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# Clinicopathological findings and disease staging of feline infectious peritonitis: 51 cases from 2003 to 2009 in Taiwan

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Fifty-one cats histopathologically confirmed to have been naturally infected by feline infectious peritonitis (FIP), were collected to analyse the clinical and laboratory findings and to characterise disease staging. Effusive FIP was found in 33 cats, non-effusive FIP in 12 cats, and mixed-type in six cats. Highly significant decreases in haematocrit and albumin levels and an increase in total bilirubin level were noted in both effusive and non-effusive FIP, at first presentation and before death. In serial blood examinations of the effusive group, anaemia and increases in bilirubin and aspartate aminotransferase (AST) were observed from 2 weeks to 0–3 days before death. The packed cell volume, bilirubin, AST, potassium, and sodium levels were established to predict disease staging and survival time. Cumulative points ranging from 0 to 4, 5 to 11 and excess of 12, indicate that the cat can survive for at least 2 weeks, less than 2 weeks and less than 3 days, respectively.

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**F**eline infectious peritonitis (FIP) is a fatal immune-mediated disease in cats that is caused by feline coronavirus (FCoV) infection. There are two major forms of FIP, an effusive and a non-effusive form. In some cases of non-effusive FIP, body effusion can develop at the terminal stage of the disease and become a mixed-type of FIP upon necropsy.<sup>1</sup> The ante-mortem diagnosis of either type of the disease is often difficult because most of the clinical signs are non-specific. An algorithm for the diagnosis of FIP that includes disease presentation signs, environment, clinical signs, laboratory findings, serological testing, and organism-specific identification has been suggested in the literature.<sup>2</sup> After the diagnosis of FIP, euthanasia is usually recommended. Most of the cats investigated in this study were diagnosed as being in the early stages of FIP at presentation. Due to religious reasons, euthanasia is difficult to perform in Taiwan.

The objectives of this study were to analyse the serial clinical and laboratory manifestations of FIP cases collected over the past 6 years in Taiwan, compare these

cases to other overseas reports, and provide a useful reference for the clinical diagnosis and staging of this disease.

## Materials and methods

### Animals

Eighty-eight cats, conformed to the diagnostic algorithm,<sup>2</sup> with full medical records and positive coronavirus reverse transcriptase-nested polymerase chain reaction (PCR) results, that were highly suspected of being infected with FIP and presented signs of the disease at National Taiwan University Animal Teaching Hospital between June 2003 and January 2009, were enrolled in this study. Fifty-one cats were confirmed to have FIP via pathological confirmation after death and were, therefore, included in the analysis. The medical records of the 51 confirmed cases were included in this study for further analysis. Six cases were excluded from the disease course and survival time analysis because of a non-disease-associated accident or a non-expected severe neurological reaction to treatment. Each cat's age, breed, and gender, as well as its disease-related history, clinical signs, physical findings, survival time, blood test results, and diagnostic tests, were recorded. All cats were grouped

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into the non-effusive, effusive, or mixed-type group based on histopathological confirmation after necropsy. All of the affected cats were also confirmed by a PCR test to be infected with coronavirus, using samples that included body effusions: nasal, tonsil, conjunctival, and rectal swabs while the animals were alive, and different organ tissues after necropsy. The complete blood counts, leukocyte differential counts, blood smear (stained by Liu's stain) and biochemistry (including total bilirubin, albumin, total protein, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, glucose, sodium, potassium, and chloride levels) of the 51 cats included in this study were regularly collected before death. Survival time was calculated from diagnosis until death or from diagnosis until euthanasia because of extremely poor clinical and laboratory findings.

Whole blood, body effusion, or nasal/oral/conjunctiva/rectal swab suspensions were collected, prepared and screened for FCoV by reverse transcriptase-PCR as described by Lin et al and Herrewegh et al, respectively.<sup>3,4</sup>

### Statistical analysis

Two of the disease-type groups were compared at a time using independent sample *t*-tests. All three disease-type groups were compared using a one-way analysis of variance (ANOVA). In the statistical analyses, a  $P < 0.05$  was considered significant. The paired *t*-test was also used to statistically differentiate between the disease-type groups in blood examinations. Statistical analyses were performed using SPSS 12.0 (SPSS, Chicago, IL, USA) and SAS 9.1 (SAS, Cary, NC, USA).

