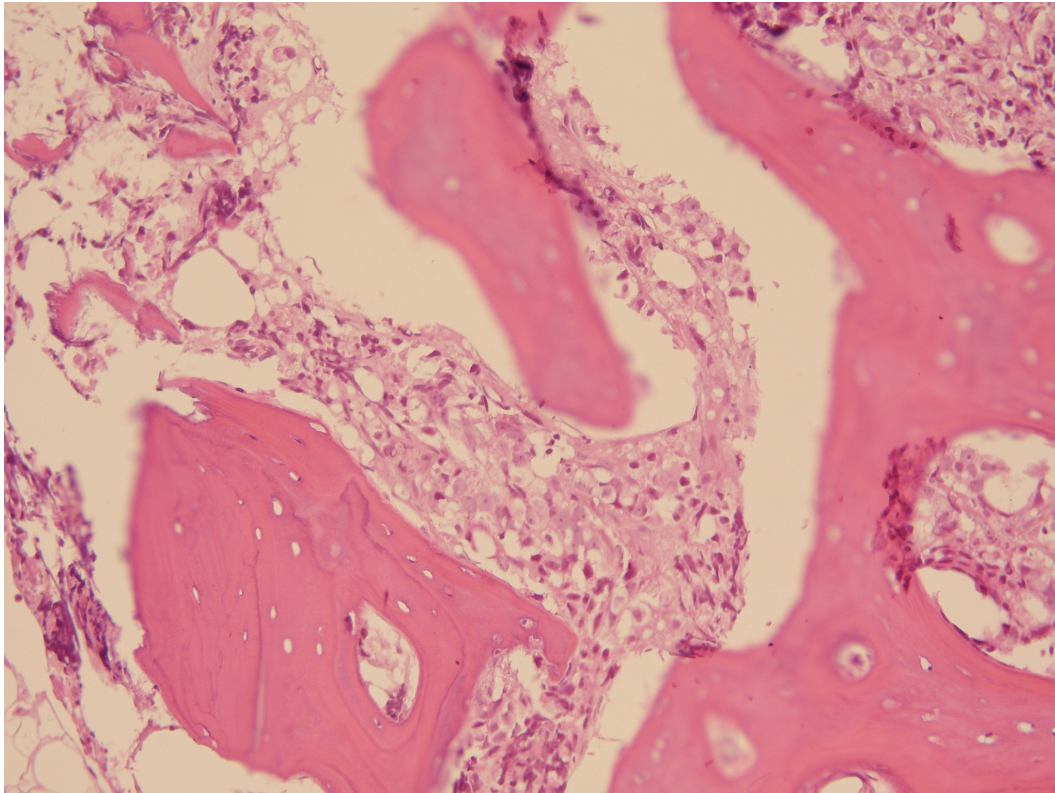
nephrectomy to remove the right kidney and para-aortic lymph nodes dissection. The microscopic slide submitted was taken from the kidney.

Case 269：國立中興大學獸醫病理學研究所 CS05-1123D

A 10-year-old, mixed breed, female dog had a greasy tumor on the abdominal area. She was nulliparous and unspayed; the date of her last estrus was unknown. The tumor was found one year previously by the owner. It grew gradually and developed some superficial ulcers in the last several weeks prior to registration at our teaching hospital. This ulcerated mass measured 5.2 x 4.8 x 3.7 cubic centimeter and was located in the left fifth mammary gland and inguinal area. There was another 2 x 1.8 x 1.5 cubic centimeter tumor just cranially to the mass mentioned above. The regional (inguinal) lymph node was moderately enlarged. Radiographically, lateral and ventro-dorsal views of thorax and abdomen showed no significant disorder. Modified radical mastectomy (regional mastectomy) was performed to remove the left 4th and 5th mammary glands completely, including the adjacent lymph nodes. During the operation, the surgeon found tumor invasion into the fascia muscularis; consequently, the excised specimen was submitted for pathologic examination. No chemotherapy was conducted after surgical removal of mammary tumors. The prognosis was guarded carefully. Two months later, the tumor was recurrent with metastasis to the iliac lymph node. She died 3 months post-operation.

Case 270：財團法人天主教耕莘醫院 (One microphotograph is attached)

A 65-year-old man was admitted to the hospital because of severe lower back pain for one week. The pain was not relieved when resting or after taking some analgesics. He felt weakness over bilateral lower legs and difficulty in walking. He had history of acute gouty arthritis and fracture of right distal radius one year ago, upper GI bleeding and anal fistula one year ago, coronary artery disease for one year and under regular medication control. No history of trauma, dysuria, frequency or urgency in urination, diarrhea or constipation recently. Physical examination showed numbness over both legs but with normal circulation of both legs. Straight leg raising test of bilateral legs were 0 degree (normal 80-90 degrees). Bilateral big toe tests of dorsiflexion and plantar flexion were severe decreased. X-ray showed lumbar spondylosis with multiple osteophytes formation over T12-S1. CT showed sclerotic change over the lower L-spine and bilateral iliac bones. MRI showed infiltrative processes over the thoracic & lumbosacral spine, paraaortic & iliac lymphadenopathy, and spinal stenosis T12-S1. Decompression operation with biopsy was performed. One microphotograph is attached.



Case 271：國立台灣大學獸醫學研究所 NTU2006-678C

An 8-year-old mixed dog had a firm mass at right axillary region noted for several years, which grew rapidly this year. The muscle under the mass was involved, lumpectomy surgery was intervened and tissue was submitted for histopathological evaluation.

Case 272：羅東聖母醫院 病理科 6232-B2

An 84 year old female suffered from cough with thick sputum recently with aggravated shortness of breath (SOB) for 2 days. Past history revealed pleurisy for 2 years Anti-tuberculosis was tried with improvement of condition. Serial X-ray and CT scans examination suggested bronchiectasis or cavitary lesions. Sputum cytology, bronchoscopic brushing and biopsy were performed. Finally, wedge resection of left upper lobe was performed on Dec 12, 2006. The specimens AB were sent for pathologic wxamination. The immunohistochemistry surveys were performed. (SW10606232 A: 2.4 x 1.3 x 1.1 cm., B: 3.2 x 1.8 x 1.4 cm.)

專題演講

Imprint cytology --- A valuable diagnostic method for fresh specimens

施 洽 雯

羅東博愛醫院病理科

Imprint cytology is a rapid diagnostic technique based upon the analysis of surface cytology of a tissue specimen. For its advantages such as simplicity, low cost, rapidity, preventing frozen artifacts in tissue, imprint cytology is used to be an initial steps in intraoperative consultation in some departments of pathology.

A total of 621 surgical specimens were submitted intraoperatively for rapid tissue diagnosis in the Department of Pathology of Lotung Pohai Hospital between January 2003 and December 2005. We report our experience with imprint cytology and investigate the value of intraoperative imprint cytology.

The average time for preparing the slides of imprint cytology was 5-6 minutes. The average time for preparing the slides of frozen section was 10-15 minutes. 92% of slides of imprint cytology are satisfactory for diagnosis. 87% of the specimens can be diagnosed within 10 minutes by the imprint technique.

The intraoperative imprint cytology is found to be particularly valuable in the following situations:

1. To confirm the gross impression of metastasis.
2. To confirm the pathologist's gross impression.
3. To determine the margin status of cancer.
4. In the diagnosis of malignancy when the submitted specimen is limited in quantity.
5. When multiple specimens are submitted within a short period of time.

Imprint cytology is an accurate, simple, fast and relatively inexpensive method of intraoperative diagnosis. We recommended that intraoperative imprint cytology should be practised in the pathologic laboratory.

Imprint cytology—
A valuable diagnostic method
for fresh specimens

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病 理 科

The frozen section is accepted as a reliable
method in intraoperative diagnosis for fresh
specimens.



The use of frozen sections for intraoperative
tissue diagnosis is a well-accepted
procedure (Ackerman and Ramirez, 1959)



Lauren V. Ackerman, MD

Imprints of fresh specimen is a rapid
diagnostic technique. The technique was
favorably reported by Dudgeon and Patrick
(1927).

Bamforth and Osborn (1958);
Pickren and Burke, 1963; Tribe, 1965;
Godwin, 1968; Silverberg, 1975;
Suen et al., 1976; Godwin, 1976.

Introduction:

The imprint cytology is an intraoperative
diagnostic method, and because of its
advantages such as simplicity, low cost,
rapidity, preventing frozen artifacts in tissue, it
is considered as initial steps in intraoperative
consultation in some centers.



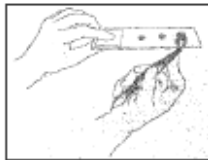
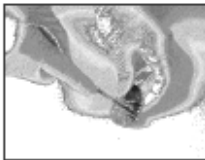
Introduction:

Imprint cytology is a rapid diagnostic
technique based upon the analysis of
surface cytology of a surgical specimen.



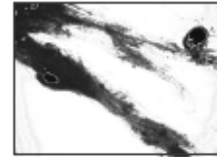
Imprints (touch preparations)

1. Direct imprints of the cut surface of the tissue or by cutting a block of tissue measure approximately 10 x 10 x 3 mm.
2. Hold the tissue gently with forceps with the fresh cut, flat surface upward.



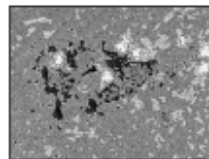
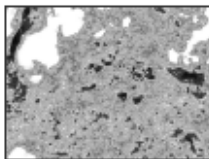
3. With the other hand, lightly touch an glass slide repeatedly in serial adjacent areas with the cut surface of the tissue.

* Just contact - do not compress, which will distort the shape of the cells.



4. If the surface touched is excessively bloody or wet, discard the slide and repeat with another slide until the touch preparations are barely opaque.

5. Prepare an average of four slides.



6. As each slide is prepared

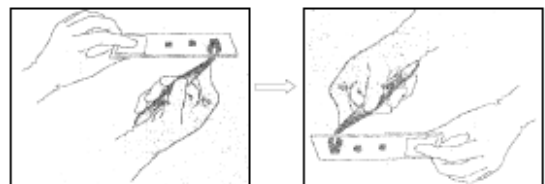
- a): Dry it rapidly by waving it in the air.

* Do not heat or blow on the slide. It should take no more than 30 to 60 seconds for the slide to dry. If it takes more; it means that the touches are too wet and that the resulting imprints will be unsatisfactory.



6. As each slide is prepared

- b): The imprint slides are immediately fixed in 95% ethyl alcohol for 5-6 seconds.



Materials :

A total of 621 surgical specimens were submitted intraoperatively for rapid tissue diagnosis in the Department of Pathology of Lotung Pohai Hospital between January 2003 and December 2005.

Methods:

1. Direct imprints of the cut surface of the tissue and several touches were made on a glass slide. Usually four to six slides were prepared.
2. Slides were immediately fixed with 95% alcohol, and then two slides were stained with hematoxylin-eosin (H&E) and two slides with standard Papanicolaou (PAP) methods.

Methods:

3. The tissues that had been used for imprint cytology were subjected to frozen section.
4. All tissues that had been used for frozen sections and imprint cytology were placed into 10% formalin, and subjected to a routine paraffin section.

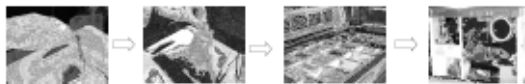
Procedure of Hematoxylin & Eosin stain for intraoperative imprint cytology

• 1. Wash	2 sec.
• 2. Hematoxylin	40 sec.
• 3. Wash	1 min.
• 4. Eosin	10 sec.
• 5. 70% alcohol	10 sec.
• 6. 80% alcohol	10 sec.
• 7. 100% alcohol	10 sec.
• 8. 100% alcohol	20 sec.
• 9. Xylene	50 sec.

3 min. 32 sec.	

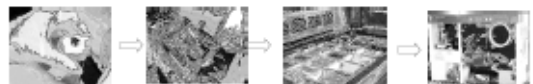
Results:

1. The average time for preparing the slides of imprint cytology was 5-6 minutes.



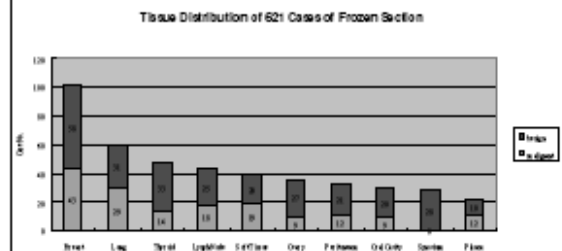
Results:

2. The average time for preparing the slides of frozen section was 10-15 minutes.



Results:

3. 92% of touch-preparation slides are satisfactory for diagnosis.
4. 87% of the specimens can be diagnosed within 10 minutes by the imprint technique.



- The specimens for frozen section included a wide range of organs with breast, lung, thyroid and lymph node presenting the most commonly four tissues.

Breast : 101 (16.26%)
 Lung : 60 (9.69%)
 Thyroid : 47 (7.57%)
 Lymph node : 43 (6.92%)

- 621 cases of frozen section

For tumor diagnosis: Benign or malignant
 528 cases.

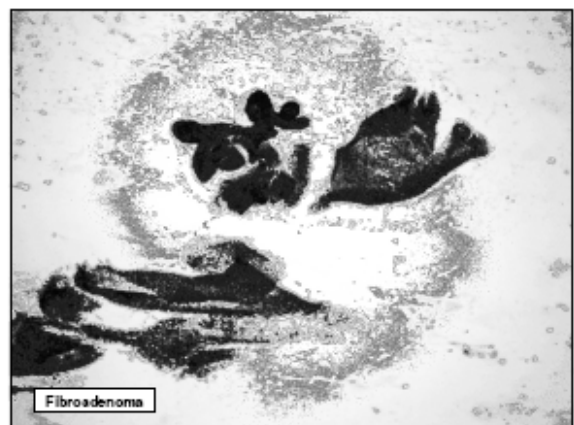
For surgical margin: 57 cases.

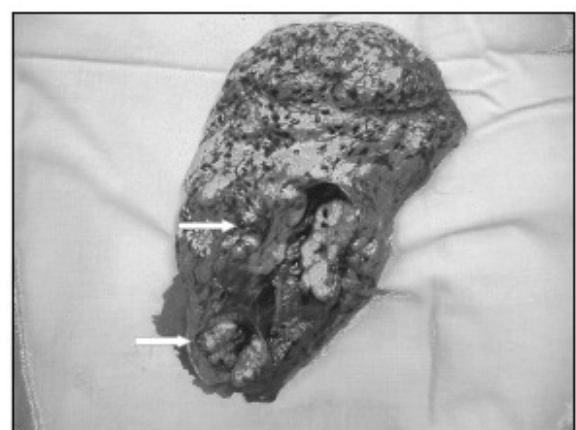
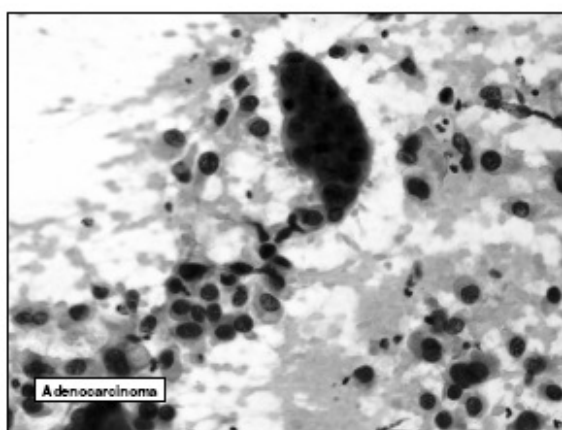
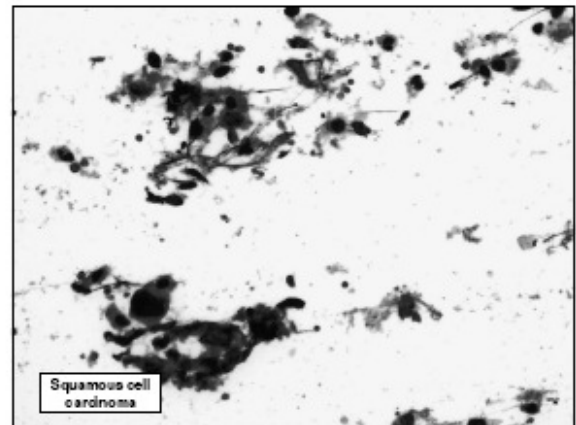
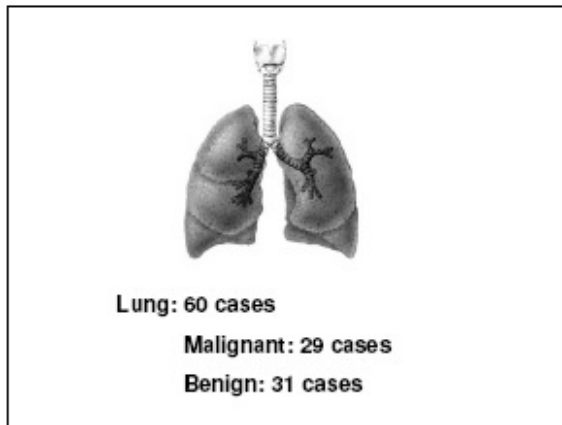
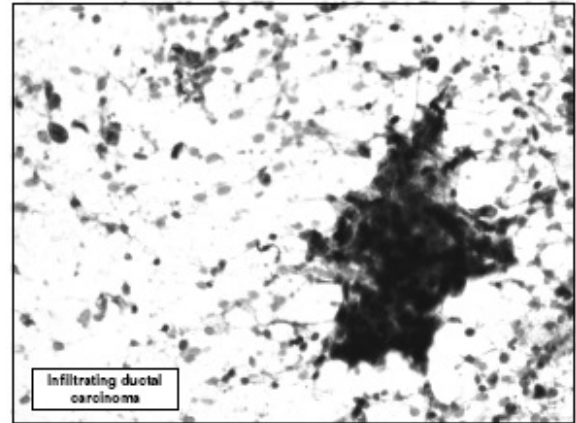
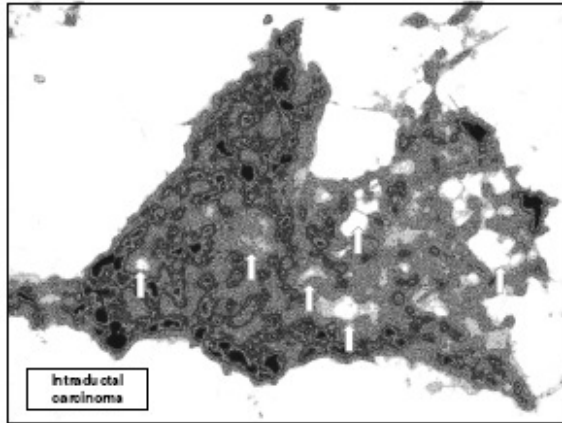
For neutrophil count: 23 cases.

