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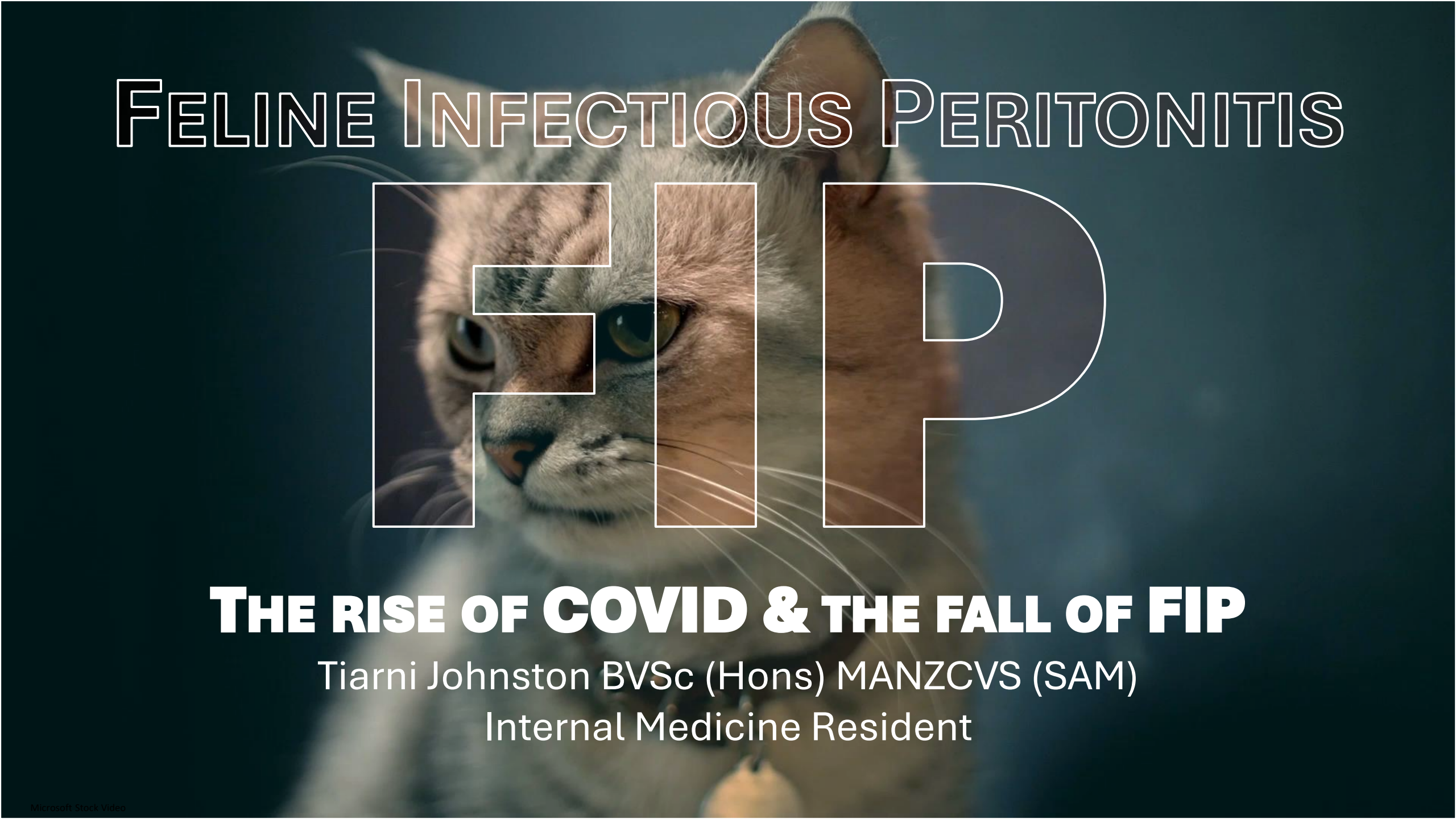
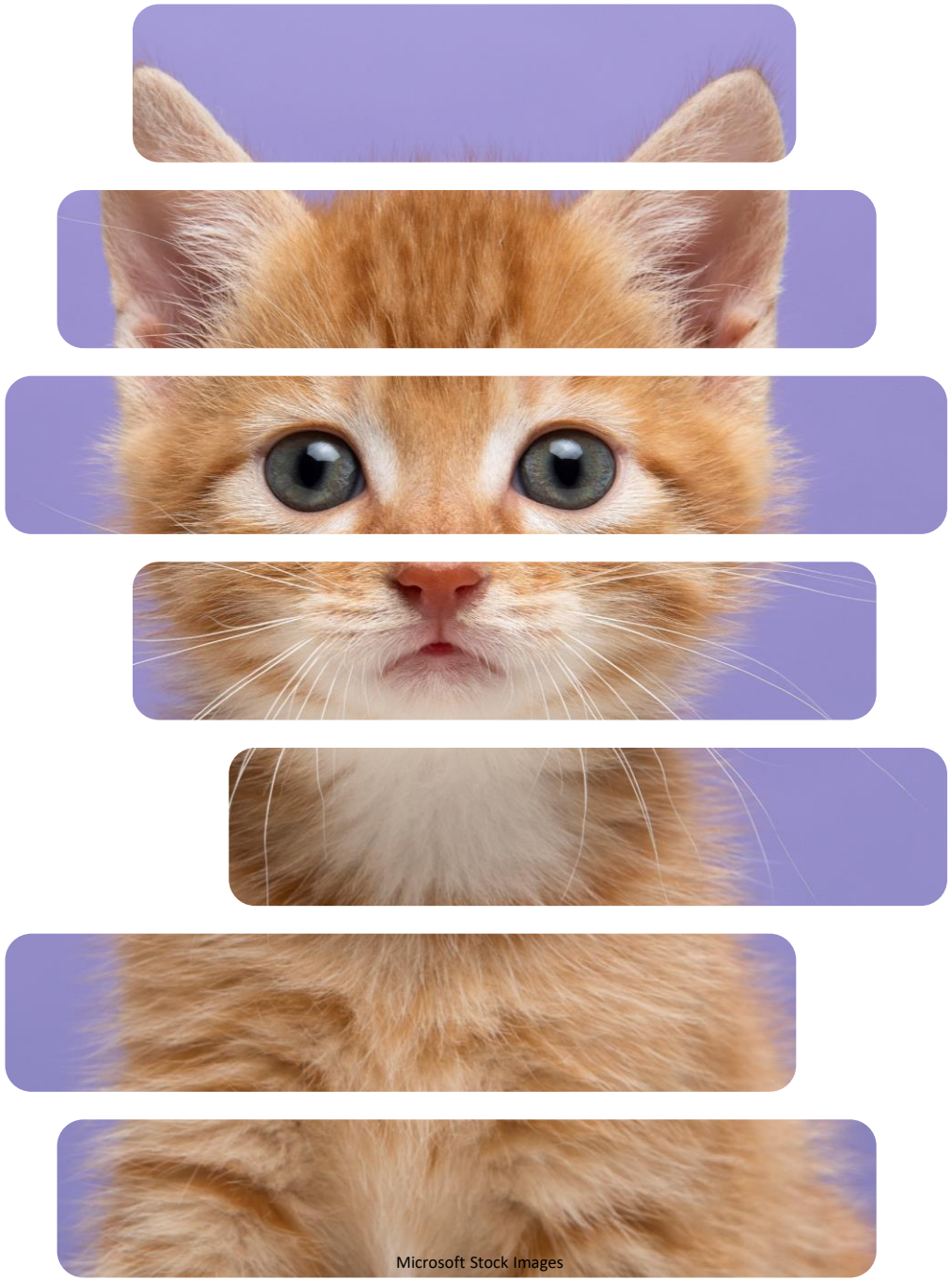