## Results

### Subject characteristics

Of the 51 cats with FIP, 38 (74.5%) were less than 1 year old and 13 (25.5%) were between 1 year and 7 years old. Twenty-two of the 38 cats less than 1 year old were younger than 6 months old. The average age of the group was  $1.22 \pm 1.56$  years old, the median was 9 months old, and the mode was 4 months old.

Twenty-six of the 51 (51%) cats were purebred, including the Persian (13), Scottish Fold (seven), American Shorthair (two), Russian Blue (two), England Fold (one), and Siamese (one) breeds. The other 25 cats were domestic shorthairs (DSHs).

Most of the purebred cats (20/26, 76.9%) were younger than 1 year old (12 of them were less than 6 months old). A total of 18/25 (72%) DSHs infected with FIP were younger than 1 year old (10 of them were less than 6 months old). Of the 51 cats with FIP, 29 (56.9%) lived with other cats (ranging from one to six other cats). Nine of the 29 (31%) affected families had

another one or two cats that also died from FIP. Eight of the 51 (15.7%) cats with FIP had another sibling die from FIP.

The clinical findings obtained in this study varied considerably between cats. The most frequently observed findings at first presentation included a reduced appetite (33), fever (31), depression (25), abdominal distension (14), uveitis (13), diarrhoea (11), panting (seven), weight loss (five), weakness (one), ataxia (one), and paralysis (one). Effusive FIP was found in 30/51 cats (58.8%), whereas non-effusive FIP was diagnosed in 12/51 cats (23.5%). The remaining nine cats were suspected to have non-effusive FIP at the initial diagnosis and effusive FIP later in their development of signs and were finally confirmed at pathology to have mixed-type FIP. Seven out of 12 (58.3%) of the non-effusive FIP-diagnosed cats simultaneously exhibited ocular changes, in comparison to only 5/30 (16.7%) effusive FIP-diagnosed cats.

In the effusive FIP group, the average survival time after presentation was  $21.3 \pm 19.9$  days, with a survival range of 1–99 days. The average survival time of the non-effusive group was  $38.4 \pm 48.8$  days, with a survival range from 1 to 171 days. The mixed-type group exhibited longer survival times in comparison to the other two groups, with an average survival time of  $110.9 \pm 172.2$  days and a survival range of 7–477 days. The average survival time of the mixed-type group was significantly longer than that of the effusive group ( $P = 0.018$ ).

### Clinicopathological findings

Six of the 51 cats were excluded because of unexpected accidents. Serial blood examinations, which were obtained from the beginning of disease presentation until immediately before death, were collected for the following analysis (Table 1). Of the 45 cats, 27 were classified as having effusive FIP, 11 as having non-effusive FIP, and seven as having mixed-type FIP.

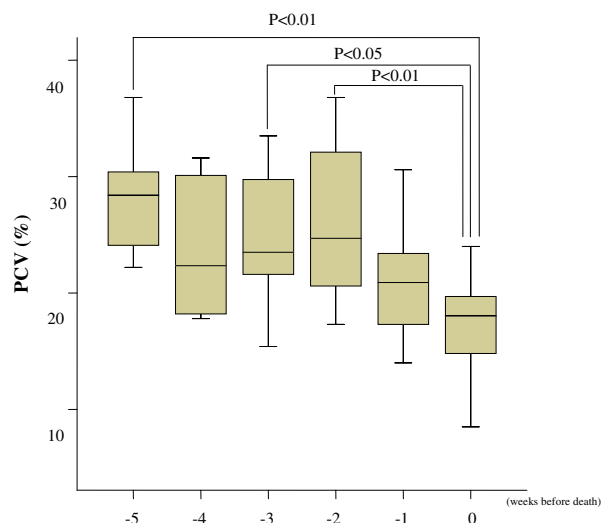
### Haematology

No blood parasites in the blood smear or positive autoagglutination were observed in the full haematological analyses of the 45 cats with FIP at their first presentation, during their therapy and before their death. Thirty cats (66.7%) exhibited mild to moderate anaemia at first presentation (21/27 [77.8%] in the effusive group, 5/11 [45.5%] in the non-effusive group, and 4/7 [57.1%] in the mixed-type group), whereas all of the cats exhibited moderate to severe anaemia by the time of their final examination before death (Table 1). In the serial blood examinations in the effusive group, the haemoglobin (Hb), packed cell volume (PCV), and red blood count (RBC) decreased with disease staging. Red blood cell count-related data dramatically decreased 2 weeks before death, whereas Hb decreased from  $8.4 \pm 2.1$  to  $5.5 \pm 1.2$  g/dl, PCV from  $25.8 \pm 6.3$  to  $17.2 \pm 4.3\%$ , and RBCs from  $5.78 \pm 1.43$  to  $3.85 \pm 1.00 \times 10^6/\mu\text{l}$  (Fig 1 and Table 2).