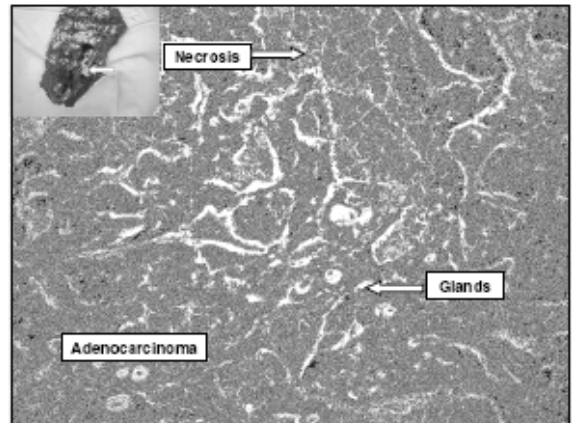
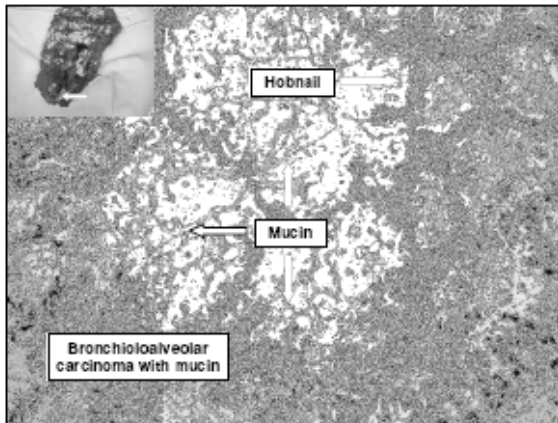
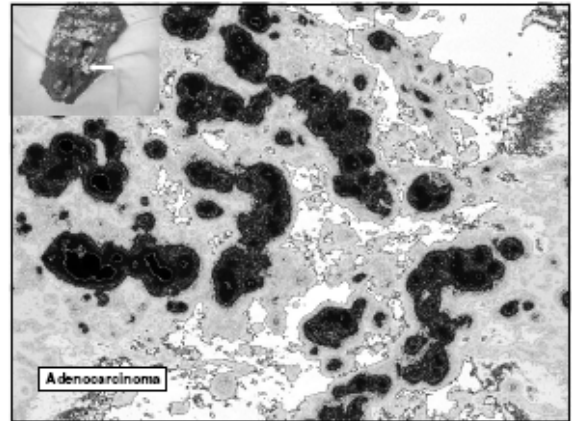
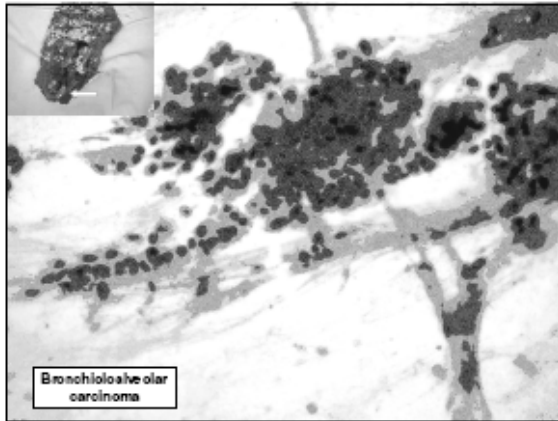
For tissue confirm: 13 cases.



Breast: 101 cases
 Malignant: 43 cases
 Benign: 58 cases







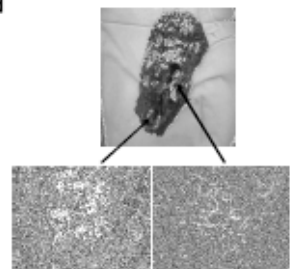
- Diagnosis: Synchronous Primary Carcinomas of Lung

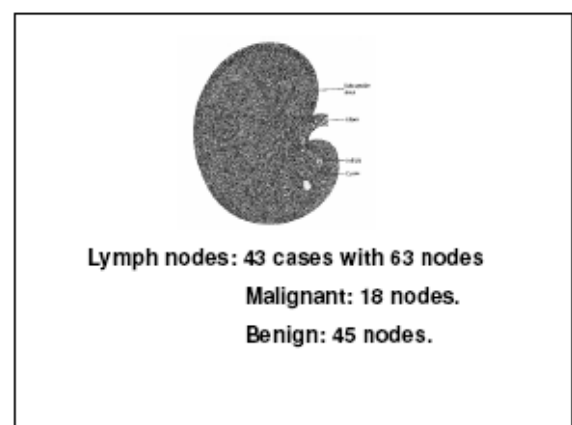
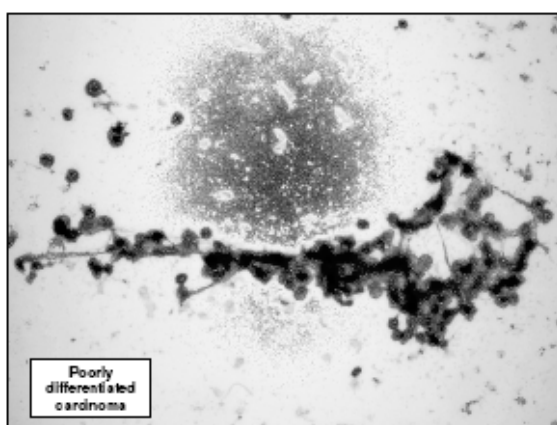
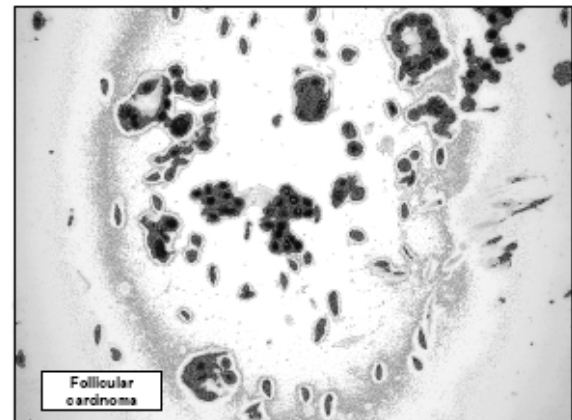
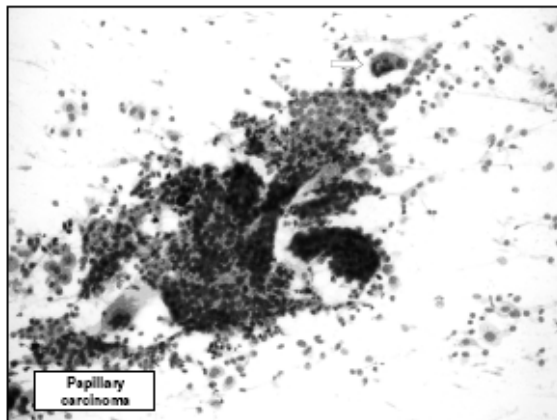
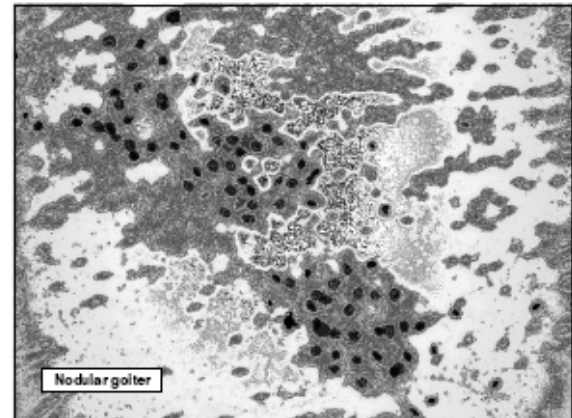
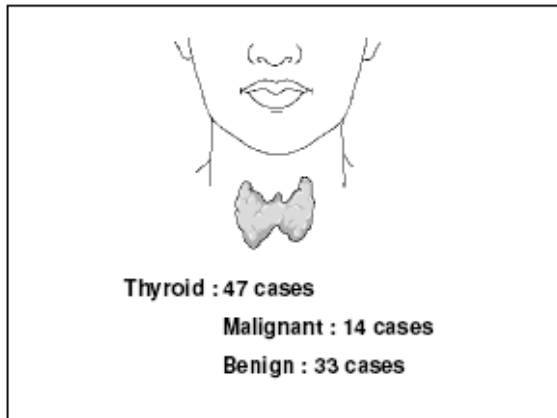
Synchronous Primary Carcinomas of Lung

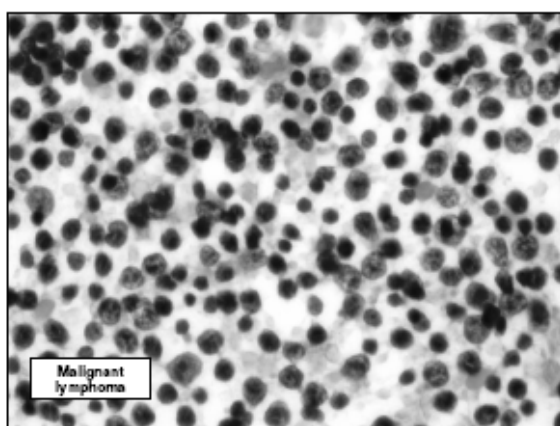
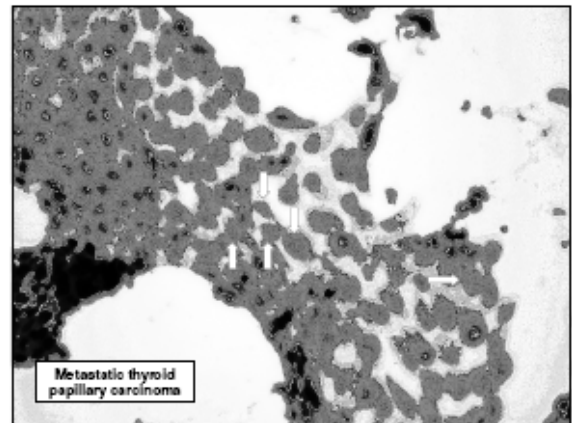
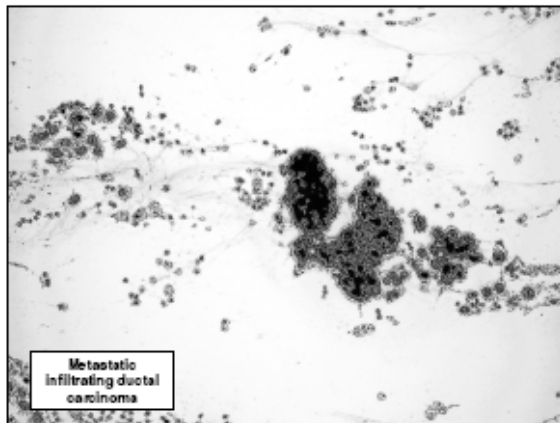
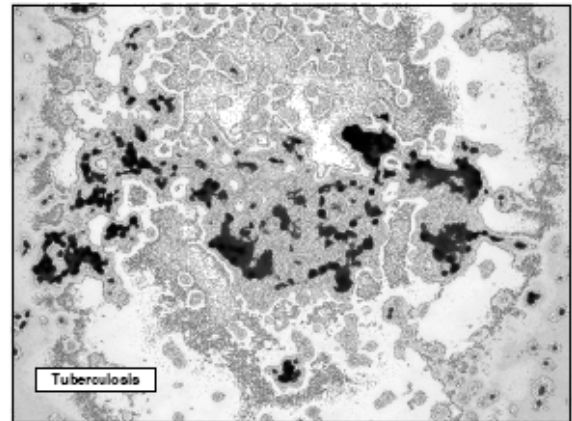
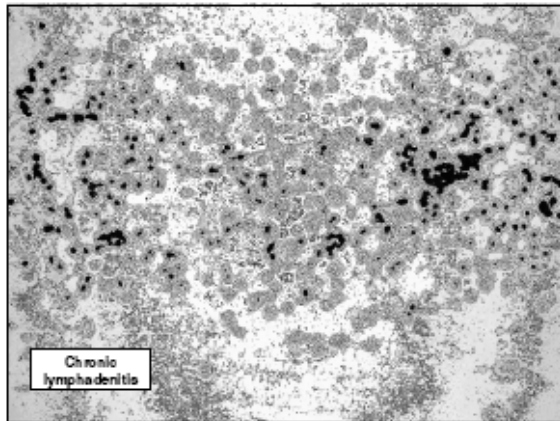
A. Tumors distinct and separate.

B. Histology

1. Different
2. Same, but in different segment, lobe or lung



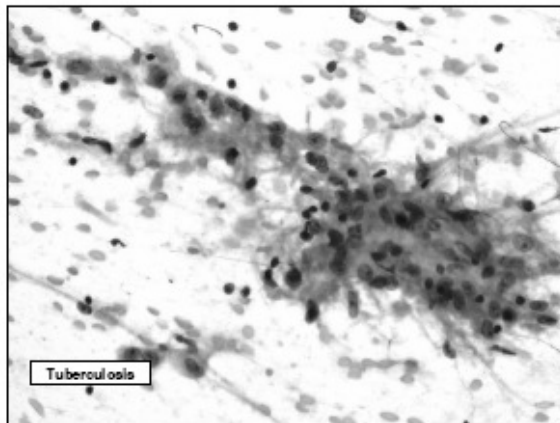
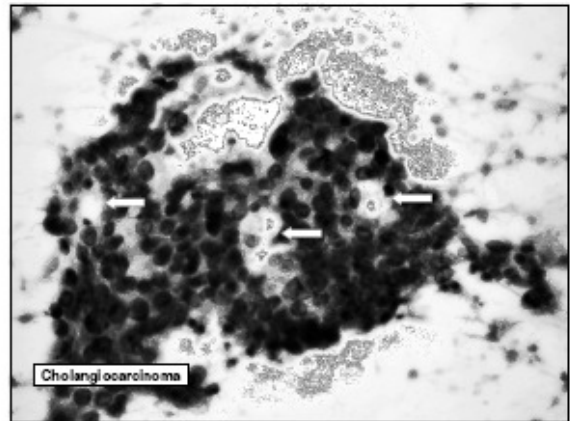
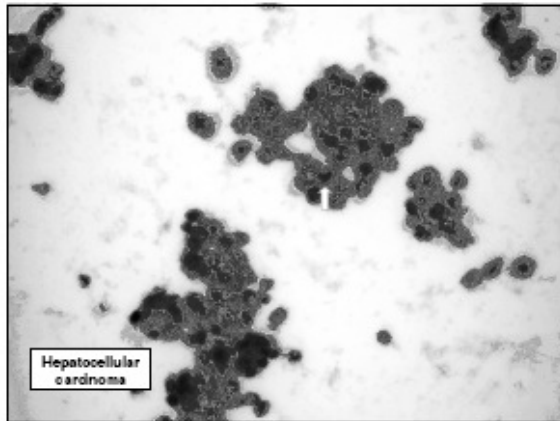




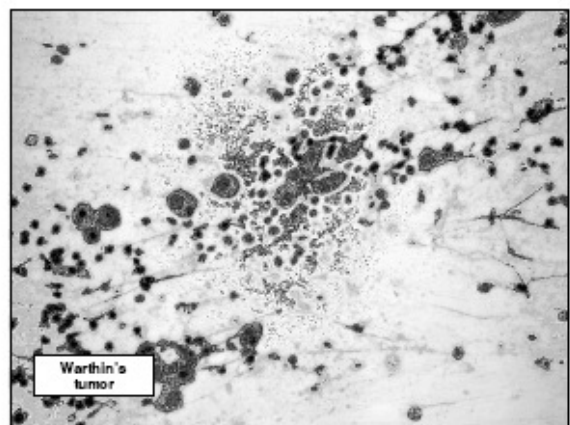
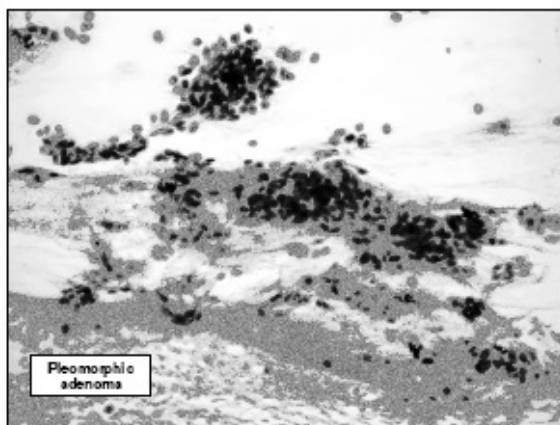
Rib cage