Feline Infectious Peritonitis
FIP
The rise of COVID & the fall of FIP
Tiarni Johnston BVSc (Hons) MANZCVS (SAM)
Internal Medicine Resident
Microsoft Stock Video

Outline

1. What is FIP?
2. Diagnosis
3. Treatment
4. Prognosis
5. Prevention

What is Feline Infectious Peritonitis?

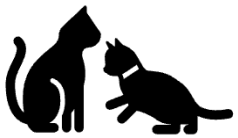


What is feline infectious peritonitis?

Feline Enteric Coronavirus (FECoV)

Epidemiology

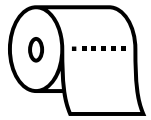
Ubiquitous in cats worldwide.



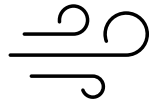
Enzootic in virtually all larger multicat environments

>50% healthy cats & 80% of cats with diarrhoea from high-risk environments = shedders over any given time

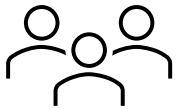
Transmission



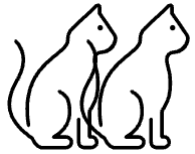
Shared litter trays.



Litter dust on fomites.



Virus on people handling cats.



Direct contact between shedding cats.

What is feline infectious peritonitis?

FECoV Infects 2 Groups of Cats

Increased FECoV replication → increased risk of FIP developing

Kittens at ~9 weeks old (<9 weeks old if high environmental viral load)

Older cats (i.e. 10+ years) associated with a weakening immunity

Disease occurs when exposure is high and innate immune defences are weakened.

Only strong adaptive immune responses will prevent viral replication and possibly disease development.

iStock Images

What is feline infectious peritonitis?

Feline Enteric Coronavirus

Pathogenesis of feline enteric coronavirus infection
Niels C Pedersen, Claire E Allen, Leslie A Lyons

There is a distinct primary stage of infection (~ 7 - 18 months)
→ the highest level of virus shedding occurs during this stage.

Recovery / No Shedding	Persistent Shedding	Intermittent Shedding
(~ 24%)	(~ 38%)	(~ 38%)

Study period performed over 24 months

Of all cats that are infected with FECoV → < 5% develop FIP

What is feline infectious peritonitis?

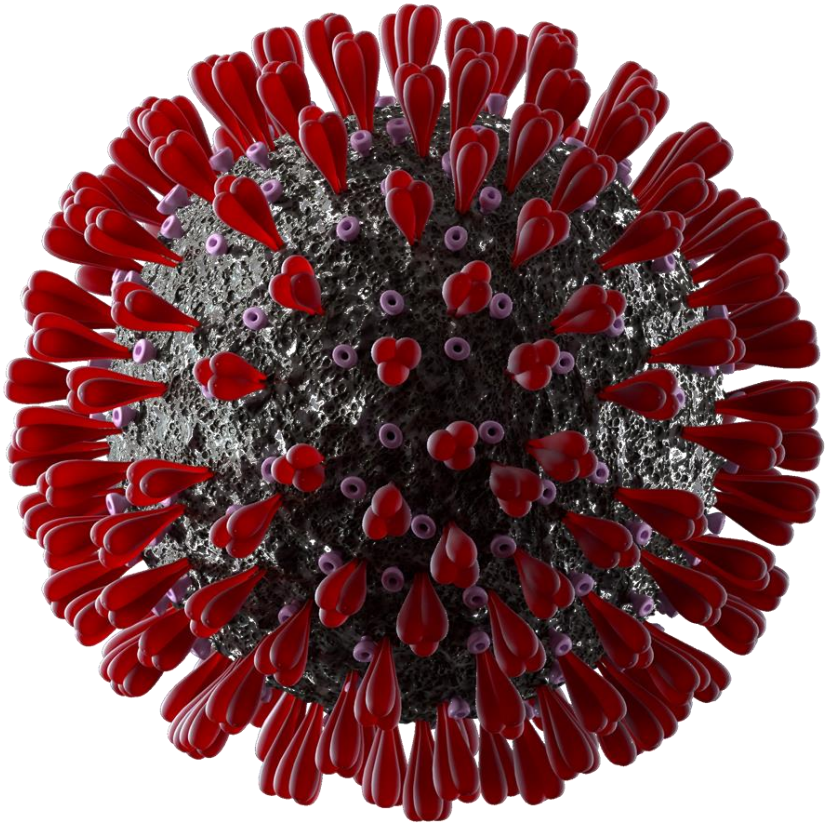
Feline Coronavirus (FCoV) – Biotype One

Feline Enteric Coronavirus

(FECoV)

VERY Contagious

Virus found frequently in the faeces of healthy cats.