**Table 1.** Blood examinations of the 45 cats with FIP at first presentation and before death.

	First presentation		0–3 days before death		Normal range
	Mean ± SD	%	Mean ± SD	%	
<b>Haematology</b>					
Haemoglobin (g/dl)	8.65 ± 2.4 ( <i>n</i> = 45)		5.64 ± 1.4† ( <i>n</i> = 30)		8–15
Anaemia	6.2 ± 1.1	40	5.5 ± 1.2	96.7	
PCV (%)	26.5 ± 7.0 ( <i>n</i> = 45)		17.0 ± 4.6† ( <i>n</i> = 30)		30–45
Anaemia	22.6 ± 4.9	66.7	17.0 ± 4.6	100	
RBC (10 <sup>6</sup> /μl)	6.06 ± 1.68 ( <i>n</i> = 45)		3.77 ± 1.12† ( <i>n</i> = 30)		5.0–10.0
Anaemia	3.98 ± 0.73	28.9	3.57 ± 0.99	90	
WBC (/μl)	18,531 ± 8356 ( <i>n</i> = 45)		14,303 ± 11,142 ( <i>n</i> = 30)		5500–19,500
Leukocytosis	27,275 ± 6054	37.8	31,729 ± 9345	23.3	
Leukopenia	4050 ± 636	4.4	4600 ± 1183	16.7	
<b>White blood cell difference</b>					
	( <i>n</i> = 39)		( <i>n</i> = 24)		
Neutrophilia	21,624 ± 4782	51.3	25,984 ± 2092	16.7	1925–14,625
Lymphocytosis	15,147	2.6		0	1100–10,725
Lymphopenia	503 ± 290	64.1	347 ± 216*	91.7	
Monocytosis	1390 ± 523	17.9	1192	4.2	0–850
Eosinocytosis	1465 ± 938	5.1		0	0–750
Thrombocytes (×10 <sup>3</sup> /μl)	311 ± 245 ( <i>n</i> = 40)		281 ± 243		300–700
Thrombocytosis	902 ± 202	7.5	807 ± 144	6.7	
Thrombocytopenia	175 ± 78	67.5	90 ± 51	53.3	
<b>Biochemistry</b>					
Total bilirubin (mg/dl)	0.7 ± 1.0 ( <i>n</i> = 36)		2.5 ± 1.3† ( <i>n</i> = 28)		0.1–0.5
Hyperbilirubinaemia	1.6 ± 1.2	36.1	2.8 ± 1.1*	89.3	
Albumin (g/dl)	2.5 ± 0.3 ( <i>n</i> = 45)		2.2 ± 0.4† ( <i>n</i> = 30)		2.2–4.0
Hypoalbuminaemia	2.0 ± 0.1	8.9	1.8 ± 0.3	43.3	
Total protein (g/dl)	8.1 ± 1.4 ( <i>n</i> = 45)		7.3 ± 1.7* ( <i>n</i> = 30)		5.5–7.1
Hyperproteinaemia	8.7 ± 1.2	71.1	8.8 ± 1.2	46.7	
Globulin (g/dl)	5.6 ± 1.3 ( <i>n</i> = 45)		5.1 ± 1.4 ( <i>n</i> = 30)		2.8–5.1
Hyperglobulinaemia	6.4 ± 1.0	57.8	6.4 ± 1.0	43.3	
A/G ratio	0.48 ± 0.13 ( <i>n</i> = 45)		0.45 ± 0.10 ( <i>n</i> = 30)		<0.7
Low A/G ratio	0.46 ± 0.10	95.6	0.44 ± 0.09	96.7	
ALP (U/l)	39 ± 15 ( <i>n</i> = 30)		63 ± 46 ( <i>n</i> = 16)		23–107
Elevated ALP		0	168 ± 23	12.5	
ALT (U/l)	61 ± 69 ( <i>n</i> = 37)		160 ± 177* ( <i>n</i> = 23)		20–107
Elevated ALT	220 ± 119	10.8	302 ± 189	43.5	
AST (U/l)	170 ± 215 ( <i>n</i> = 16)		562 ± 348*		6–44
Elevated AST	170 ± 215	100	562 ± 348	100	
BUN (mg/dl)	22 ± 22 ( <i>n</i> = 37)		34 ± 41 ( <i>n</i> = 24)		15–29
Elevated BUN	62 ± 43	13.5	93 ± 46	25	
Creatinine (mg/dl)	1.1 ± 0.5 ( <i>n</i> = 37)		1.1 ± 1.2 ( <i>n</i> = 24)		0.8–2.4
Elevated creatinine		0	6.2	4.2	
Glucose (mg/dl)	140 ± 36 ( <i>n</i> = 41)		116 ± 48* ( <i>n</i> = 28)		74–159
Hyperglycaemia	192 ± 29	22	182 ± 29	21.4	
Hypoglycaemia	69	2.4	53 ± 20	17.9	
Potassium (mmol/l)	3.9 ± 0.8 ( <i>n</i> = 34)		3.5 ± 1.0 ( <i>n</i> = 28)		3.5–5.8
Hypokalaemia	2.5 ± 0.1	17.6	2.8 ± 0.4	53.6	
Sodium (mmol/l)	154 ± 7 ( <i>n</i> = 34)		152 ± 12 ( <i>n</i> = 27)		150–165
Hyponatraemia	145 ± 3	26.5	145 ± 3.5	55.6	
Chloride (mmol/l)	117 ± 9 ( <i>n</i> = 17)		112 ± 7 ( <i>n</i> = 15)		112–129
Hypochloraemia	96 ± 6	11.8	107 ± 4	53.3	
Na/K ratio	41.24 ± 9.43 ( <i>n</i> = 34)		45.83 ± 11.96 ( <i>n</i> = 27)		