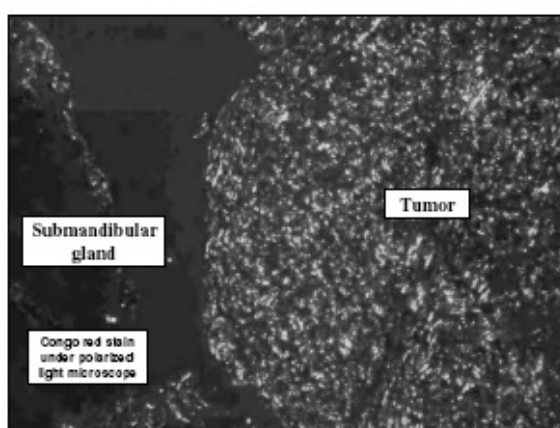
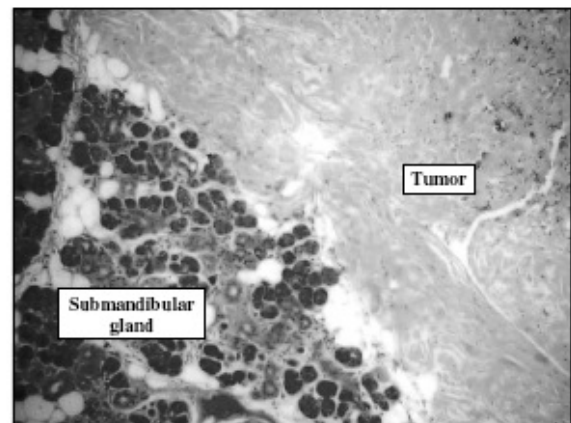
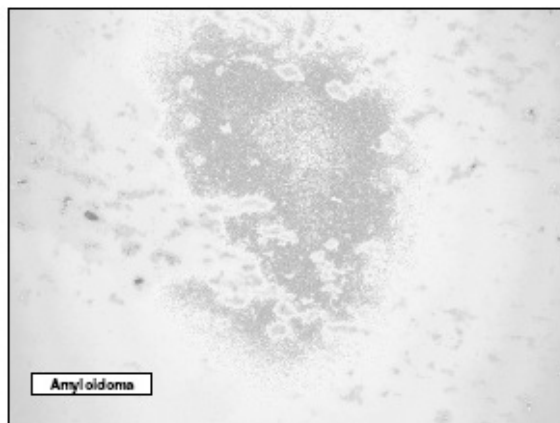
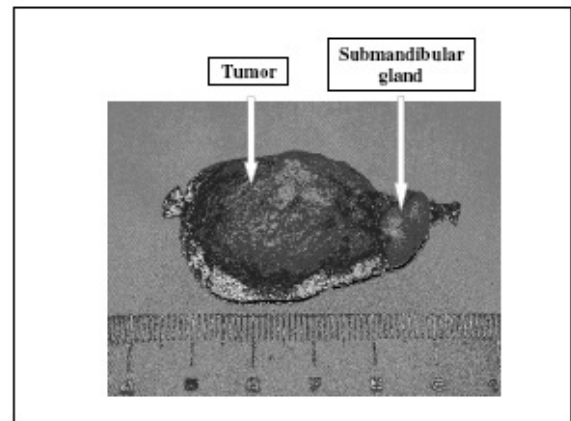
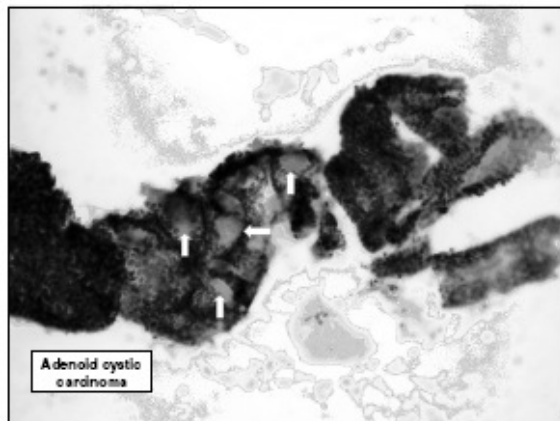
Liver

Liver: 14 cases
Benign : 6 cases
Malignant: 8 cases



Salivary gland: 11 cases
 Malignant: 2 cases
 Benign: 9 cases





Conclusion: (1)

The imprint technique was found to be particularly valuable in the following situations:

1. To confirm the gross impression of metastasis.
2. To confirm the pathologist's gross impression.
3. To determine the margin status of cancer.

Conclusion: (2)

4. In the diagnosis of malignancy when the submitted specimen is limited in quantity.
5. When multiple specimens are submitted within a short period of time.

Conclusion: (3)

Imprints should always be interpreted in the light of gross findings; a negative diagnosis should be disregarded if the gross appearance of the lesion suggests malignancy.

Conclusion: (4)

False-negative reports are generally due to one of the following two reasons:

(a) Interpretative errors:

These occur in cytologically well-differentiated tumors. The morphological changes of the neoplastic cells in these tumors are often subtle.

Conclusion: (5)

(b) Insufficient cells:

There is a dense fibrous stroma in some tumors. In these cases the number of neoplastic cells transferred to the slide is insufficient to enable the observer to make a correct diagnosis.

Conclusion: (6)

- Touch imprint cytology is an accurate, simple, fast and relatively inexpensive method of intraoperative diagnosis.
- We recommended that intraoperative imprint cytology should be practised in the pathologic laboratory.

Electron Microscopy for Emerging Disease Diagnosis

San Duo Chen

陳 三 多

National Chung Hsing University

EM Outlook EMERGING INFECTIOUS DISEASES

A Peer-Reviewed Journal Tracking and Analyzing Emerging Issues

Vol. 1, No. 1, Jan 2002



Emerg Infect Dis 2003 Mar

Electron Microscopy for Rapid Diagnosis of Infectious Agents in Emergent Situations

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*University of Manitoba, Canada

†Robert Koch-Institut, Germany

Bioterrorism attack

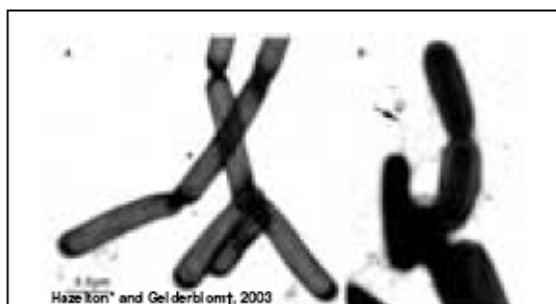
In late September 2001

a letter containing spores of *Bacillus anthracis* resulted in the death of one employee from inhalation anthrax.

Over the next 6 weeks,

similar letters were delivered to television news centers in New York City and government offices

Ultimately >32,000 suspected exposures and five deaths were recorded in the United States.



Bacillus anthracis was inactivated, and negatively stained with uranyl acetate which do not have flagella. Contrastly the *B. subtilis* shows distinct flagella.

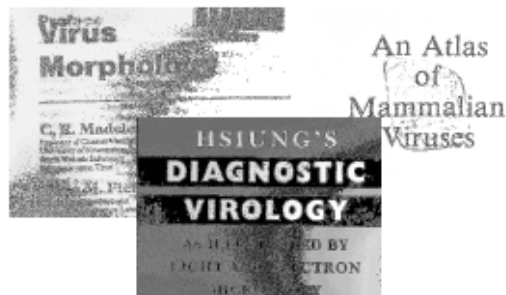
Role of Electron Microscopy in Virus Identification

1938 first EM micrograph of poxvirus

1941 immunologic procedures were first used in EM studies of tobacco mosaic virus

1940 EM was successfully in the differential diagnosis of smallpox and chickenpox

Currently, **>30,000 viruses** comprising 56 separate families have been identified



1950s negative staining and the wider availability of EM, electron microscopy became essential in characterizing many new isolates detected in diagnostic cell cultures and clinical samples, e.g., stool, urine, and biopsied specimens

Electron microscopic diagnosis is **“uniquely”** suited for **rapid** identification of infectious agents

A specimen can be ready for examination and identify by EM **within 10 minutes** of arrival in the EM laboratory

The **“open view”** of EM testing allows rapid detection of viruses and other agents if sufficiently high particle concentrations exist

Because of this capability, EM testing can be a frontline method, applied to samples from a suspected lesion, body fluids, or biopsies samples.

Specimen Collection

Syringe collection
collection into the barrel of a 26-gauge needle attached to a tuberculin syringe.
Directly touch
coated grids may be lightly touched directly to the vesicle fluid, lesion base
Tissue for thin section
Samples in buffer without fixatives should be stored at 4°C

Thin and ultrathin section

Gross lesion
↓
Examine by histological pathology
↓
Select the lesion area for thin section
↓
Ultrathin section

Causes of insufficient sampling

1. The collection of lesion exudates with swab samples and placed in transport medium
2. Failure to collect an adequate volume of sample.
At least 1 g of fecal material.
A minimum of 5.0 ml of blood.
less than 1 mm³ each block

Infectious agents **inactivation**

Most infectious agents may be inactivated in formaldehyde or glutaraldehyde.

Samples mounted on the grid may be inactivated by fixative, or ultraviolet irradiation

The syringe with infectious materials should be placed in a rigid sterile container, sealed with Parafilm

Grid for negative-stain

1. 400-mesh grid coated with Formvar film
2. Carbon-coated films have higher thermal stability. However, they may be more hydrophobic than plain films.
3. Glow discharge the films to improve hydrophilicity, particle adherence, and distribution of both sample and stain.

Negative-stain method

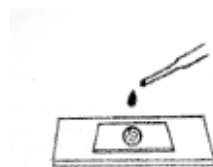
1. Suspension cleared by low-speed centrifugation (1,000 x g for 5 min).
2. Grid is floated with the coated surface on a drop of UA or PTA
3. Rinse the grid with Distilled H₂O



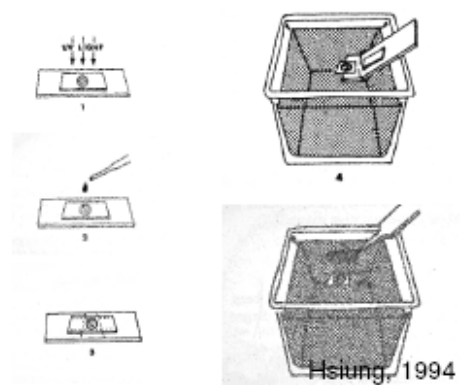
STEP 2

Pseudoreplica method

1. drops of sample are placed on the solidified agar
2. Grid are placed over the drops on agar
3. Viral particles adsorb to the grid as diluent volume is reduced.



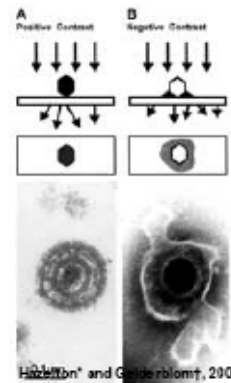
Hsiung, 1994



Negative Staining Solution

1. 1% aqueous uranyl acetate, pH 2-4.5
2. 1% phosphotungstic acid, pH 7.0
3. Staining solution should be relatively fresh and stored in brown glass bottles at 4°C
4. Grids must be protected from dust

Comparison of herpesvirus after positive and negative stain



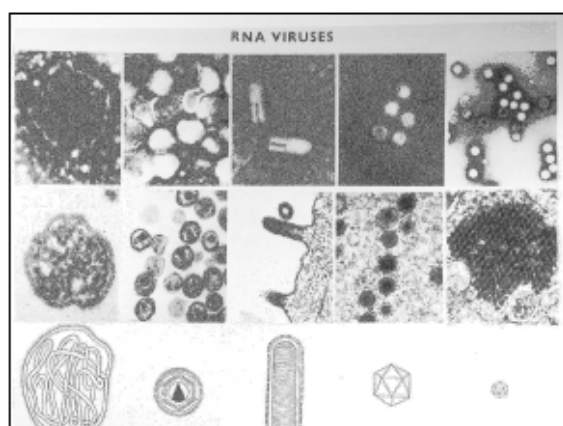
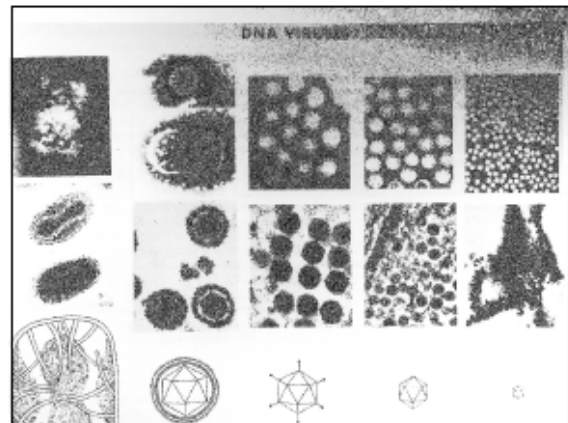
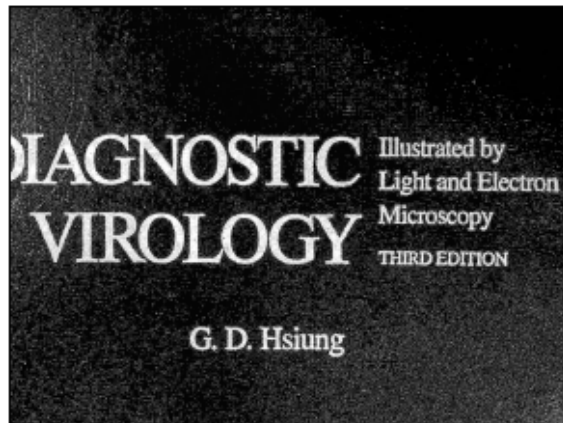
A. Positive staining

Samples undergo a process of fixation, osmium, dehydration, embedment, ultrathin sectioning, and staining

B. Negative staining

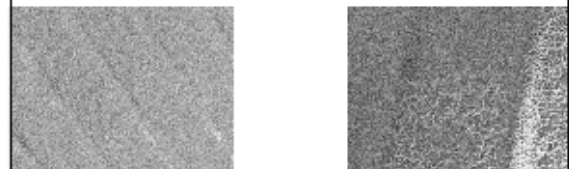
After a brief fixation, samples are mounted on grids and stained with phosphotungstic acid

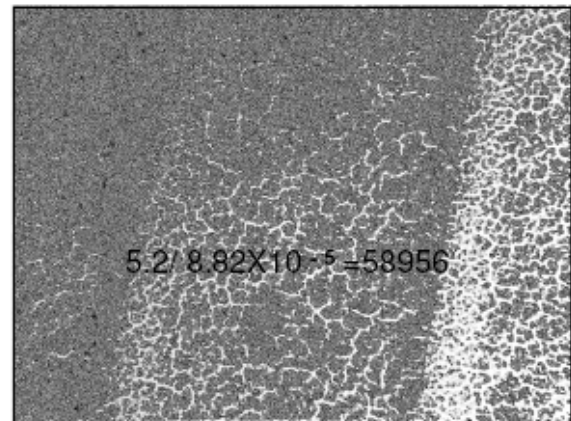
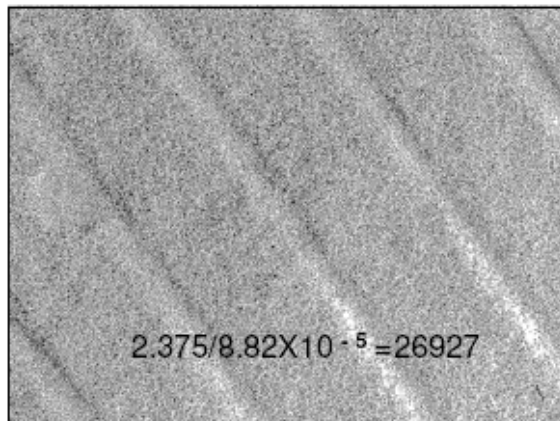
Hall and G. and G. and G., 2003



Measure the size of viral particles precisely

Grating replica
28800 line per inch
 8.82×10^{-5} cm





Immunoelectron microscopy

Immunoabsorption

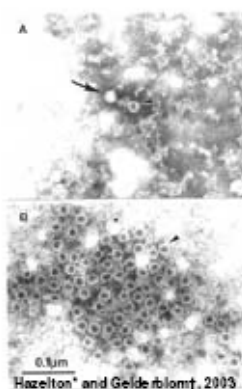
- Grid is floated on a drop of antiserum for 10 min
- Washed on 6 drops PBS
- Floated on the specimen for 30–60 min at 37°C.
- Washed on 6 drops of PBS
- negative stained, and examined.

Immunoaggregation

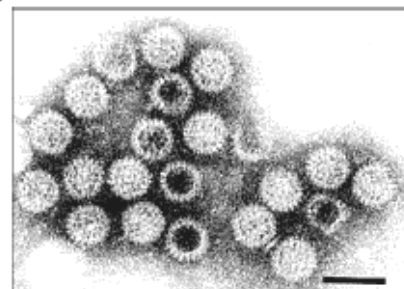
1. Specific antibody is added to sample to form the antigen:antibody complexes
2. Centrifuge and drops of sample are placed on grid
3. Or drops of sample are placed on the solidified agar – pseudoreplica method
4. Grid are placed over the drops on agar
5. Antigen:antibody complexes adsorb to the grid as diluent volume is reduced.

A. Human parvovirus with erythema infectiosum

B. Immunoelectron microscopic. The serum mixed with matched serum (1:100), incubated for 90 min, and virions/immune complexes centrifuged directly to grid



Rotavirus visualized by immune electron microscopy in stool from child with acute gastroenteritis.