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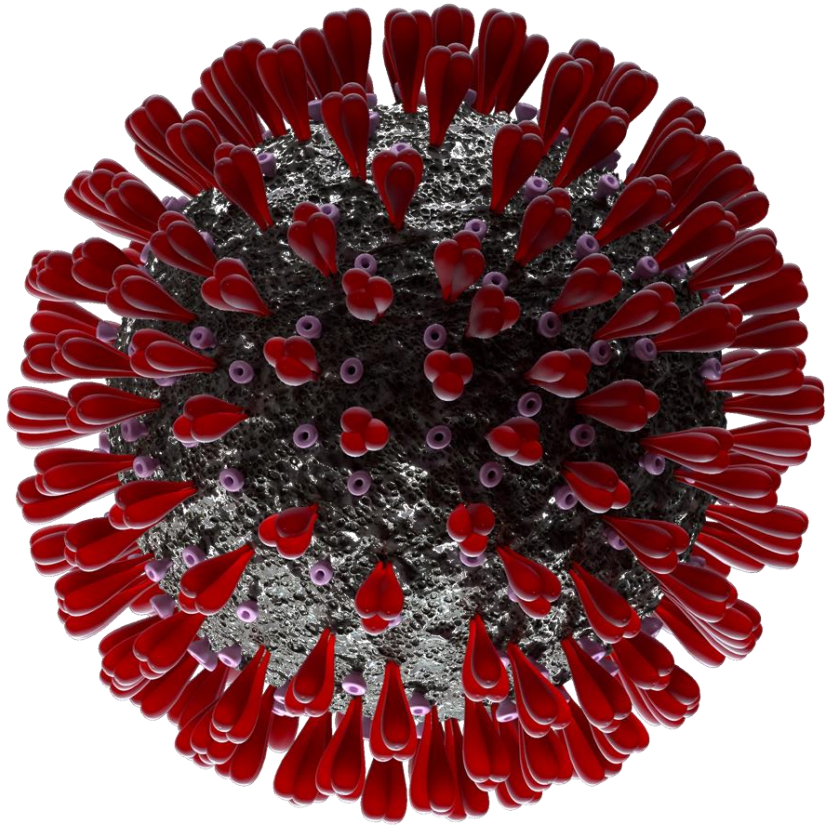
What is feline infectious peritonitis?

Feline Coronavirus (FCoV) – Biotype Two



Feline Infectious Peritonitis

(FIPV)

NOT Contagious

Virus found in tissues and effusions of cats with FIP.

Microsoft stock images

What is feline infectious peritonitis?