\*Significantly (*P* < 0.05) different from the value obtained at first presentation.†Significantly (*P* < 0.01) different from the value obtained at first presentation.



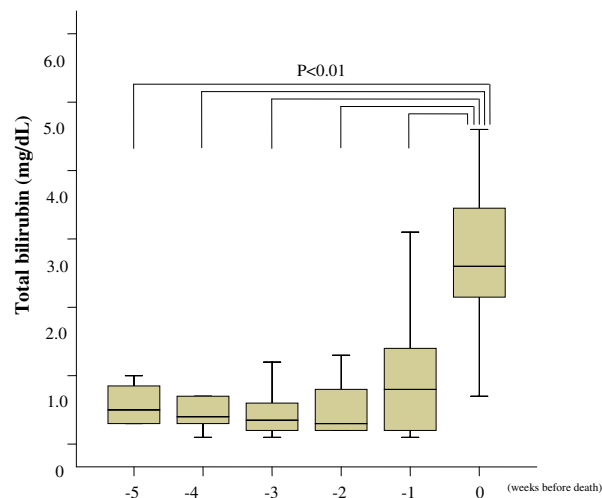
**Fig 1.** Comparison of serial haematocrit levels in cats with effusive FIP. The *x*-axis represents the weeks before death. Starting from the origin, the first point marked '-5' indicates 5 weeks before death, whereas the last point marked '0' indicates 0–3 days before death. The *y*-axis represents haematocrit level. Haematocrit levels dramatically decreased beginning 2 weeks before death. Significant differences were noted between 0–3 days and 2 weeks ( $P < 0.01$ ), between 0–3 days and 3 weeks ( $P < 0.05$ ), and between 0–3 days and 3 weeks, between 0–3 days and 4 weeks, and between 0–3 days and 5 weeks ( $P < 0.01$ ) before death.

### Biochemistry

Serial plasma biochemistry analyses were performed in 45 cats (Table 1).

At first presentation, 13/36 cats (36.1%) exhibited hyperbilirubinaemia, which increased to 89.3% (25/28) just before death. Of these 13 cats, 11 were infected with effusive-type FIP and the remaining two were infected with mixed-type FIP. In 3/11 effusive-type cats, total bilirubin levels were greater than 2.2 mg/dl. At final examination, 100% of the effusive group exhibited hyperbilirubinaemia, and 14 of the cats had bilirubin levels in excess 2.2 mg/dl, whereas only two cats in the non-effusive group and four cats in the mixed-type group exhibited such high bilirubin levels. In the serial blood examinations of the effusive group, bilirubin levels were observed to significantly increase from  $1.0 \pm 0.9$  to  $2.8 \pm 1.2$  mg/dl 1 week prior to death ( $P < 0.01$ ) (Fig 2 and Table 2).