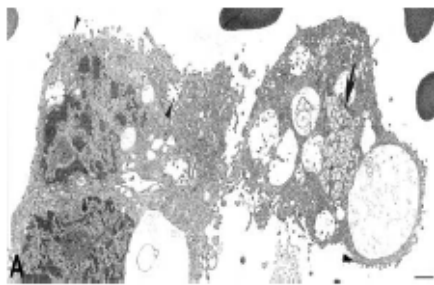
Specific Antibodies for Immunoelectron Microscopy

Appropriate antibodies are available from the World Health Organization Collaborating Centers at the Centers for Disease Control and Prevention, and VECTOR, Koltsovo, Novosibirsk Region, Russia.

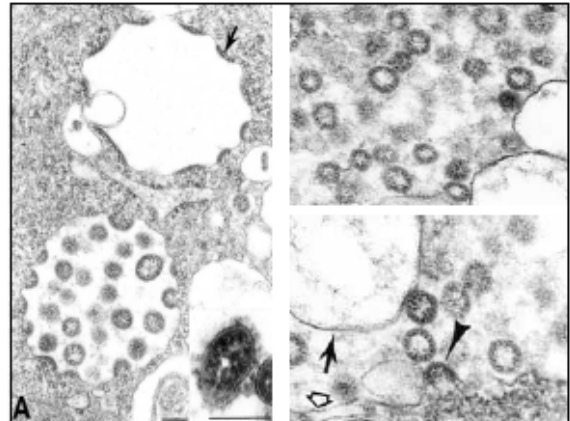
Morphology is the Truth

Find the diagnostic evidence directly on the lesion
Observe the pathogen directly in the cells of the lesion

Ultrastructural Characterization of SARS Coronavirus

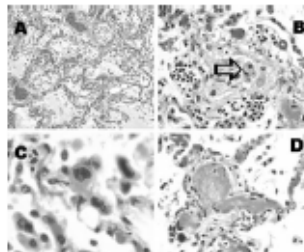


Goldsmith et al. 2004



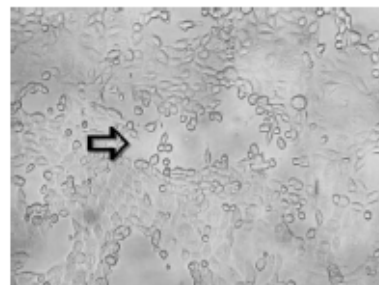
Human Metapneumovirus Detection in Patients with Severe Acute Respiratory Syndrome

Pathologic
findings of
lung
tissue
sections



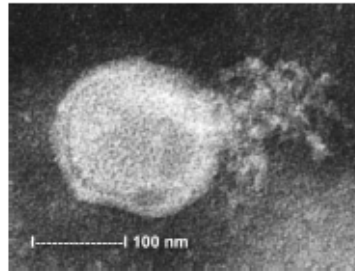
Paul K.S. Chan et al. 2002

Cytopathic effect of human metapneumovirus
in rhesus monkey kidney cell monolayers.



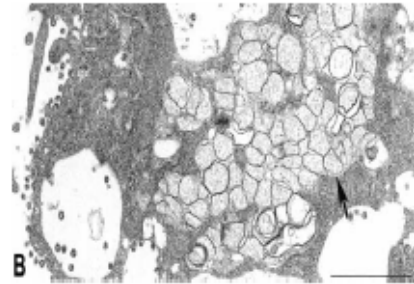
Paul K.S. Chan et al. 2002

Human Metapneumovirus in SARS



Paul K.S. Chan et al. 2002

Ultrastructural characteristics of a bronchial alveolar lavage from a patient with SARS



Goldsmith et al. 2004

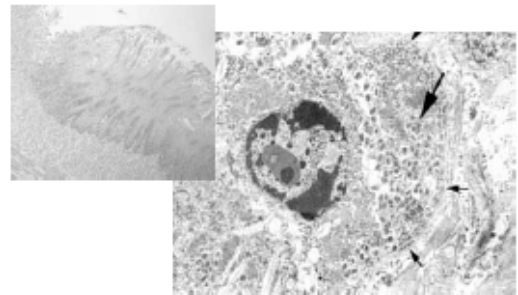
Choose the **Appropriate** Technique

EM is essential for observe the viral particles

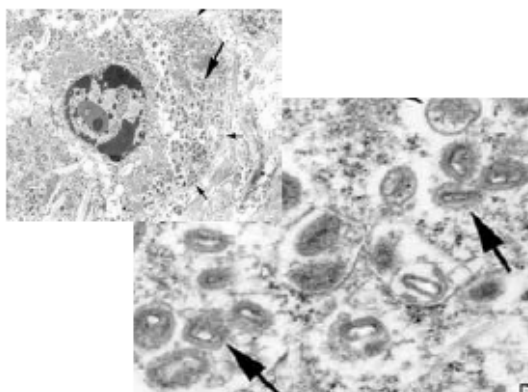
Eyes are good for watching the girl

Meter is too short, inch is too long

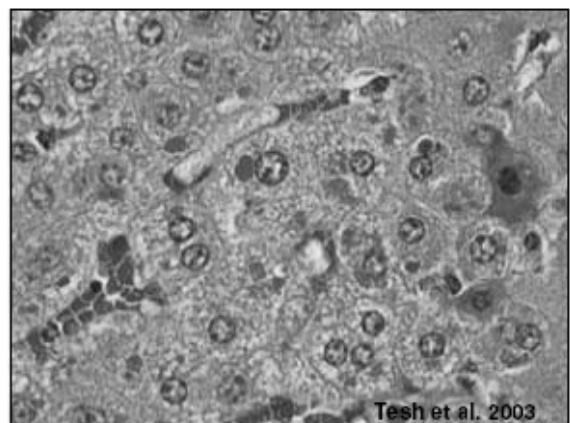
Experimental Infection of Ground Squirrels with Monkeypox Virus



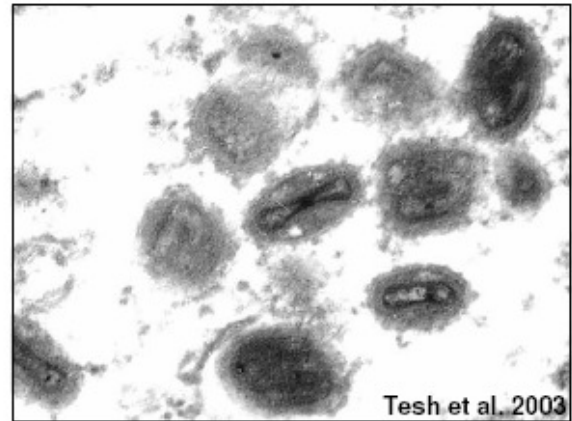
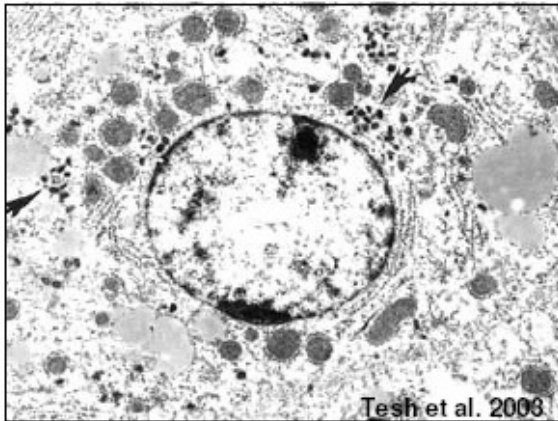
Tesh et al. 2003



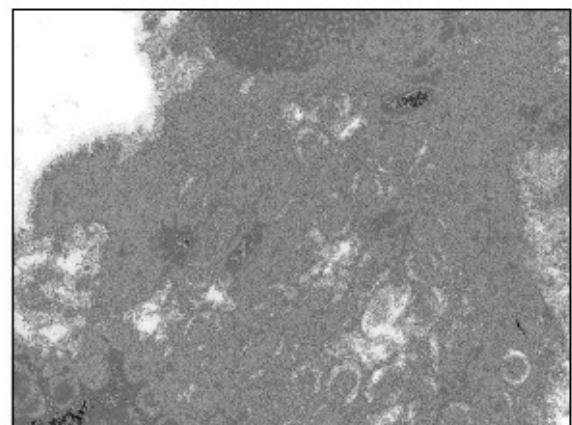
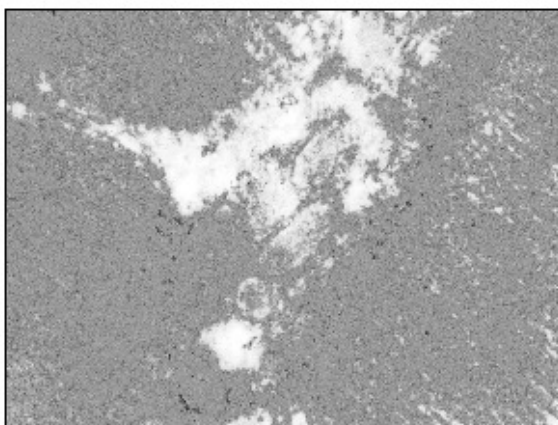
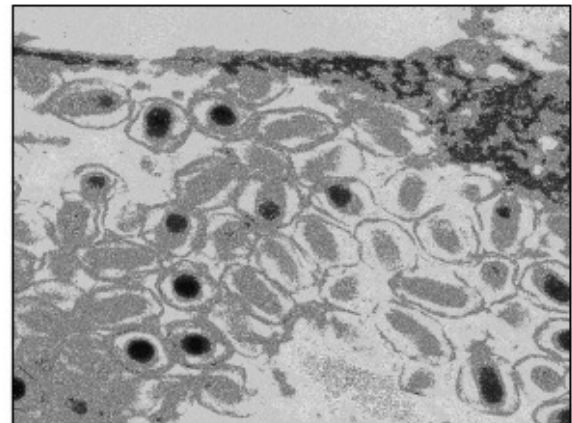
Tesh et al. 2003



Tesh et al. 2003

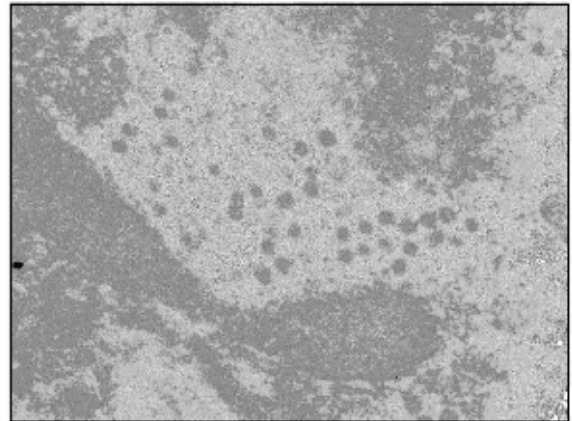


White spot syndrome virus
 Herpesvirus ?
 Baculovirus ?



Dog died with
conversion and coma

Tetanus?
Infectious canine hepatitis ?
adenovirus



Shieh et al. 2002
Definitive diagnoses are
sometimes very difficult to
establish without further
pathologic studies.

**Pathologic Studies of Fatal Cases in
Outbreak of Hand, Foot, and Mouth
Disease, Taiwan
Shieh et al. 2002**

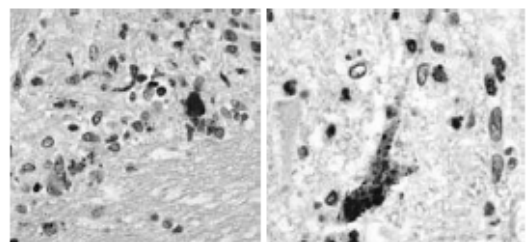
Two cases were admitted to the same
hospital with a similar clinical course.

Histopathologic features were similar
in both cases and showed severe and
extensive encephalomyelitis.

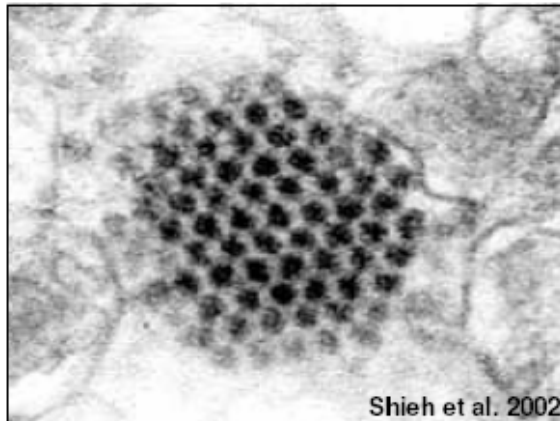
In first case, positive staining of
enteroviral antigens EV71 was
observed in neurons.

Electron microscopy evaluation
of spinal cord tissues showed a
highly vacuolated neuron
containing scattered picornavirus-
like particles and viral inclusions.

Positive immunostaining of EV71
antigens in neuron



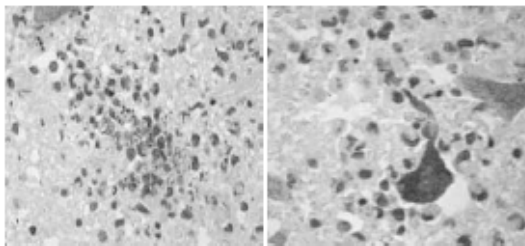
Shieh et al. 2002



The second case was negative for EV71 by IHC, in situ hybridization, polymerase chain reaction, and viral isolation.

An IHC test showed intense immunostaining of flaviviral antigens in neurons, neuronal processes, and inflammatory foci at various CNS sites.

Positive immunostaining in neuron

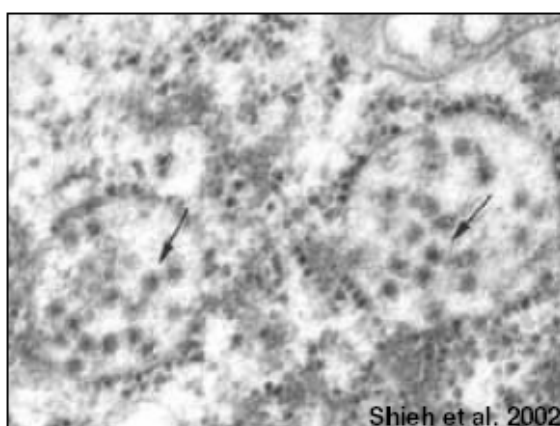


Shieh et al. 2002

Further study was conducted by injecting neurologic tissue of the patient into suckling mice.

CNS material from an inoculated mouse was passed onto Vero-E6 cells and produced cytopathic effect.

Electron microscopy examination of mouse brain and infected cell culture revealed flavivirus particles, and polymerase chain reaction with sequencing confirmed the isolate as Japanese encephalitis virus.



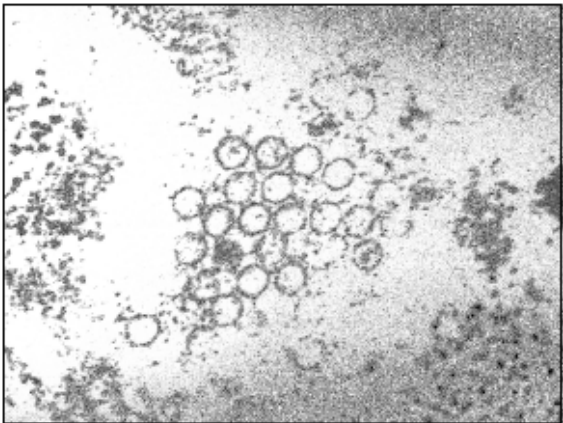
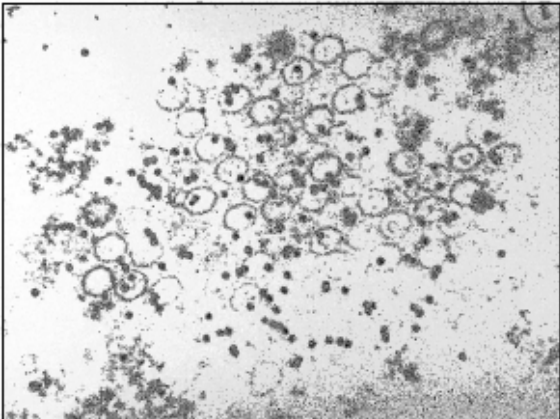
Conclusion

The neurologic disorders and clinical courses of acute viral CNS infections can be very similar regardless of causative agents

Definitive diagnoses are sometimes very difficult to establish without further pathologic studies.