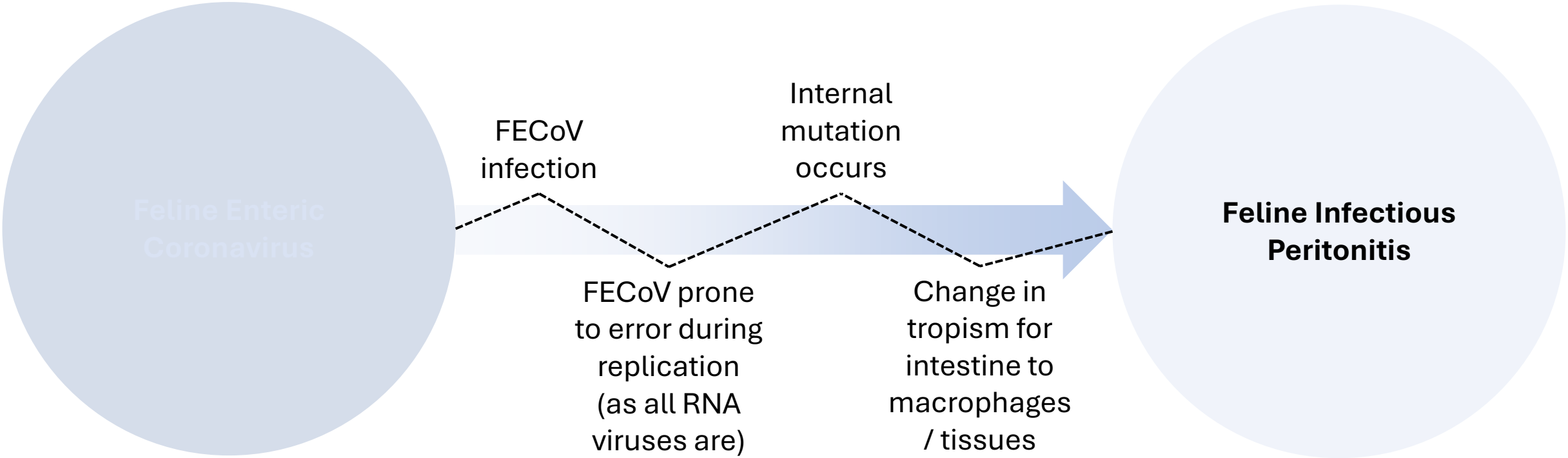
Feline Enteric Coronavirus

So how do we get from FECoV to FIP?

Feline Infectious Peritonitis

What is feline infectious peritonitis?

Internal Mutation Hypothesis

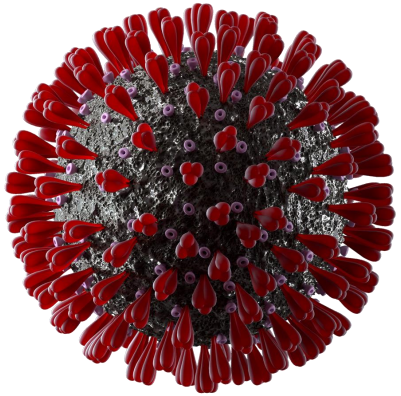


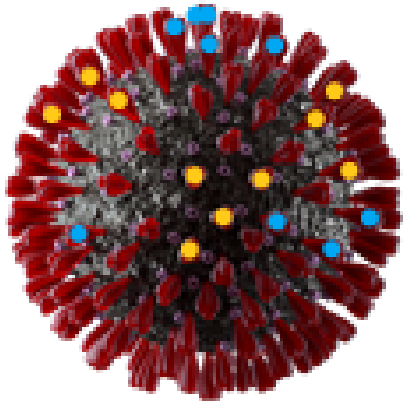
Outbreaks?

Internal Mutation Hypothesis

+

Circulating Strain Hypothesis





Increasing evidence that multiple mutations are required to change tropism.

So, if you have a strain of FECoV already with ≥1 mutations → FIP is more likely to develop in multiple individuals at once.

What is feline infectious peritonitis?

Abdominal Effusion

Effusive "Wet" Form

→ The classic presentation of FIP

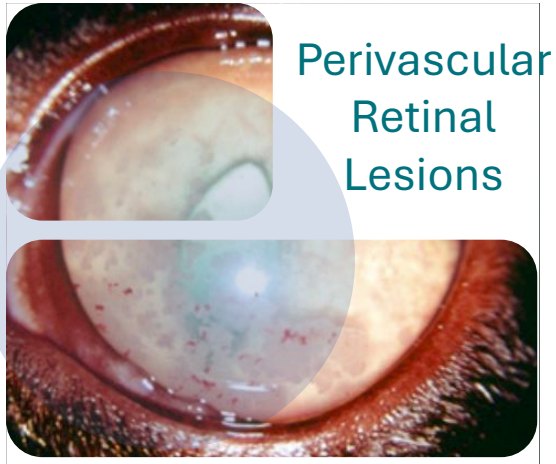
→ Results in a viscous effusion within body cavities

Non-Effusive "Dry" Form

→ Focal and organised granulomatous lesions in organs

→ Mesenteric lymph nodes, caecum, colon, kidney, lungs, pericardium, eyes, brain / spinal cord, and miscellaneous sites.

→ Inflammatory lesions induced by FCoV (pyogranulomatous vasculitis)



Perivascular Retinal Lesions

Keratic Precipitates

How is FIP Diagnosed?