Only 4/45 cats (8.9%) exhibited hypoalbuminaemia at first presentation, whereas 13/30 cats (43.3%) exhibited hypoalbuminaemia ( $2.2 \pm 0.4$  g/dl) at their last examination. There was a significant difference in albumin concentration between the initial presentation and last examination ( $P < 0.01$ ). A total of 32/45 (71.1%) cats exhibited hyperproteinaemia at first presentation, in comparison to 14/30 cats (46.7%) at the final examination. The total protein concentration significantly decreased from  $8.1 \pm 1.4$  g/dl at first presentation to  $7.3 \pm 1.7$  g/dl before death ( $P < 0.05$ ). The



**Fig 2.** Comparison of serial total bilirubin in cats with effusive FIP. The *x*-axis represents the weeks before death. Starting from the origin, the first point marked '-5' indicates 5 weeks before death, whereas the last point marked '0' indicates 0–3 days before death. The *y*-axis represents total bilirubin concentration. Total bilirubin concentration dramatically increased beginning 1 week before death. Significant differences ( $P < 0.01$ ) were noted between 0–3 days and 1 week, between 0–3 days and 2 weeks, between 0–3 days and 3 weeks, between 0–3 days and 4 weeks, and between 0–3 days and 5 weeks before death.

A/G ratio was below 0.7 in 95.6% of the cats at first presentation and in 96.7% of the cats at their last examination. The A/G ratio means were  $0.46 \pm 0.10$  and  $0.44 \pm 0.09$  at the first presentation and final examination, respectively.

Hepatic enzyme concentrations were observed to increase as the disease progressed. ALT levels significantly increased from  $61 \pm 69$  U/l at first presentation to  $160 \pm 177$  U/l before death ( $P < 0.05$ ). According to the serial blood examination of the effusive group, AST levels were observed to significantly increase from  $141 \pm 48$  U/l to  $673 \pm 322$  U/l at 1 week before death (Table 2).

Six of 34 cats (17.6%) exhibited hypokalaemia at first presentation. More cats (15/28, 53.6%) exhibited abnormal potassium concentrations at their last examination than at their first presentation. A total of 9/34 (26.5%) cats exhibited hyponatraemia at first presentation, in comparison to 15/27 (55.6%) cats at their last examination (Table 1). Abnormal sodium and potassium concentrations were observed in all three groups.

### Reverse transcriptase-nested PCR for coronavirus

Coronavirus was most effectively detected in pleural effusion (9/9, 100%) and ascites (17/18, 94.4%). In addition, rectal swabbing exhibited higher detection rates in both effusive (18/30, 60%) and non-effusive (12/18, 66.7%) groups in comparison to nasal (4/15,

**Table 2.** Serial haematological and biochemical findings in cats with effusive FIP.

	Last examination (0–3 days before death)		One week before death		Two weeks before death		Normal range
	Percentage	Mean $\pm$ SD	Percentage	Mean $\pm$ SD	Percentage	Mean $\pm$ SD	
Haemoglobin (g/dl)		5.5 $\pm$ 1.2		7.0 $\pm$ 1.6		8.4 $\pm$ 2.1*	8–15
Anaemia	100 (20/20)	5.5 $\pm$ 1.2	76.5 (13/17)	6.3 $\pm$ 0.9	44.4 (8/18)	6.5 $\pm$ 0.8	
PCV (%)		17.2 $\pm$ 4.3		21.7 $\pm$ 5.0		25.8 $\pm$ 6.3*	30–45
Anaemia	100 (20/20)	17.2 $\pm$ 4.3	88.2 (15/17)	20.5 $\pm$ 3.9	72.2 (13/18)	22.7 $\pm$ 4.2	
Red cell count ( $10^6/\mu\text{l}$ )		3.85 $\pm$ 1.00		4.92 $\pm$ 1.29		5.78 $\pm$ 1.43*	5.0–10.0
Anaemia	90 (18/20)	3.7 $\pm$ 0.9	58.8 (10/17)	4.03 $\pm$ 0.71	27.8 (5/18)	4.00 $\pm$ 0.73	
Total bilirubin (mg/dl)		2.8 $\pm$ 1.2		1.0 $\pm$ 0.9*		0.5 $\pm$ 0.4*	0.1–0.5
Hyperbilirubinaemia	100 (19/19)	2.8 $\pm$ 1.2	57.1 (8/14)	1.6 $\pm$ 0.8	40 (6/15)	1.0 $\pm$ 0.3	
Albumin (g/dl)		2.2 $\pm$ 0.4		2.3 $\pm$ 0.3		2.5 $\pm$ 0.3	2.2–4.0
Hypoalbuminaemia	45 (9/20)	1.9 $\pm$ 0.3	29.4 (5/17)	2.0 $\pm$ 0.1	5.6 (1/18)	1.8	
Total protein (g/dl)		6.9 $\pm$ 1.2		7.3 $\pm$ 0.8		8.1 $\pm$ 0.9	5.5–7.1
Hyperproteinaemia	35 (7/20)	8.2 $\pm$ 0.7	52.9 (9/17)	7.9 $\pm$ 0.7	86.7 (13/15)	8.4 $\pm$ 0.6	
AST (U/l)		673 $\pm$ 322		141 $\pm$ 48*		103 $\pm$ 63*	6–44
Elevated AST	100 (6/6)	673 $\pm$ 322	100 (7/7)	141 $\pm$ 48	85.7 (6/7)	117 $\pm$ 56	
Potassium (mmol/l)		3.5 $\pm$ 1.1		4.2 $\pm$ 0.6		4.3 $\pm$ 0.8	3.5–5.8
Hypokalaemia	52.6 (10/19)	2.7 $\pm$ 0.4	0 (0/15)		13.3 (2/15)	3.0 $\pm$ 0.5	
Sodium (mmol/l)		150 $\pm$ 7		154 $\pm$ 6		156 $\pm$ 4	150–165
Hyponatraemia	57.9 (11/19)	145 $\pm$ 3	26.7 (4/15)	147 $\pm$ 4	13.3 (2/15)	147 $\pm$ 3	