How to identify the disease
pathogen by EM

Pseudorabies and
Cytomegalovirus



Comparison of viral agents associated with skin lesions. A-C show cowpox viruses indistinguishable in appearance from variola virus, the agent of smallpox

Hazleton* and Gelderblom†, 2003

Cowpox with Severe Generalized Eruption, Finland

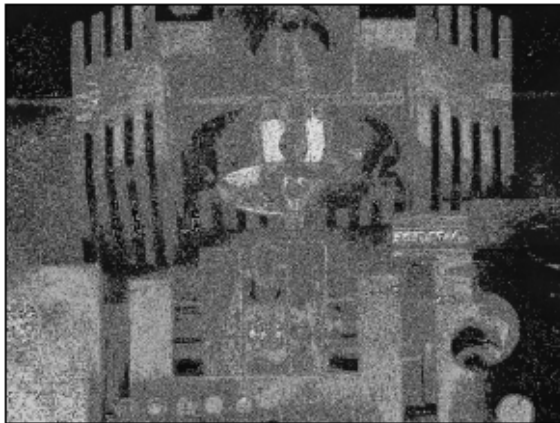
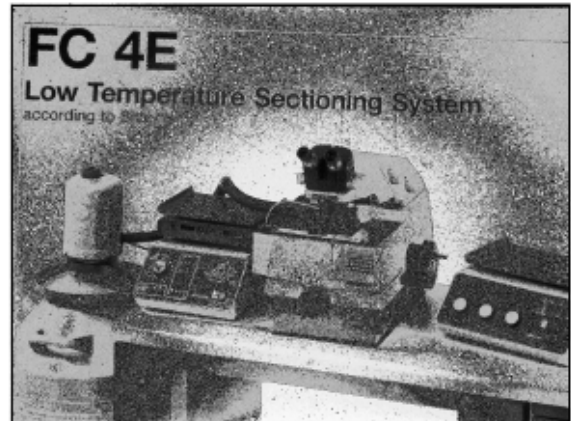
Peikonen et al. 2003

Cowpox lesions on patient's forearm on day 7



Cryoultrasectioning

Rapid diagnosis
Immunocytochemistry
Immunolabelling

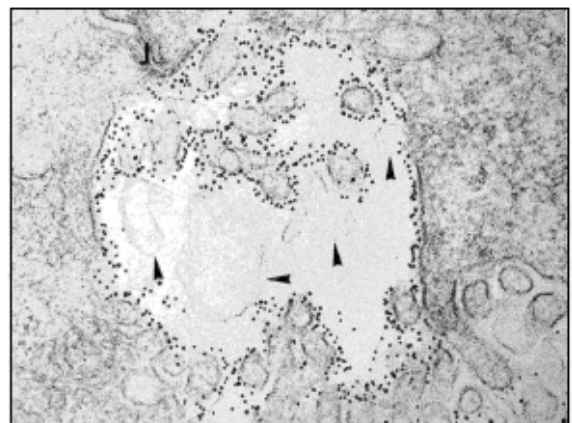
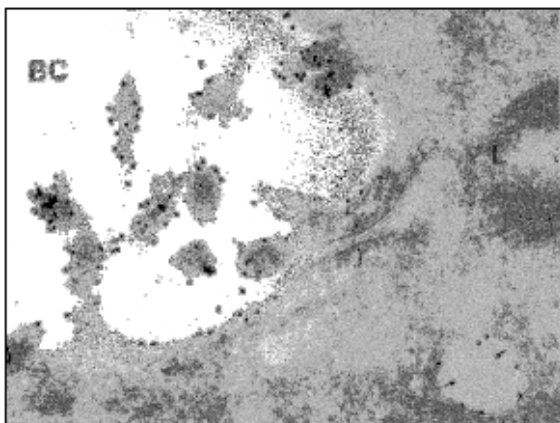


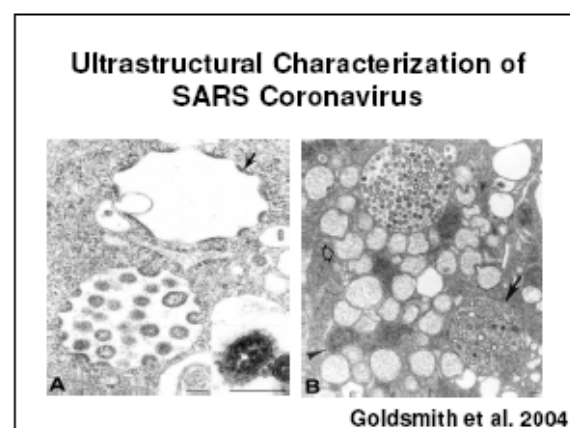
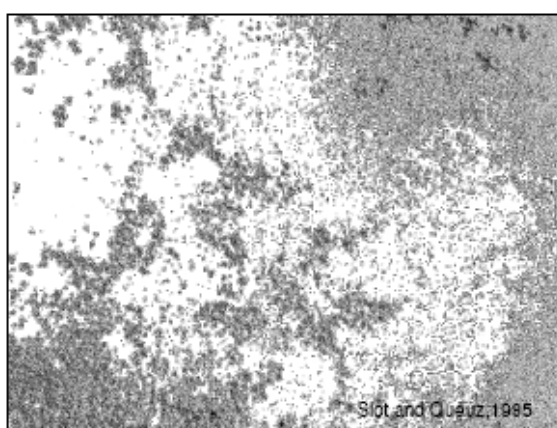
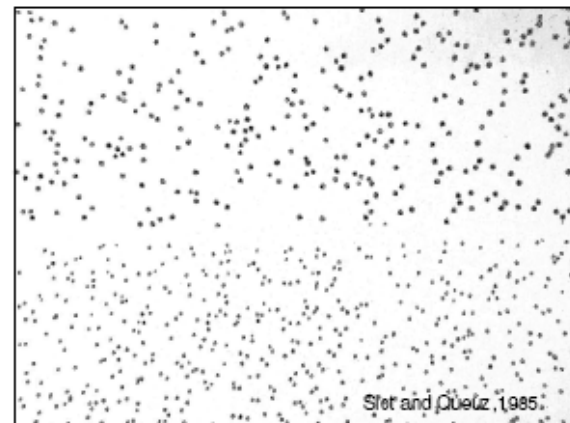
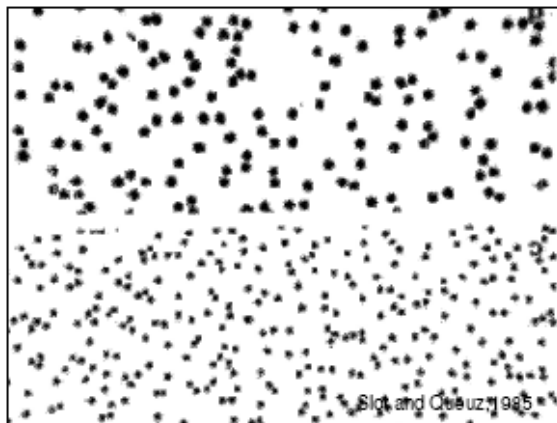
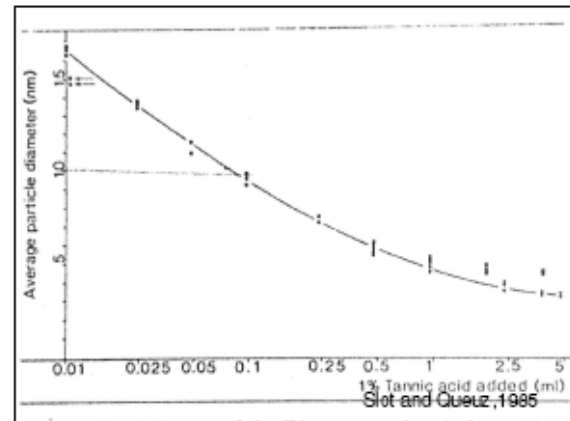
Immunolabelling

Pre-embedding method
Post-embedding method
Cryoultrasectioning

Marker

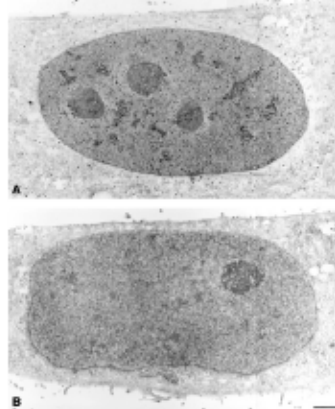
Ferritin
Peroxidase
Colloidal gold
nanogold





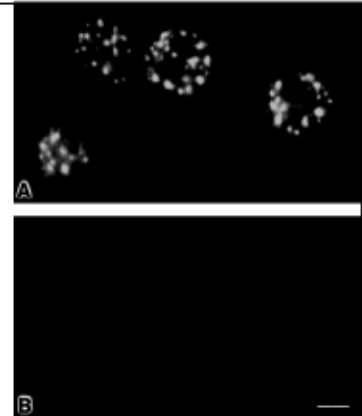
Transmission EM
of labeled HeLa
cells.

(A) Stained with
primary antibody
followed by
fluorescein and
Nanogold-labeled
anti-mouse Fab'.
(B) Control



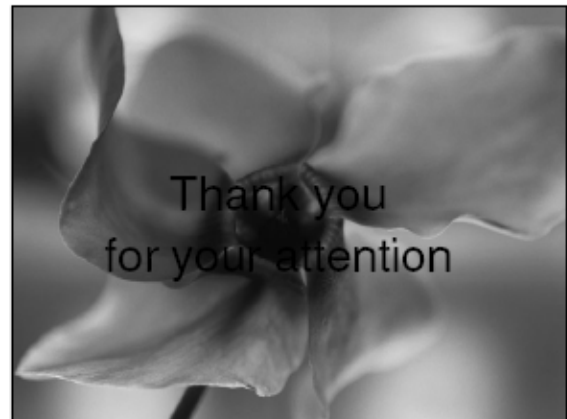
Fluorescence
micrographs of
labeled HeLa
cells.

(A) Stained with
primary antibody
followed by
fluorescein and
Nanogold-
labeled anti-
mouse Fab'.
(B) Control



Rapid, Direct evidence
Differentiation by immunogold

Electron microscopy is a
very useful technique
for emerging infectious
disease diagnosis



原位雜交及非生物素過氧化酵素 (non-biotin) horseradish peroxidase (HRP) 應用於犬瘟熱病毒感染診斷

梁鍾鼎^{1,2} 李泔泓¹ 廖秀鈴¹ 劉振軒²

1.國家實驗動物中心，國家實驗研究院

2.國立台灣大學生農學院獸醫學系

實驗動物的病毒性疾病往往呈現不顯性感染，所呈現的病理變化常為非特異性或無顯著病變，血清學抗體僅表示過去動物曾接觸此病原，不能表示最近兩週內動物的健康狀態，所以全力發展分子病理及分子病理技術應用於實驗動物病毒性疾病診斷實乃當務之急。

原位雜交 (in situ hybridization, ISH) 技術是基於核酸探針會和細胞內特異的 DNA 或 RNA 發生互補所發展出的技術，被偵測的核酸可以是細胞的內源性 DNA、mRNA、病毒核酸序列或細菌的核酸。在應用上，目前原位雜交主要的應用範圍包括藉由偵測 mRNA 進行基因表現的研究、傳染性病原的診斷 (尤其是病毒性疾病)、cell cycle 及 apoptosis 領域的研究。相較於免疫化學染色，原位雜交的優點在於探針獲得比抗體方便，尤其在新發現的病原研究，此外探針的保存時間較久，但其缺點則是操作流程繁瑣，且影響雜交敏感性的因素繁多 (Chueh et al., 1999)。

傳統的免疫化學染色方法(梁等,2000)是利用初級抗體辨認組織中的病原 (抗原)，然後再接上生物素化 (biotinylated)的二級抗體，利用卵白素 (avidin)與 4 個生物素分子的親和力，與過氧化 形成複合物，再利用呈色劑呈色。但是因為卵白素是一種糖蛋白，等電點 (pI)為 10，所以極易與切片中帶負電荷的組織或血球凝集素 (lectin) 形成非特異性鍵結，如腎臟、肝臟、中樞神經組織及肥大細胞等器官。為了避免此一內源性生物素在診斷上的干擾及誤判，所以發展非生物素性 HRP 的免疫染色方法，應用於病毒性疾病診斷。

在免疫化學染色及診斷上有一些技術的問題，因為在水溶液培養基中，分子彼此間有忌水 (hydrophobic)作用，尤其是在其分子表面張力較水分子小時，如一些中性芳香族胺基酸如苯氨基丙酸 (phenylalanine)、酪氨酸 (tyrosine)、色氨酸 (tryptophan) 等之側鏈，因為它們彼此之間會產生忌水作用，所以相對地這些胺基酸或彼此鍵結，形成複合物，影響免疫複合物形成的穩定度。

組織中的蛋白質，會經由福馬林的固定作用而增加其忌水性，因為相鄰的蛋白質會形成雙鍵。這些組織包括結締組織、鱗狀上皮、脂肪細胞等。很不幸的是大部份的血漿蛋白質或免疫球蛋白(IgG)抗體皆是忌水性，尤其是 IgG3，IgG1 分子忌水性遠大於 IgG2，IgG4。這些抗體分子在儲存時，會增加其忌水性，相對地在解凍時會影響其染色效力。抗體稀釋液的 pH 與抗體的等電點越接近時，此時抗體的忌水性越強；反之，則越弱。其它降低組織及抗體液的忌水性的物質包括 Tween 20 或是直接將抗體

稀釋液 pH 值調高。一般最常用的方法是在加入初級抗體前加入次級抗體來源血清，或是初級抗體直接用胎牛血清稀釋(1% BSA, non-fat milk, casein 等)。

大部份的多源性抗體 IgG 的等電點在 pH5.8-8.5 之間，所以在生理性 pH 值時(pH 7.0) ，抗體分子可能帶正電或負電。當組織帶負電時如內皮細胞及膠原纖維等，會與帶正電的抗體分子形成複合物，常易與組織中膠原或彈性纖維形成非特異性結合，造成誤判。內源性過氧化酶素的去除可藉由過氧化氫(H₂O₂)，這些內源性酶素出現在所有血液性蛋白質或血紅素(紅血球)、肌紅素(肌肉細胞)、細胞色素(顆粒球、單核球)、觸 (肝、腎臟)等組織。

另一個代替的方法就是使用血清鹼性磷酸酶(alkaline phosphatase) 系統取代傳統過氧化酶素染色(Liang et al., 2004)，但必須加入 5 mM levamisole 於呈色劑中破壞內源性生物素多的組織如肝、腎、淋巴組織、中樞神經組織、脂肪組織、乳腺等易產生非特異性鍵結。所以可考慮在染色前切片先以 0.01-0.1% avidin 及 0.001-0.01% biotin 處理，或是以 streptavidin 取代卵白素。因為它沒有糖，等電點僅有 5。另外在染色時要注意二級抗體是 F(ab)₂ 結構或是全部的 IgG 抗體分子，因為後者含 FcR。FcR 是一種糖蛋白分子，分子量為 50-70KD，易在冷凍組織染色呈非特異性陽性反應。組織呈死後變化易與任何抗體產生非特異性反應。

利用非生物素過氧化酶素方法(Liang et al., 2007)，可在犬瘟熱病毒感染患犬的肺臟小支氣管上皮及肺泡巨噬細胞、腎盂上皮細胞、膀胱上皮細胞、脾臟巨噬細胞、大腦皮層外錐狀細胞及樹狀突細胞質、胃腸道黏膜上皮細胞、小腦白質層星狀細胞及細胞質、皮膚海綿層細胞及細胞質等器官發現特異性 CDV 抗原。

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Comparative Pathology Case 264

Contributors: Chu-Teh Chen (陳朱德) MD; Chia-Wen Shih (施洽雯) MD, MS
Department of pathology, Lotung Poh Ai Hospital (羅東博愛醫院病理科)

Clinical history: A 80-year-old woman visited our OPD for the problem of protruding neck mass. There is a bulging out reddish mass at anterior aspect of neck with fragile looking, sized about 2.0 cm in diameter. It was found that the tumor enlarged rapidly in recent weeks. Neck CT scan was arranged and It shows a solid cutaneous mass at ant neck, sized about 1.5 X 1.9 cm. No cervical lymphadenopathy was found. Wide total excision was done smoothly. Clinically, there is no lung or liver metastasis noted.

Pathological diagnosis: Merkel cell carcinoma

Gross findings: The resected specimen is 4.3 X 2.4 X 2.2 cm in size and the tumor is gray and 2.5 X 2.0 X 1.9 cm in size.

Histopathological findings: The tumor is characterized by a spectrum of small blue cell tumors that are found usually within the dermis. They have histologic feature of epithelial cells and neuroendocrine cells. The lesion fills the entire dermis with sparing of the epidermis by a thin Grenz zone, and showing solid pattern. The nuclei are relatively uniform, and exhibit nuclear molding, finely granulated dusty chromatin, small nucleoli, scanty cytoplasm and similar to small cell carcinomas. Mitotic figures are frequently seen..

Immunohistochemical study: The tumor cells are stained positive for AE1/AE3, chromogranin A, cytokeratin 20, and negative for LCA, S100, CK7, TTF-1

Discussion: Merkel cell carcinoma of the skin was first described by Toker as trabecular carcinoma. It is a rare malignant primary cutaneous neoplasm with

epithelial and neuroendocrine differentiation. Tumor cells share morphologic, immunohistochemical and ultrastructural features with merkel cells, but a direct histogenetic link is unproven. Other synonyms include neuroendocrine carcinoma of the skin, primary small-cell carcinoma of the skin, and cutaneous APUDoma.

The diagnosis of Merkel cell carcinoma can be made on the basis of the cytologic features in a good HE stained slide. The histopathologic differential diagnosis includes basal cell carcinoma, malignant melanoma, cutaneous lymphoma, eccrine carcinoma, poorly differentiated squamous cell carcinoma, metastatic neuroblastoma, primary peripheral primitive neuroectodermal tumor and metastatic small cell carcinoma. Distinction from metastatic small cell carcinoma is often the most difficult., and a chest radiography is suggested.

Merkel cell carcinoma shows epithelial and neuroendocrine differentiation. The tumor is uniformly positive for broad-spectrum cytokeratins such as AE1/AE3, CAM5.2, pan-cytokeratin), EMA and BER-EP4., and positive for neuroendocrine differentiation include NSE, chromogranin, synaptophysin. All Merkel cell carcinomas are positive for NSE. Chromogranins B and A are found in 100% and 72% of the tumors, respectively.. The tumor cells are negative for LCA and S100, and cutaneous lymphoma and malignant melanoma are excluded.