\*Significantly ( $P < 0.01$ ) different from the last value obtained before death.

26.7%), oral (4/16, 25%), and conjunctival (4/42, 9.5%) samples.

## Discussion

Cats aged less than 2 years were the most significantly FIP-affected age group according to a worldwide survey.<sup>5</sup> Norris and Pesteanu-Somogyi reported that 55% of 42 FIP-infected cats and 67% of 60 FIP-infected cats, respectively, were less than 2 years old.<sup>6,7</sup> This result is consistent with our findings where 88.2% of 51 FIP-infected cats were less than 2 years old. Furthermore, 38 of the diseased cats were less than 1 year old, and 22 of these 38 cats were younger than 6 months old. This phenomenon may be due to the fact that most kitten purchases and adoptions from animal shelters in Taiwan involve cats that are 2–3 months old. In the current study, the oldest cat diagnosed with FIP was 7 years old, and the average of age of diagnosis was  $1.22 \pm 1.56$  years. This finding is not consistent with earlier studies, which have reported a secondary increased incidence in cats aged 14–15 years.<sup>8</sup> A lower older cat population in Taiwan in comparison to other countries could explain this discrepancy.

In this study, there was no significant difference in representation between purebred (49%) and DSH (51%) cats. The most commonly observed purebred cat breeds with FIP were Persians and Scottish Folds in the study, the former being the most popular purebred type in Taiwan. The first Scottish Fold FIP case was diagnosed in June 2007, and seven more Scottish Fold cases were among the 21 following cases diagnosed as of

January 2009. Prior to June 2007, no other FIP diagnoses involving Scottish Fold cats had been reported.<sup>6,7</sup> FIP has been reported to occur most often in cats from catteries, pet shops, and multi-cat households. Furthermore, certain bloodlines and intra-breed mating may more strongly predispose cats to FIP than the breeds themselves.<sup>2,9</sup> All of the purebred cats involved in this study were purchased from pet shops. In the current study, 15.7% of the diseased cats had siblings who had died from FIP, indicating that a heredity predisposition may exist. In addition, Scottish Fold cats appeared to be over-represented in this study, which could be a result of the small Scottish Fold breeding population in Taiwan; however, this correlation requires further study.

Our results disagree with those obtained by Norris, who reported that 45% of her 42 cases were effusive FIP and 55% were non-effusive FIP, suggesting that the effusive form is not as frequently observed as the non-effusive form in Australia.<sup>7</sup> In the current study, 58.8% of the 51 cases were effusive FIP, 23.5% were non-effusive FIP, and 17.6% were mixed-type FIP. Our observations in Taiwan mostly agree with the findings of Lutz and Harmann,<sup>10,11</sup> who observed that the effusive form was more common than the non-effusive form.