To exclude the metastatic small cell carcinoma, TTF-1 and CK20 are important markers. Cytokeratin 20 is a sensitive and quite specific marker for Merkel cell carcinoma and also useful for the detection of occult micrometastases in sentinel lymph nodes. CK20 is useful in combination with TTF-1 to differentiate between Merkel cell carcinoma (CK20 positive, TTF-1 negative) and small cell carcinoma of lung (< 10% CK20 positive, TTF-1 positive). Lack of CK20 immunoreactivity is found in small cell carcinomas from various sites including gastrointestinal, pancreas, prostate, bladder, thymus, and orbit. Other small cell malignancies that may exhibit variable CK20 positivity include bronchogenic small cell carcinoma (0.03%), small cell cervical carcinoma (9%) and small cell carcinomas of salivary gland origin (60%). CK7 has been reported to be positive in 25% of cases of Merkel cell carcinoma. Merkel cell tumors are variably positive for CK7, CD99, and CD117.

Merkel cell carcinoma is an aggressive neoplasm. Regional nodal metastases are common, and distant metastases also occur, particularly to the lungs, liver and bones. Wide resection of the primary site and regional lymph node dissection are recommended for initial treatment. Radiation therapy can be effective as an adjunct, and chemotherapy is employed for metastatic tumors.

Diagnostic criteria:

1. cutaneous carcinoma with neuroendocrine character
2. exclude metastatic small cell carcinoma

References:

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Comparative Pathology Case 265

Contributors: Chun-Ming Lin (林俊明), DVM; Victor Fei Pang (龐飛), DVM, PhD; Chian-Ren Jeng (鄭謙仁), DVM, PhD

Division of Pathobiology, Graduate Institute of Veterinary Medicine, National Taiwan University, Taipei (國立台灣大學獸醫學研究所病理生物組)

Clinical history: Five pigs from a conventional farm located in Chiayi were euthanized for sampling. These pigs were observed to have loss of appetite, progressive wasting and worsening respiratory distress. The clinician performed the necropsy and submitted lung samples for pathological examination.

Diagnosis: Bronchointerstitial pneumonia, lymphohistocytic and necrotizing, multifocal to coalescing, severe, chronic with a moderate degree of proliferation of type 2 pneumocytes and active bronchio-epithelium. Etiology is partial related with porcine circovirus type II infection

Gross findings: The cut section of the wet tissues submitted varies in color from tan to dark red with areas of rubbery mixture on longitudinal section.

Histopathological findings: Microscopically, there are numbers of inflammatory cells, chiefly lymphohistocytic cells infiltration with a moderate degree of proliferation of type 2 pneumocytes and coagulates of necrotic cells in the alveoli. There are also abundant of inflammatory exudate, cellular debris presenting in the bronchus along with active bronchio-epithelium.

In situ hybridization (ISH): PCV2 nucleic acid labelling varied from low to moderate amounts. PCV2 genome was mostly detected in clusters of necrotic cells, macrophages (intracytoplasmatic location, mainly) and intra-bronchial inflammatory cells.

Indirect in situ polymerase chain reaction (Indirect ISPCR):

Massive amounts of PCV2 nucleic acid located in clusters of necrotic inflammatory cells, widely distributed for the whole lung parenchyma. Aggregated

positive signals can be specially detected in the germinal center of peri-bronchial lymphoid follicles. In addition, viral nucleic acid was also found in other cells, such as bronchial epithelial cells, blood monocytes within pulmonary vessels, smooth muscle cells (mainly in the nucleus), lymphocytes and/or plasma-like cells, endothelial cells, and fibroblast-like cells around peribronchial/olar areas. PCV2 nucleic acid was also present in the intra-bronchial and/or intra-epithelial inflammatory cells. The signal of PCV2 nucleic acid detected by indirect ISPCR is generally significant than routine ISH.

Discussion: PCV2 was newly associated with pigs exhibiting proliferative necrotizing pneumonia (PNP) and postweaning multisystemic wasting syndrome (PMWS) and others swine diseases worldwide. In dense-pig raising regions, PCV2 infection is consistently persist. A close 84 to 100% of PCV2 nucleic acid or serum antibody detection rate was frequently seen in most PNP or PMWS-affected pig farms, and only partial population of the infected pigs would suffer from typical PNP or PMWS. To date, still little is known regarding the immunological response of pigs suffering from PNP/ PMWS or the mechanism by what PCV2 infection might result in the development of PNP/ PMWS (Darwich et al., 2004).

Traditionally, apply immunohistochemistry staining (IHC) or in situ hybridization (ISH) on paraffin-embedded tissue specimens were used for investigate the virus distribution in PNP or PMWS-affected pigs. These studies indicate the PCV2 loading is consistent correlated with the lesional stages and the monocyte/macrophage lineage cells as well as other antigen-presenting cells such as follicular dendritic cells are the main site of PCV2 distributed. Occasionally, limited numbers of lymphocytes are susceptible to PCV2 (Rosell et al., 1999). However, these methods only provide limited resolution, mainly because of its inability to detect and quantitate target nucleic acid sequences present at levels below which the signal can be clearly distinguished from background. For example, Brunborg *et.al.*, (2004) described that minimum 108 PCV2 genomes per 500 ng DNA in most tissues was an estimated viral load required in order to give a visible staining in IHC (Brunborg et al., 2004). On the contrary, the polymerase chain reaction (PCR), advanced real time PCR or even nested PCR were extremely sensitive methods to detect limited viral containment in various samples. This is particularly important in diagnosis of latent or persistent occult viral infections, where very low virus loads are normally encountered within infected cells. Unfortunately, PCR is limited to obtain the information about the virus distribution in vivo because the cells or tissue need to be destroyed in order to extract the DNA or RNA. More recent study has indicated all cell subpopulations, especially B lymphocytes from peripheral blood mononuclear cells (PBMCs) and bronchial lymph nodes in early PCV2 infected pigs could support virus replication based on the evidence of cell sorted and real time PCR (Yu et al., 2007).

Use of the polymerase chain reaction (PCR) in conjunction with in situ hybridization (in situ PCR or ISPCR) has allowed specific amplification of previously undetectable sequences (Haase et al., 1990; Embretson et al., 1993). Over the past several years, ISPCR has been used successfully by a number of research groups to identify the presence of targets that fall below the threshold of detection of traditional in situ hybridization. Thus, in situ amplification technology has been exploited to confirm the presence in specific cells of various subfamilies of retroviruses, including lentivirus (Haase et al., 1990) and HIV-1 (Nuovo et al., 1994). ISPCR has also been used to study elements involved in shifting an integrated virus from a latent to an infectious state (Chieu et al., 1992). Herein, our work was to develop this more sensitive method to characterize the cellular tropism of PCV2. Therefore, we modified a routinely ISH processed in paraffin-embedded tissue specimen to an indirect in situ polymerase chain reaction (ISPCR) program for the identification of PCV2 in lymphoid tissue of healthy carrier and PNP/ PMWS pigs.

Diagnostic criteria:

1. Histopathologic findings: hypertrophy and proliferation of type 2 pneumocytes with varying degrees of lymphohistiocytic interstitial inflammation and necrotic debris in the alveoli
2. In situ hybridization / Indirect in situ PCR: PCV2 positive

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Comparative Pathology Case 266

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Clinical history: A 72-year-old woman was admitted to the hospital because of intermittent poor appetite, upper abdominal pain and insomnia for one to two week. She also noted color urine. Her eyeball and skin have turned to yellow recently. Body weight has lost about 15 Kg(110 to 95 Kg) within 2 months. Ultrasound revealed CBD (9-10 cm) bilateral IHD dilatation and gall stone, distal CBD lesion was highly suspected. CT showed a hilar mass of liver with proximal CBD, common hepatic duct and bilateral distal IHDs compression. ERCP revealed significant narrowing at the bilateral hepatic ducts common bile duct and proximal CBD, that compatible tumor invasion and compression. Exp. Laparotomy with tube cholecystostomy, omentum and hilar LN biopsy was performed. A 115 Gm brownish gray and friable omentum tissue with necrosis and multiple small white small mass was removed from omentum.

Diagnosis: Cholangiocarcinoma.

Gross findings: The resected specimen submitted consisted of multiple pieces of soft tissue with the largest one measuring 115 gm in weight. Grossly they showed yellowish gray with small white small mass. These tissues are friable. All for section

Histopathological findings:

PAP stains:

- 1) area #1: CKAE1/AE3(+) CEA(-) Calretinin(+) Cytokeratin
- 2) area #2: CKAE1/AE3(+) PCEA(+) CK7(+) CK20(+)

Special stain: PAS(+) and GMS(+) for candida.

Discussion: Cholangiocarcinoma occurs with equal frequency in males and

females; the average age of presentation is 60 years. About 90% of patient present with jaundice. These tumor can developed at any level of biliary tree. Cytological procedures yield diagnostic material in about 70% of cases.

Diagnostic criteria:

1. Criteria of adenocarcinoma.
2. CEA(+) CK7(+) CK20(+)
3. Clinical finding.

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Comparative Pathology Case 267

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Clinical history: Soft turtles, less than one year old. There were lack of apparent clinical signs, but the turtles have been frequently captured due to long-time staying on the feeding boards.

Diagnosis: Mycobacteriosis in pond-cultured soft turtles.

Gross findings: The turtles show grayish-white miliary nodules or patches, variable in size, were found scattered on the various organs.

Histopathological findings: In the liver section, Histiocytic granulomas contained an admixture of epithelioid cells and Langhan's giant cells without the formation of a necrotic center. Gradually, necrogranulomas were formed, characterized by the appearance of epithelioid cells, Langhan's giant cells and lymphocytes surrounding a necrotic center. Finally, fibrous encapsulation was also found in advanced lesions. Occasional lesions were the aggregation of epithelioid cells and Langhan's giant cells without formation of a necrotic center, but encircled by layers of fibrous tissues. Yellowishbrown pigments were frequently found in situ. Dystrophic calcification was not observed.

Laboratory results :

- Ziehl-Neelsen staining method

Acid-fast, unbranching bacilli were usually detected in both organ smears and tissue sections by the Ziehl–Neelsen staining method.

- Polymerase chain reaction

Mycobacterial marinum: *hsp65* sequencing show positive in various organs.

Discussion: Organize granulomas may be induced by bacterial, fungal, protozoan and metazoan parasitic organisms. Several pathogens have been found in reptiles, including *Salmonella spp* (Kenneth W. Angus, 2005), *Mycobacteria spp*, *Ascarops sp.* (Stephen R. Goldberg et al., 1988) and *Chlamydia spp* (G. SOLDATI, 2004). These are associated with organized granulomas.

Recent investigation indicates that *hsp65* sequencing is a potential tool for identifying both fast- and slow- growing mycobacteria (McNabb et al., 2004). Several species of mycobacteria including *M. avium*, *M. chelonae*, *M. marinum*, and *M. kansasii* have been identified in turtles (Brock et al., 1976; Rhodin and Anver, 1977; Schildger et al., 1991; Orós et al., 2003). Amongst them, *M. chelonae* is the most prevalent (Rhodin and Anver, 1977). However, all of our strains were identified as *M. marinum*.

The source of the organisms in the present study was still uncertain. According to Taiwan farmer's custom, trash fish mixed with eel feed was frequently used as the main food for Chinese soft shell turtles. It might play an important role for transmission route, because *M. marinum* was the largest proportion of all mycobacteria isolated from fish (Durborow, 1999).

Generally, chronic mycobacteriosis is the most frequent form of the disease in amphibians and reptiles (Rhodin and Anver, 1977; Brownstein, 1984; Schildger et al., 1991). Chelonian mycobacteriosis can induce osteoarthritis or plastral ulceration and visceral granulomas in the lung, liver and spleen of the infected turtles (Brock et al., 1976; Rhodin and Anver, 1977; Schildger et al., 1991; Orós et al., 2003). *M. marinum* in our cases induced a systemic infection characterized by visceral granuloma formation in the various organs such as the spleen, liver, lung, intestine, kidney, stomach and pancreas. Neither osteomyelitis nor plastral ulceration was found in the present study.

M. marinum can induce granulomatous lesions in human skin (Ang et al., 2000). Due to the poor growth of the organism at 37 °C, systemic dissemination is rare but has been reported in the immunocompromised patients (Lacaille et al., 1990; Tchorobay et al., 1992; Decostere et al., 2004). From June 1999 to November 2000, fourteen isolates of *M. marinum* have been collected at the Chang Gung Memorial Hospital, Taoyuan, Taiwan (Wu et al., 2002). One patient had septic arthritis and the other thirteen had skin infections and/or tenosynovitis, mainly involving the upper extremities. Because of its rarity, most physicians are not familiar with this infection (Chow et al., 1987; Tchorobay et al., 1992; Wu et al., 2002).

Chinese soft shell turtles are a delicious food and regarded as good for the health in

Southeast Asia, particularly for the Chinese and Japanese cultures. Our study revealed that mycobacteriosis due to *M. marinum* infections was not uncommon in turtles. Therefore, more attention should be paid to this important zoonotic disease (Wheeler and Graham, 1989).

Diagnostic criteria:

- Histopathologic findings: In the liver section, characterized by the appearance of epithelioid cells, Langhan's giant cells and lymphocytes surrounding a necrotic center. Finally, fibrous encapsulation was also found in liver.
- Ziehl-Neelsen staining method

Acid-fast, unbranching bacilli were usually detected in both organ smears and tissue sections by the Ziehl–Neelsen staining method.
- Polymerase chain reaction

Mycobacterial marinum show positive in various organs

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Comparative Pathology Case 268

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Clinical history: A 67 year old female patient, admitted due to bilateral renal stones, was found to have a tumor at the pelvis of right kidney during ureteroscopic examination. CT scan showed a hypodense lesion at the lower pole of right kidney with enlarged para-aortic lymph nodes. Needle biopsy proved malignancy. She received radical nephrectomy to remove the right kidney and para-aortic lymph nodes dissection. The microscopic slide submitted was taken from the kidney.

Diagnosis: Sarcomatoid carcinoma of renal pelvis

Gross findings:

- (1) Hydronephrosis with markedly dilated pelvis
- (2) Polypoid tumor, 8.0 x 7.0 x 5.0 cm in size, in the pelvis
- (3) Staghorn stone, 3.0 x 3.0 x 2.0 cm in size, in the pelvis

Histopathological findings:

- (1) Epithelioid like tumor nests with frequent mitosis and tumor necrosis; CK (++) and Vimentin (+++)
- (2) Spindle cell proliferation with frequent mitosis, tumor necrosis and myxoid stroma; only Vimentin (+++)
- (3) Lymph node metastasis with only epithelioid part; CK (++) and Vimentin (+++)

Discussion:

- (1) Sarcomatoid carcinoma, also known as spindle cell carcinoma, anaplastic carcinoma, or carcinosarcoma, was reported to occur in various organs, mostly

in the upper aerodigestive tract. (Respiratory tract: sinonasal cavity, larynx, lung; Digestive tract: esophagus, stomach, small bowel, colon, rectum, liver, gall bladder, pancreas ; Other organs: thymus, thyroid gland, adrenal cortex)

- (2) Epithelial differentiation may not be apparent under routine light microscopic examine, immunohistochemical staining for epithelial markers would disclose an epithelial origin in the spindle cells part. Also, the sarcomatous part showed strong positivity for vimentin.
- (3) In contrast to sarcomatoid renal cell carcinoma, sarcomatoid carcinoma of renal pelvis showed overexpression of p53 protein and relatively low *ki-67* index.
- (4) Some tumors contain osteoclast-like multinucleated giant cells, which were CD68 positive and p53 negative and were regarded as reactive rather than neoplastic.
- (5) It was regarded as high grade urothelial carcinoma and should be treated as it was staged.

Diagnostic criteria:

- (1) Spindle cell tumor with coexpression of keratin and vimentin.
- (2) Polypoid protrusion into renal pelvis rather than intra-renal location favors urothelial origin.
- (3) Overexpression of p53 protein.

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Comparative Pathology Case 269

Slide code: CS05-1123D

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Clinical history: A 10-year-old, mixed breed, female dog had a greasy tumor on the abdominal area. She was nulliparous and unspayed; the date of her last estrus was unknown. The tumor was found one year previously by the owner. It grew gradually and developed some superficial ulcers in the last several weeks prior to registration at our teaching hospital. This ulcerated mass measured 5.2 x 4.8 x 3.7 cubic centimeter and was located in the left fifth mammary gland and inguinal area. There was another 2 x 1.8 x 1.5 cubic centimeter tumor just cranially to the mass mentioned above. The regional (inguinal) lymph node was moderately enlarged. Radiographically, lateral and ventro-dorsal views of thorax and abdomen showed no significant disorder. Modified radical mastectomy (regional mastectomy) was performed to remove the left 4th and 5th mammary glands completely, including the adjacent lymph nodes. During the operation, the surgeon found tumor invasion into the fascia muscularis; consequently, the excised specimen was submitted for pathologic examination. No chemotherapy was conducted after surgical removal of mammary tumors. The prognosis was guarded carefully. Two months later, the tumor was recurrent with metastasis to the iliac lymph node. She died 3 months post-operation.

Diagnosis: Mammary Carcinoma with Sebaceous Differentiation, Mammary gland, Dog

Gross findings: Grossly, the masses were firm, whitish to light brown and superficially ulcerated. On cut surface, they were multilobulated with foci of necrosis. The inguinal lymph node was enlarged with whitish areas on the cut surface.

Histopathological findings: Microscopically, the mammary masse consisted of two dominating types of tumor. The first type of the mammary tumor was characterized by intraductal papillary-like nests with fibrovascular stroma and mild lymphoid cell infiltration. The tumor cells were pleomorphic with prominent nucleolus. Mitosis was frequent. The second type of the mammary tumor showed sebaceous differentiation. The areas of this sebaceous tumor were characterized by multilobulated growth of sebaceous and keratinized epithelial cells, which were clumped with each other and surrounded by few to several layers of basaloid cells. The sebaceous cells were characterized by small discrete cytoplasmic vacuoles that produced scalloping or rounded indentations in the nuclear membrane. Numerous mitotic cells were also found in the layers of basaloid cells. A few foci of clumped cells with an abundant foamy cytoplasm, resembling sebaceous cells, were also noticed within the intraductal papillary-like nests of mammary carcinoma, supporting the sebaceous metaplasia. Large areas of invasive sebaceous carcinoma were commonly seen surrounding small-sized intraductal papillary tumor nests. Disseminated lymphatic spread to the lymph node was found especially of the sebaceous carcinoma.

Immunohistochemistry: In the tumor cells with sebaceous differentiation, the Periodic Acid Schiff's (PAS) stain for glycogen and mucicarmine stain for mucin were negative, while Oil Red O stain for lipid was positive.

Discussion: Sebaceous differentiation of mammary carcinoma, to our knowledge, has not been documented in veterinary literature yet, although there have been a few cases reported in human.^{5,6,10,12,13} In humans, sebaceous metaplasia has been reported in intraductal carcinoma of breast,^{5, 6,10,12,13} or has a concurrent presence of squamous differentiation.^{5,10,12} However, due to the rarity of the peculiar variant the prognosis of the sebaceous phenotype in mammary carcinoma remains unsettled.¹³ Similarly, there is a variant exhibiting lipid-rich carcinoma of mammary gland in dogs.^{3,8,9} The lipid-rich tumor cells contain either multiple and

small or large and solitary vacuoles that pushed the nucleus to the periphery of the cell as the signet-ring cell.^{3,7} Moreover, the lipid-rich carcinomas of the mammary gland in human¹¹ and dog³ have a poor prognosis.

Mammary gland is developed from a specialized sweat gland.¹ Both skin appendages and the secretory and ductal apparatus of mammary gland share a common embryonic ectodermal anlagen.¹³ The origin and pathway of the sebaceous metaplasia in mammary carcinoma remains unclear. It was suggested that there was an association between sebaceous gland metaplasia and squamous metaplasia.⁵ However, in our case neoplastic glandular cells became toward cells that contained lipid droplets within the cytoplasm displaying scalloping or rounded indentations in the nuclear membrane, represented the sebaceous metaplasia, although they were looked like squamous appearance. Therefore, we propose that the sebaceous metaplasia probably was derived from mammary stem cells (basaloid cells) with a pluripotentiality of differentiation. Some previous studies also concluded that the mammary stem cells were converted into sebaceous cells or adenosquamous cells.^{5,12}

Metaplastic sebaceous carcinoma of mammary gland should be distinguished from primary sebaceous carcinoma of skin adnexal origin. In fact, sebaceous carcinomas arising from skin sites are uncommon and show seldom widespread metastasis in the dog.^{2,4} The features which militate against a skin appendage origin in our case were metaplastic transition of the predominantly intraductal papillary carcinoma from only a small area of sebaceous differentiation to a large area of invasive sebaceous carcinoma with associated squamous differentiation.

Lipid-rich carcinoma, a variant of mammary carcinoma, has been documented in dogs recently.^{3,8,9} It is characterized by tumor cells, arranged in solid nests and cords separated by a moderate amount of stroma, with an abundant foamy cytoplasm which contained a large amount of neutral lipid.⁷ In contrast, the mammary carcinoma with sebaceous differentiation in our case showed the characteristics of sebaceous tumor with multilobulated clumps and central areas of keratinized epithelial cells. These lipid vacuoles in sebaceous differentiation produce scalloping or rounded indentations in the nuclear membrane which are different to those found in lipid-rich carcinoma. Either sebaceous or lipid-rich mammary carcinomas may display positive staining results for Oil Red O stain from frozen section.

In our patient, the mammary carcinoma with sebaceous differentiation had a poor prognosis. In humans, it has been suggested that the prognosis of this tumor is more favorable with little propensity for metastatic spread.^{5,6,13}

Diagnostic criteria:

1. Histopathologic findings: Sebaceous tumor were characterized by multilobulated growth of sebaceous and keratinized epithelial cells, which were clumped with each other and surrounded by few to several layers of basaloid cells.
2. Special staining: The tumor cells with sebaceous differentiation, the Periodic Acid Schiff's (PAS) stain for glycogen and mucicarmine stain for mucin were negative, while Oil Red O stain for lipid was positive.

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Comparative Pathology Case 270

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Clinical history: A 65-year-old man was admitted to the hospital because of severe lower back pain for one week. The pain was not relieved when resting or after taking some analgesics. He felt weakness over bilateral lower legs and difficulty in walking. He had history of acute gouty arthritis and fracture of right distal radius one year ago, upper GI bleeding and anal fistula one year ago, coronary artery disease for one year and under regular medication control. No history of trauma, dysuria, frequency or urgency in urination, diarrhea or constipation recently. Physical examination showed numbness over both legs but with normal circulation of both legs. Straight leg raising test of bilateral legs were 0 degree (normal 80-90 degrees). Bilateral big toe tests of dorsiflexion and plantar flexion were severe decreased. X-ray showed lumbar spondylosis with multiple osteophytes formation over T12-S1. CT showed sclerotic change over the lower L-spine and bilateral iliac bones. MRI showed infiltrative processes over the thoracic & lumbosacral spine, paraaortic & iliac lymphadenopathy, and spinal stenosis T12-S1. Decompression operation with biopsy was performed.

Diagnosis: Metastatic prostatic adenocarcinoma of the iliac and lumbar bones.

Gross findings: Rt iliac and lumbar spine L3-5 biopsies shows tiny pieces of soft and bony tissue fragments containing blood clots not remarkable grossly. They were totally embedded after decalcification.

Histopathological findings:

PAP stains: Cytokeratin Focally +. PSA +++ . PAS stain: +.

There shows bone tissue exhibiting some dysplastic and also atypical cells infiltration. There is fibroblasts proliferation and increase of collagen fibers. Focal

nests of atypical cells exhibiting prominent nucleolus are found. PSA shows highly reactive. But the background staining is also very strong. Prostatic adenocarcinoma is highly suspected.

Discussion: With advances in the treatment of heart disease, stroke, and other malignancies, men are living longer; this change in life expectancy increases the risk of having and dying from prostate cancer.

McNeal et al (1988) first proposed the histologic division of the prostate into an outer PZ, a central zone (CZ), and an inner TZ. In the young adult prostate, approximately 5% of prostatic glandular tissue is in the TZ located on both sides of the prostatic urethra. This is the area where benign hyperplasia develops in older patients. The TZ is separated from the PZ and CZ by the surgical capsule, in which calcified corpora amylacea may be found. The CZ is situated at the base of the prostate, and the ejaculatory ducts reach the verumontanum by passing through CZ tissue. The CZ is relatively resistant to disease processes and constitutes approximately 25% of the glandular tissue of the prostate in the young adult. The PZ constitutes 70% of the prostate and lies on the posterior and lateral aspects of the gland surrounding the TZ. Its ducts drain into the urethra distal to the verumontanum. Approximately 75% of prostate cancers occur in the ultrasonic PZ, and 25% occur in the TZ. Because of the typical location of prostatic carcinoma (posterior aspects of the peripheral zone), urinary symptoms occur late; asymptomatic tumors are often detected by digital rectal exam or following routine examination that detects elevated prostate-specific antigen (PSA).

PSA is a single-chain glycoprotein with a molecular weight of 34,000 daltons. Physiologically, PSA is produced in the prostatic ductal epithelium by both abnormal and normal prostate tissue, secreted into the prostatic ducts, then concentrated in the seminal plasma. This glycoprotein acts to liquefy the seminal coagulum formed with ejaculation. In serum, PSA reaches the circulation by diffusing through the prostatic stroma. PSA screening is currently the single best test for prostate cancer and is widely used in the diagnosis of prostate cancer, but it does not help in determining whether the detected cancer will cause clinically significant disease. Whereas PSA is an excellent marker for the follow-up of patients with established prostate cancer, some men with prostate cancer may have normal PSA levels, a moderate elevation of the PSA level (4-10 ng/mL) has a low specificity for prostate cancer, and an elevated PSA level is not specific for prostate cancer. Elevated serum PSA levels may also be associated with prostatitis, prostate infarction, PIN, prostate biopsy, transurethral resection of the prostate, and urethral catheterization.

The free-to-total PSA ratio measures both bound and free PSA as a percentage of total PSA and is a useful additional discriminator between cancer and benign

pathology, especially in patients with moderately elevated serum PSA levels (4-10 ng/mL). This ratio is also useful in determining whether a repeat biopsy is appropriate in a patient with a moderately elevated PSA level whose initial systematic biopsy results are negative. The lower the percentage of free PSA, the higher the likelihood of cancer. An assay for cPSA is now available and primarily measures alpha1-antichymotrypsin cPSA. Some studies have shown an increased specificity with the cPSA assay for the diagnosis of prostate cancer compared with the specificity of total PSA and free-total PSA. In the future, cPSA could conceivably replace total PSA measurements.

In a man aged 50 years, risk analysis shows that the lifetime risk of microscopic prostate cancer is approximately 42%, the risk of clinical prostate cancer is 10%, and the risk of fatal prostate cancer is 3%. Mortality for prostate cancer has decreased in the United States since 1992, and it has decreased in the United Kingdom since 1995. The decrease in the United States is greater than that in the United Kingdom. Maximum mortality (ie, the greatest rate of mortality) is in those aged 85 years and older.

Diagnostic criteria:

1. Most common primary malignancies in adults to metastasize to bone are prostate, kidney, thyroid, lung, pancreas, and breast
2. In children the most common are rhabdomyosarcoma, clear cell carcinoma of kidney, and neuroblastoma
3. Osteolytic lesions on radiographs are usually thyroid, kidney, lung, or gastrointestinal tract in origin
4. Osteoblastic lesions on radiographs are usually metastatic prostate, medulloblastoma, or carcinoid
5. Tumor cells in metastatic prostatic adenocarcinoma to bone in patients previously treated may appear histiocytic and require immunohistochemistry (PSA, PAP) to identify prostatic origin

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Comparative Pathology Case 271

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Clinical history: An 8-year-old mixed dog had a firm mass at right axillary region noted for several years, which grew rapidly this year. The muscle under the mass was involved, lumpectomy surgery was intervened and tissue was submitted for histopathological evaluation.

Diagnosis: Malignant canine peripheral nerve sheath tumors (MPNST), right axillary region, canine.

Gross findings: The submitted mass was well demarcated from the surrounding adipose tissue but it invaded into the muscular layer. Gross examination revealed that the cut surface was gray to white and firm and soft texture from areas to areas.

Histopathological findings: Microscopically, the subcutaneous mass submitted is well defined, none capsulated and poorly circumscribed. The tumor is incompletely separated by thin to thick collagenous stroma mixed with mucinous matrix. The tumor cells in the tumor mass are characterized by the presence of perivascular whorls of fusiform cells which exhibit storiform pattern. In some areas, the tumor cells show onion or finger print pattern. These structures consist of pericytes proliferating around vascular channels lined with endothelium and wherever there are capillaries. The mitotic figures are observed rarely. The tumor cells invading into the muscular layer are seen. The infiltrations of plasma cells and lymphocytes are present among the tumor mass.

Discussion: Canine peripheral nerve sheath tumors (PNSTs) arise from Schwann cells, perineurial fibroblasts, or both. These tumors including schwannomas (neurilemmoma) and neurofibromas were classified as PNSTs by the World Health Organization (WHO) in 1999. In dogs and cats, peripheral nerve sheath tumors of the skin are found in older animals. In cattle, they have a suspected genetic basis, may be multiple, can develop in both the young and old, and are generally an incidental finding at slaughter; they arise from the deep nerves of the thoracic wall and viscera, and cutaneous involvement is rare. Regardless of the species, these tumors appear as white, firm, nodules. Attachment to a peripheral nerve may occasionally be noted. Both benign and intermediate-grade malignant variants are recognized. In dogs, cats, and horses, most are locally infiltrative but do not metastasize. Complete excision is the treatment of choice. Where margins are narrow or insufficient, followup radiation therapy may increase the tumor-free interval.

Based on the morphologic and biologic behavior, PNSTs are divided into benign PNST (BPNST) and malignant PNST (MPNST) forms with several pathomorphologic features. In human MPNSTs, variable histologic patterns and heterogenous differentiation have been reported, including epithelioid MPNST and MPNST with divergent differentiation such as rhabdomyoblastic (malignant Triton tumor) cartilaginous, osseous, angiomatous, and glandular forms or their complex.

Immunohistochemically, PNSTs are generally positive for vimentin and S-100, whereas anaplastic or heterogenous MPNSTs tend to be negative for S-100. Nerve growth factor receptor (NGFR), expressed in the perineurium of normal peripheral nerves and neoplastic Schwann cells, was frequently demonstrated in human PNSTs.

Recently, morphologic and immunohistochemical varieties of canine BPNSTs and MPNSTs, and immunohistochemistry for neurofilament, NGFR and α -SMA might be helpful for differentiating canine PNSTs from other sarcomas including RMSs or CHPs. In addition, immunostains for S-100, GFAP, NSE and myoglobin have only limited value in distinguishing between canine MPNSTs with divergent differentiations and other related sarcomas.

The differential diagnosis of MPNSTs in dogs should include fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma and hemangiopericytoma (CHP) because of their histological similarities. The most important differential diagnosis of canine PNST might be CHP, which is characterized by concentric whorls or fingerprint of spindle cells around capillaries and has been categorized as tumors of unknown origin in the current WHO classification. Immunohistochemical investigations of CHP have been described in several previous reports, and these unique canine tumors expressed various markers including vimentin, α -SMA, desmin, factor VIII-related

antigen, S-100, NSE, and GFAP. Usually, the result of α -SMA positive signals is observed in CHP.

The reason for diverse differentiation in MPNSTs still remains unclear. Many pathologists have introduced the concept of ectomesenchyme. Migratory neural crest cells can differentiate not only into melanocytes, Schwann cells, and ganglion cells but also to cells in the leptomeninges and some mesenchymal cells contributing to the formation of muscle, bone, or cartilage in the neck and head regions. This might provide a reasonable explanation for the degree of divergent differentiation observed in MPNSTs.

Diagnostic criteria:

1. Morphopathology: Spindle neoplastic cells are often arranged as interwoven bundles of small, wavy spindle cells with palisading and whorls. In contrast to hemangiopericytoma, whorls are less prominent in PNST and most encircle sclerotic collagen rather than capillaries. The spindle cells are more delicate and often have more intercellular fibrillar or mucinous matrix than hemangiopericytoma.
2. Immunohistochemistry: Immunoreactive with vimentin, neurofilament, S-100 and fail to factor VIII-related antigen and α -SMA antibody.

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Comparative Pathology Case 272

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Clinical history: An 84 year old female suffered from cough with thick sputum recently

with aggravated shortness of breath (SOB) for 2 days.

Past history revealed pleurisy for 2 years. Anti-tuberculosis was tried with improvement

of condition. Serial X-ray and CT scans examination suggested bronchiectasis or cavitary lesions.

Sputum cytology, bronchoscopic brushing and biopsy were performed..

Diagnosis: Sarcomatoid carcinoma, lung.

Gross findings: Wedge resection of LLL with 2 pieces of lung tissues, up to A: 2.4 x 1.3 x 1.1cm, B: 3.2 x 1.8 x 1.4 cm., were submitted.

Histopathological findings:

1. sarcomatous cells in the parenchyma and epithelial components of neoplastic cells
lining on the cystic spaces and with papillary fronds.
2. the tumor cells contains huge irregular vesicular nuclei.
3. extensive necrosis and anthracosis are noted.

Discussion: Primary malignant pleuropulmonary tumors showing sarcomatoid features are exceedingly uncommon. Overwhelmingly, such lesions are typically epithelial in nature; therefore, named as sarcomatoid carcinoma(SC). Neoplasms with a mesenchymal lineage in the lung and pleura are most often proven to be

secondary, emanating deep soft tissue sites or female genital tract. Sarcomatoid carcinoma (SC) is rare (1 % of all lung malignancy) and in elderly (60 Y/O) and heavy smokers with a short history but bulky tumor(5 cm). Ninety percent cases are resectable with 5YS to be 20 %. The WHO classification of SC includes 1. spindle cell ca (only spindle cells present), 2. giant cell ca (large cell ca with only giant cells) (1+2= monophasic SC in Wick), 3. pleomorphic ca (adeno-squamous cell ca with spindle cell and/or giant cells), 4. carcinosarcoma (ca with sarcoma containing heterologous elements, CS), 5. pulmonary blastoma.(3+4+5= biphasic SC).1. In spindle cell ca, it is rare, but most common spindle cell malignancy in lung is SC and more possible than primary pulmonary sarcoma. Therefore, one usually considers a cytologically atypical spindle cel tumor of lung to be a sarcomatoid carcinoma (SC), instead of sarcoma, unless thorough IHC or EM studies indicate otherwise. IHC shows epithelial markers (CK, EMA, CEA): (+). The D/D is soft tissue sarcoma, eg. synovial sarcoma which can be diagnosed by IHC: CEA(+), bcl2: (+). 2. giant cell ca is very rare (0.08-0.1 % of lung ca) and contains only giant cells, 700-800 um with well-defined cell borders. Mitosis is frequent and emperipolesis (active penetration of leukocyte into tumor cells) are noted. The D/D includes large cell lung ca, metastatic MFH etc. 3. pleomorphic ca consists of 0.3 % of lung ca with adeno-squamous cell ca and more than 10 % spindle or giant cells. IHC is required only if the tumor lacks an obvious epithelial component. 4. carcinosarcoma contains epithelial component (SQCC> adenoca> large cell ca) and sarcoma elements(osteoid, bone, muscel) (cf: SQCC with osteocartilaginous stroma metaplasia). IHC and EM support CS is basically an epithelial tumor that shows varying degrees of mesenchymal differentiation. In IHC, epithelial (CK, EMA, CEA, TTF-1) and mesenchyma (vimentin) may positive but any of these IHC markers may be found in either component. In EM, epithelial features (desmosome) may be found in spindle cells—close relation between CS and spindle cell ca. The metastasis of CS may be ca or sarcoma component.