There was no significant difference ( $P = 0.07$ ) in the average survival times of effusive and non-effusive FIP cats; however, mixed-type FIP cats survived significantly longer ( $110.9 \pm 172.2$  days) than the effusive FIP cats ( $P = 0.018$ ). One of the accidentally killed cats survived nearly 5 months (139 days) after being diagnosed with effusive FIP from an immunofluorescent assay of ascites. Interestingly, the volume of ascites

gradually decreased during therapy (the cat received 0.5 mg/kg of prednisone, once daily, 0.5 mg/kg of benazepril, once daily, and human interferon  $\alpha$ ). The cat died due to acute lung bleeding and shock. During the necropsy, approximately 20 ml of ascites and FIP-associated granulomatous lesions on the liver were observed.

Six cats in the mixed-type FIP group originally had non-effusive FIP; five of them developed ascites and one developed pleural effusion 2 to 19 days before death at an average of 9.7 days. These FIP cats also exhibited a concomitant aggravation of clinical signs. All of the PCR tests of the effusion obtained from these cats were positive. One cat was diagnosed with non-effusive FIP at 1.5 years old, and the disease was controlled with prednisolone and human interferon  $\alpha$  for about 1 year. After that year, the cat exhibited waxing and waning clinical signs, and nelfinavir was added to control virus replication.<sup>12</sup> Three months later, the cat presented with ascites and survived 477 days after therapy. Cat 6 was treated with prednisolone, nelfinavir, and interferon, and survived for 181 days. According to Pedersen's report, the dry form of FIP sometimes develops into effusive FIP, as has primarily been observed in cases of artificial laboratory infection;<sup>5,9</sup> this has also been observed in naturally infected cats in this study.

Non-regenerative anaemia has been reported as a common finding in many chronic feline diseases and is commonly observed in cats with FIP.<sup>13</sup> One study has reported that 60% of FIP-diseased cats have anaemia, with 2/42 FIP cats dying of acute haemolytic anaemia.<sup>7</sup> In the current study, no cats were observed to have acute haemolytic anaemia; however, 66.7% of the cats exhibited mild to moderate anaemia at first presentation, which increased to 100% at their last examination before death. There were significant differences in the haematological examinations between the first presentation and the last examination. In our serial blood observation of the effusive group, Hb, PCV, and RBC decreased with disease stage and displayed the most significant decrease 2 weeks before death. The PCV count 3 days before death was significantly different from the PCV counts 2, 3, and 5 weeks before death. The reasons for progressing anaemia were most likely malnutrition and long-term energy consumption. We could not find any significant differences in reticulocyte counts between the time of disease presentation and the time just prior to death. The use of interferon has been described to induce anaemia<sup>14</sup>; however, in this study, cats treated with interferon exhibited the same anaemia as those receiving no interferon treatment.

In the current study, hyperbilirubinaemia was observed in 36.1% (13/36) of the cats at first presentation, which significantly increased to 89.3% (25/28) of the cats before death. Approximately 45.8% of effusive FIP-diseased cats exhibited hyperbilirubinaemia at first presentation in comparison to 100% before death. None of the cats in the non-effusive FIP group exhibited hyperbilirubinaemia at first presentation and only two

developed hyperbilirubinaemia before death. A greater prevalence of hyperbilirubinaemia was noted in the effusive group relative to the other two groups. In the serial blood examination of the effusive group, there were significant differences in hyperbilirubinaemia between 3 days before death and 1, 2, 3, 4, and 5 weeks before death. Therefore, hyperbilirubinaemia could be used as an additional parameter to predict poor prognosis and to serve as an indicator for disease stage, especially in the effusive group. The cause of hyperbilirubinaemia in FIP cats is not clearly understood.<sup>1,7,13</sup> Hyperbilirubinaemia is frequently a reflection of hepatic necrosis despite the fact that ALP and ALT activities are often not as increased as dramatically in hepatic necrosis as they are with other liver diseases, such as cholangiohepatitis and hepatic lipidosis.<sup>2</sup> In this study, hyperbilirubinaemia was not well correlated with hepatic necrosis in any of the icteric cats. Some cats with icterus did not exhibit any obvious hepatic necrotic lesions. Furthermore, hyperbilirubinaemia could be caused by haemolysis as a result of secondary immune-mediated haemolytic anaemia; however, in our observation, there was no evidence of immune-mediated haemolytic anaemia. Bilirubin is sometimes increased in cats with FIP without evidence of haemolysis, liver disease, or cholestasis. It has been speculated that bilirubin metabolism and excretion into the biliary system are compromised in cats with FIP.<sup>1</sup>

According to the serial examination of the effusive group, we developed assessment criteria for the prediction of survival time. A total of 92.2% of the effusive cases satisfied the assessment criteria (Table 3). Cumulative points ranging from 0 to 4 indicate that the cat can survive for at least 2 weeks. Cumulative points ranging from 5 to 11 indicate a survival time

**Table 3.** Algorithm for the staging of effusive FIP.

Parameter	Range	Score*
PCV (%)	>26	0
	20–26	2
	<20	4
AST (U/l)	<150	0
	150–300	2
	>300	4
Total bilirubin (mg/dl)	≤0.5	0
	0.6–2.2	2
	>2.2	4
Potassium (mmol/l)	4.0–5.8	0
	3.0–3.9	2
	<3.0	4
Sodium (mmol/l)	156–165	0
	150–155	2
	<150	4

\*0–4: survival time more than 2 weeks; 5–11: survival time less than 2 weeks; ≥12: survival time less than 3 days.

of less than 2 weeks, whereas cumulative points in excess of 12 indicate a survival time of less than 3 days. These criteria could be used to assess survival time at first presentation in a clinical setting.

In conclusion, anorexia and a fever that was not responsive to antibiotics were the most frequently observed clinical signs in each type of FIP. In non-effusive FIP, uveitis was more often observed than neurological signs. A low A/G ratio (<0.7), anaemia, elevated hepatic enzyme levels, and hyperbilirubinaemia were the most frequently observed abnormal laboratory findings. Assessment criteria, including PCV, bilirubin, AST, potassium, and sodium levels, can be used to predict disease staging and survival time. The results obtained in the present study provide clinically useful parameters for the ante-mortem diagnosis of FIP.

## References

- Hartmann K. Feline infectious peritonitis. *Vet Clin North Am Small Anim Pract* 2005; **35**: 39–79.
- Addie DD, Jarrett O. Feline coronavirus infections. In: Greene GE, ed. *Infectious diseases of the dog and cat*. 3rd edn. Oxford: Elsevier, 2006: 88–102.
- Lin CN, Su BL, Wang CH, Hsieh MW, Chueh TJ, Chueh LL. Genetic diversity and correlation with feline infectious peritonitis of feline coronavirus type I and II: a 5-year study in Taiwan. *Vet Microbiol* 2009; **136**: 233–9.
- Herrewegh AA, de Groot RJ, Cepica A, Egberink HF, Horzinek MC, Rottier PJ. Detection of feline coronavirus RNA in feces, tissues, and body fluids of naturally infected cats by reverse transcriptase PCR. *J Clin Microbiol* 1995; **33**: 684–9.
- Pedersen NC. An overview of feline enteric coronavirus and feline infectious peritonitis virus infection. *Feline Pract* 1995; **23**: 7–22.
- Pesteanu-Somogyi LD, Radzai C, Pressler BM. Prevalence of feline infectious peritonitis in specific cat breeds. *J Feline Med Surg* 2006; **8**: 1–5.
- Norris JM, Bosward KL, White JD, Baral RM, Catt MJ, Malik R. Clinicopathological findings associated with feline infectious peritonitis in Sydney, Australia: 42 cases (1990–2002). *Aust Vet J* 2005; **83**: 666–73.
- Pedersen NC. Feline infectious peritonitis and feline enteric coronavirus infections. *Feline Pract* 1983; **13**: 5–20.
- Pedersen NC. A review of feline infectious peritonitis virus infection: 1963–2008. *J Feline Med Surg* 2009; **11**: 225–58.
- Lutz H, Hauser B, Horzinek MC. Feline infectious peritonitis (FIP): the present state of knowledge. *J Small Anim Pract* 1986; **27**: 108–16.
- Hartmann K, Binder C, Hirschberger J, et al. Comparison of different tests to diagnose feline infectious peritonitis. *J Vet Intern Med* 2003; **17**: 781–90.
- Hsieh LE, Lin CN, Su BL, et al. Synergistic antiviral effect of Galanthus nivalis agglutinin and nelfinavir against feline coronavirus. *Antiviral Res* 2010; **88**: 25–30.
- Sparkes AH, Gruffydd-Jones TJ, Harbour DA. Feline infectious peritonitis: a review of clinicopathological changes in 65 cases, and a critical assessment of their diagnostic value. *Vet Rec* 1991; **129**: 209–12.
- Sleijfer S, Bannink M, Van Gool AR, Kruit WH, Stoter G. Side effects of interferon-alpha therapy. *Pharm World Sci* 2005; **27**: 423–31.

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