Immunohistochemistry: (SW10606252B)

1. TTF-1: (+), Ber-EP4: (+), vimentin: (+)
2. calretinin: (-)

Differential diagnosis:

1. metastatic carcinoma.
2. primary sarcoma of lung: rare in respiratory tract.

Kaposi's sarcoma, fibrosarcoma, leiomyosarcoma, rhabdosarcoma,
epithelioid hemangioendothelioma, hemangiopericytoma,,MFH
chondrosarcoma, synovial sarcoma,

3. metastatic sarcoma: no epithelial differentiation by LM or EM.

A. Synovial sarcoma: CEA (+), bcl2: (+).

B. Pleura: monomorphic sarcomatoid ca vs sarcomatoid mesothelioma

4. carcinosarcoma: ca+ sarcoma (malignant CT: osteoid, cartilage, muscle)

Diagnostic criteria:

1. carcinoma shows foci of malignant spindle or giant cells.

2. carcinoma shows connective tissue differentiation.

3. IHC, EM show tumor cells are entirely epithelial origin.

CK, EMA CEA: (+)

4. molecular survey shows identical mutation in spindle cells and epithelial components.

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中華民國比較病理學會
第一次至第三十八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	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	中興大學獸醫學系
	43.	Phyllodes tumor	Human	台中榮民總醫院
	44.	Canine oral papilloma	Dog	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
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	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	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
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	中興大學獸醫學系
129.	Kaposi's sarcoma	Human	華濟醫院
131.	Basal cell carcinoma (BCC)	Human	羅東聖母醫院
132.	Transmissible venereal tumor	Dog	臺灣大學獸醫學系
137	Canine Glioblastoma Multiforme in Cerebellopontine Angle	Dog	中興大學獸醫病理研究所
143	Osteosarcoma associated with metallic implants	Dog	紐約動物醫學中心
144	Radiation-induced osteogenic sarcoma	Human	花蓮慈濟綜合醫院
145	Osteosarcoma, osteogenic	Dog	臺灣大學獸醫學系
146	Pleomorphic rhabdomyosarcoma	Human	行政院衛生署新竹醫院
147	Papillary Mesothelioma of pericardium	Leopard	屏東科大學獸醫學系
148	Cystic ameloblastoma	Human	台北醫學院
149	Giant cell tumor of bone	Canine	中興大學獸醫學院
150	Desmoplastic small round cell tumor (DSRCT)	Human	華濟醫院
152	Hepatocellular carcinoma	Human	羅東聖母醫院
158	Hemangiopericytoma	Human	羅東聖母醫院
160	Cardiac fibroma	Human	高雄醫學大學病理學科
166	Nephroblastoma	Rabbit	紐約動物醫學中心
168	Nephroblastoma	Pig	台灣動物科技研究所

169	Nephroblastoma with rhabdomyoblastic differentiation	Human	高雄醫學大學病理科
172	Spindle cell sarcoma	Human	羅東聖母醫院
174	Juxtaglomerular cell tumor	Human	新光醫院病理檢驗科
190	Angiosarcoma	Human	高雄醫學大學病理學科
192	Cardiac myxoma	Human	彰化基督教醫院病理科
194	Kasabach-Meritt syndrome	Human	慈濟醫院病理科
195	Metastatic hepatocellular carcinoma, right atrium	Human	新光醫院病理科
197	Papillary fibroelastoma of aortic valve	Human	新光醫院病理科
198	Extraplacental chorioangioma	Human	耕莘醫院病理科
208	Granulocytic sarcoma (Chloroma) of uterine cervix	Human	高雄醫學大學病理學科
210	Primary non-Hodgkin's lymphoma of bone, diffuse large B cell, right humerus	Lymphoma	彰化基督教醫院病理科
213	Lymphoma, multi-centric type	Dog	中興大學獸醫系
214	CD30 (Ki-1)-positive anaplastic large cell lymphoma (ALCL)	Human	新光醫院病理科
215	Lymphoma, mixed type	Koala	台灣大學獸醫學系
217	Mucosal associated lymphoid tissue (MALT) lymphoma, small intestine	Cat	臺灣大學獸醫學研究所
218	Nasal type NK/T cell lymphoma	Human	高雄醫學大學病理科
222	Acquired immunodeficiency syndrome (AIDS) with disseminated Kaposi's sarcoma	Human	慈濟醫院病理科
224	Epithelioid sarcoma	Human	彰化基督教醫院病理科
226	Cutaneous B cell lymphoma, eyelid, bilateral	Human	羅東聖母醫院病理科
227	Extramammary Paget's disease (EMPD) of the scrotum	Human	萬芳北醫皮膚科, 病理科
228	Skin, back, excision, CD30+diffuse large B cell lymphoma, Soft tissue, leg, side not stated, excision, vascular leiomyoma	Human	高雄醫學大學附設醫院病理科
231	Malignant melanoma, metastasis to intra-abdominal cavity	Human	財團法人天主教耕莘醫院病理科
232	Vaccine-associated rhabdomyosarcoma	Cat	台灣大學獸醫學系

	233	1. Pleura: fibrous plaque, 2. Lung: adenocarcinoma, 3. Brain: metastatic adenocarcinoma	Human	高雄醫學大學附設中和醫院病理科
	235	1. Neurofibromatosis, type I 2. Malignant peripheral nerve sheath tumor (MPNST)	Human	花蓮慈濟醫院病理科
	239	Glioblastoma multiforme	Human	羅東聖母醫院
	240	Pineoblastoma	Wistar rat	綠色四季
	241	Chordoid meningioma	Human	高醫病理科
	243	Infiltrating lobular carcinoma of left breast with meningeal carcinomatosis and brain metastasis	Human	花蓮慈濟醫院病理科
	245	Microcystic Meningioma.	Human	耕莘醫院病理科
	247	Well-differentiated fetal adenocarcinoma without lymph node metastasis	Human	新光吳火獅紀念醫院
	249	Adenocarcinoma of lung.	Human	羅東聖母醫院
	252	Renal cell carcinoma	Canine	國立台灣大學獸醫學系獸醫學研究所
	253	Clear cell variant of squamous cell carcinoma, lung	Human	高雄醫學大學附設中和醫院病理科
	256	Metastatic adrenal cortical carcinoma	Human	耕莘醫院病理科
	258	Hashimoto's thyroiditis with diffuse large B cell lymphoma and papillary carcinoma	Human	高雄醫學大學附設中和醫院病理科
	262	Medullar thyroid carcinoma	Canine	臺灣大學獸醫學系
細菌	6.	Tuberculosis	Monkey	臺灣大學獸醫學系
	7.	Tuberculosis	Human	省立新竹醫院
	12.	H. pylori-induced gastritis	Human	台北病理中心
	13.	Pseudomembranous colitis	Human	省立新竹醫院
	26.	Swine salmonellosis	Pig	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

	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	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
	134.	Swine salmonellosis with meningitis	Swine	中興大學獸醫學系
	135.	Meningoencephalitis, fibrinopurulent and lymphocytic, diffuse, subacute, moderate, cerebrum, cerebellum and brain stem, caused by <i>Streptococcus</i> spp. infection	Swine	國家實驗動物繁殖及研究中心
	140	Coliform septicemia of newborn calf	Calf	屏東縣家畜疾病防治所
	161	Porcine polyserositis and arthritis (Glasser's disease)	Pig	中興大學獸醫學院
	162	Mycotic aneurysm of jejunal artery secondary to infective endocarditis	Human	慈濟醫院病理科
	170	Chronic nephritis caused by <i>Leptospira</i> spp	Pig	中興大學獸醫學院
	173	Ureteropyelitis and cystitis	Pig	中國化學製藥公司
	254	Pulmonary actinomycosis.	Human	耕莘醫院病理科
	259	Tuberculous peritonitis	Human	彰化基督教醫院病理科
	260	Septicemic salmonellosis	Piglet	國立屏東科技大學
	261	Leptospirosis	Human	慈濟醫院病理科
病毒	21.	Newcastle disease	Chickens	台灣大學獸醫學系
	22.	Herpesvirus infection	Goldfish	台灣大學獸醫學系
	30.	Demyelinating canine distemper	Dog	台灣養豬科學研究所

	encephalitis		
31.	Adenovirus infection	Malayan sun bears	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	中興大學獸醫學系
133.	Japanese encephalitis	Human	花蓮佛教慈濟綜合醫院
136	Viral encephalitis, poliovirus infection	Lory	美國紐約動物醫學中心
138	1.Aspergillus spp. encephalitis and myocarditis 2.Demyelinating canine distemper encephalitis	Dog	台灣大學獸醫學系
153	Enterovirus 71 infection	Human	彰化基督教醫院
154	Ebola virus infection	African Green monkey	行政院國家科學委員會實驗動物中心
155	Rabies	Longhorn Steer	台灣大學獸醫學系
163	Parvoviral myocarditis	Goose	屏東科技大學獸醫學系
199	SARS	Human	台大醫院病理科
200	TGE virus	swine	臺灣動物科技研究所
201	Feline infectious peritonitis(FIP)	Feline	台灣大學獸醫學系
209	Chicken Infectious Anemia (CIA)	Layer	屏東防治所
219	1.Lymph node:Lymphadenitis, with lymphocytic depletion and intrahistiocytic basophilic cytoplasmic inclusion bodies. Etiology consistent with Porcine Circovirus(PCV)infection. 2.Lung: Bronchointerstitial	Pig	臺灣動物科技研究所

	pneumonia, moderate, lymphoplasmacytic, subacute.		
220	Cytomegalovirus colitis	Human	彰化基督教醫院病理科
221	Canine distemper virus Canine adenovirus type II co-infection	Canine	國家實驗動物繁殖及研究中心
223	1. Skin, mucocutaneous junction (lip): Cheilitis, subacute, diffuse, sever, with epidermal pustules, ballooning degeneration, proliferation, and eosinophilic intracytoplasmic inclusion bodies, Saanen goat. 2. Haired skin: Dermatitis, proliferative, lymphoplasmacytic, subacute, diffuse, sever, with marked epidermal pustules, ballooning degeneration, acanthosis, hyperkeratosis, and eosinophilic intracytoplasmic inclusion bodies.	Goat	台灣動物科技研究所
238	Hydranencephaly	Cattle	國立屏東科技大學獸醫學系
248	Porcine Cytomegalovirus (PCMV) infection	Swine	國立屏東科技大學獸醫學系
250	Porcine respiratory disease complex (PRDC) and polyserositis, caused by co-infection with pseudorabies (PR) virus, porcine circovirus type 2 (PCV 2), porcine reproductive and respiratory syndrome (PRRS) virus and <i>Salmonella typhimurium</i> .		屏東縣家畜疾病防所
255	Vaccine-induced canine distemper	gray foxes	國立台灣大學獸醫學系
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	台灣大學獸醫學系
	52. Aspergillosis	Goslings	屏東縣家畜疾病防治所
	53. Intracavitary aspergilloma and cavitary tuberculosis, lung.	Human	羅東聖母醫院

寄生蟲	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
	138	1.Aspergillus spp. encephalitis and myocarditis 2.Demyelinating canine distemper encephalitis	Dog	台灣大學獸醫學系
	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	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 Toxocara canis larvae migration	Dog	臺灣養豬科學研究所
	139	Disseminated strongyloidiasis	Human	花蓮佛教慈濟綜合醫院
	141	Eosinophilic meningitis caused by Angiostrongylus cantonensis	Human	台北榮民總醫院病理檢驗部
	156	Parastrongylus cantonensis infection	Formosan gem-faced civet	中興大學獸醫學院
	157	Capillaria hepatica, Angiostrongylus cantonensis	Norway Rat	行政院農業委員會農業藥物毒物試驗所
	202	Colnorchiasis	Human	高雄醫學院附設醫院
	203	Trichuriasis	Human	彰化基督教醫院
原蟲	204	Psoroptes cuniculi infection (Ear mite)	Rabbit	農業藥物毒物試驗所
	205	Pulmonary dirofilariasis	Human	和信治癌中心醫院
	206	Capillaries philippinesis	Human	和信治癌中心醫院
	207	Adenocarcinoma with schistosomiasis	Human	花蓮佛教慈濟綜合醫院
	4.	Cryptosporidiosis	Goat	臺灣養豬科學研究所

	15.	Amoebiasis	Lemur fulvus	台灣養豬科學研究所
	16.	Toxoplasmosis	Squirrel	台灣養豬科學研究所
	17.	Toxoplasmosis	Pig	屏東技術學院獸醫學系
	51.	Pneumocystis carinii pneumonia	Human	台北病理中心
	57.	Cecal coccidiosis	Chicken	中興大學獸醫學系
	65.	Cryptosporidiosis	Carprine	台灣養豬科學研究所
	211	Avian malaria, African black-footed penguin	Avian	臺灣動物科技研究所
	242	Neosporosis	Cow	國立屏東科技大學獸醫學系
	263	Intestinal amebiasis	Human	彰化基督教醫院病理科
立克次體	229	Necrotizing inflammation due to scrub typhus	Human	佛教慈濟醫院病理科
	251	Scrub typhus with diffuse alveolar damage in bilateral lungs.	Human	佛教慈濟醫院病理科
皮膚	216	Cytophagic histiocytic panniculitis with terminal hemophagocytic syndrome	Human	佛教慈濟綜合醫院病理科
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	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
	151	Osteodystrophia fibrosa	Goat	台灣養豬科學研究所 & 台東縣家畜疾病防治所
	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
	83.	Phagolysosome-overload nephropathy	SD rats	實驗動物繁殖中心
	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	中興大學獸醫學系
	91.	Hypervitaminosis D	Orange-rumped agoutis	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
142	Avian encephalomalacia (Vitamin E deficiency)	Chicken	國立屏東科技大學獸醫學系
159	Hypertrophic cardiomyopathy	Pig	台灣大學獸醫學系
165	Chinese herb nephropathy	Human	三軍總醫院病理部及腎臟科
167	Acute pancreatitis with rhabdomyolysis	Human	慈濟醫院病理科
171	Malakoplakia	Human	彰化基督教醫院
183	Darier's disease	Human	高雄醫學大學病理科
191	1. Polyarteritis nodosa 2. Hypertrophic Cardiomyopathy	Feline	台灣大學獸醫學系
193	Norepinephrin cardiotoxicity	Cat	台中榮總
196	Cardiomyopathy (Experimental)	Mice	綠色四季
212	Kikuchi disease (histiocytic necrotizing lymphadenitis)	Lymphadenitis	耕莘醫院病理科
225	Calcinosis circumscripta, soft tissue of the right thigh, dog	Dog	台灣大學獸醫所
230	Hemochromatosis, liver, bird	Bird	台灣大學獸醫學系
234	Congenital hyperplastic goiter	Holstein calves	屏東縣家畜疾病防治所
236	Hepatic lipidosis (fatty liver)	Rats	中興大學獸醫學病理學研究所
237	Arteriovenous malformation (AVM) of cerebrum	Human	耕莘醫院病理科
244	Organophosphate induced delayed neurotoxicity in hens	Hens	中興大學獸醫學病理學研究所
257	Severe lung fibrosis after chemotherapy in a child with Ataxia-Telangiectasia	Human	慈濟醫院病理科

會員資料更新服務

各位會員：

您好！如果您的會員資料有更新或誤刊情形，麻煩您填妥表格後寄回學會秘書處或電話連絡：

中華民國比較病理學會秘書處

350 苗栗縣竹南鎮頂埔里科東二路 52 號

台灣動物科技研究所動物醫學組 病理室收

Tel: (037) 585872

Fax: (037) 585850

e-mail address: hic01@mail.atit.org.tw

-----中華民國比較病理學會-----

會員資料更改卡

姓 名：_____ 會員類別：☐一般會員

☐學生會員

☐贊助會員

最高學歷：_____

服務單位：_____職 稱：_____

永久地址：_____

通訊地址：_____

電 話：_____傳 真：_____

E-Mail Address：_____

中 華 民 國 比 較 病 理 學 會

誠摯邀請您加入

入 會 辦 法

一、 本會會員申請資格為：

- (一) 一般會員：贊同本會宗旨，年滿二十歲，具有國內外大專院校（或同等學歷）生命科學及其它相關科系畢業資格或高職畢業從事生命科學相關工作滿兩年者。
- (二) 學生會員：贊同本會宗旨，在國內、外大專院校生命科學或其他相關科系肄業者（請檢附學生身份證明）。
- (三) 贊助會員：贊助本會工作之團體或個人。
- (四) 榮譽會員：凡對比較病理學術或會務之推廣有特殊貢獻，經理事會提名並經會員大會通過者。

二、 會員：

- (一) 入 會 費：一般會員新台幣一仟元，學生會員一百元，贊助會員伍仟元，於入會時繳納。
- (二) 常年會費：一般會員新台幣伍佰元，學生會員一百元。

【註：學生會員身份變更為一般會員時，只需繳交一般會員之常年會費】

三、請填妥入會申請表郵寄或傳真方式寄回中華民國比較病理學會秘書處收。地址：

350 苗栗縣竹南鎮頂埔里科東二路 52 號 台灣動物科技研究所動物醫學組 電話：037-585872、傳真 037-585850。