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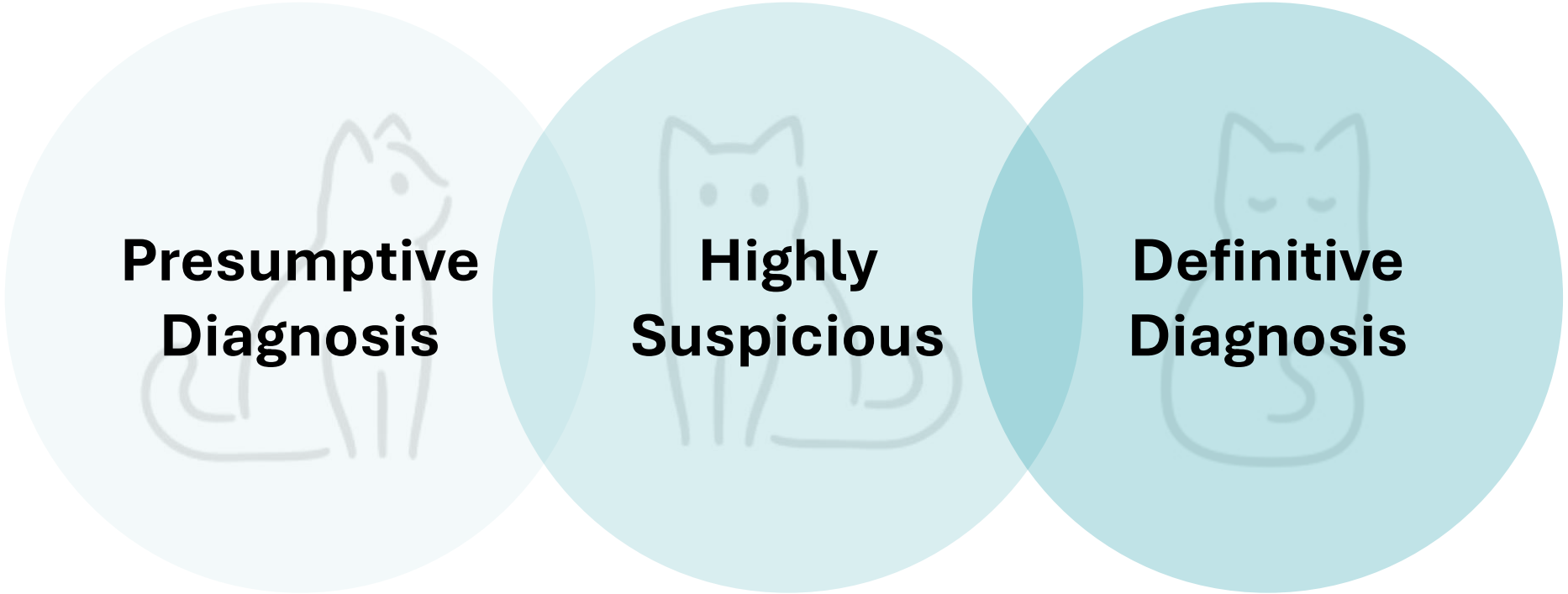
How is FIP Diagnosed?



Presumptive Diagnosis

Baseline Diagnostics:

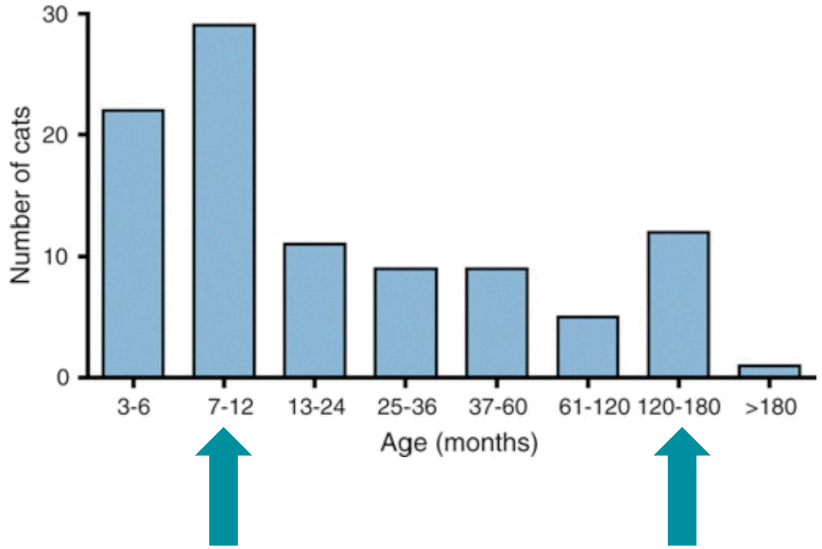
1. Signalment
2. Disease History
3. Physical Examination Abnormalities
4. CBC & Serum Chemistry
5. Effusion/Tissue Assessment

This is often enough for a presumptive diagnosis.

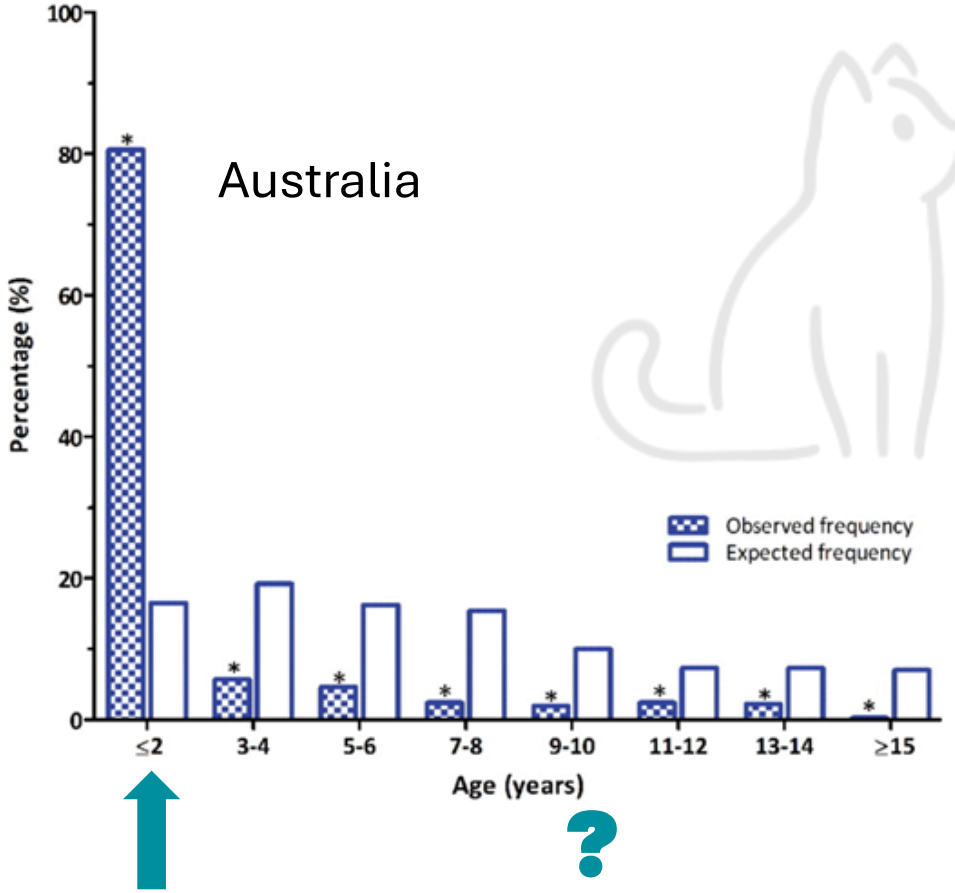
Presumptive Diagnosis

Signalment: Age:

Europe & The Americas



Australia



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Presumptive Diagnosis

Signalment

Breed:

- Cats of any breed or age can develop FIP.
- Often in pedigree cats.

Sex / Neuter Status:

- In some studies, males are more likely to develop FIP than females.

Genetic Factors:

- Inbreeding = the most significant genetic risk factor.

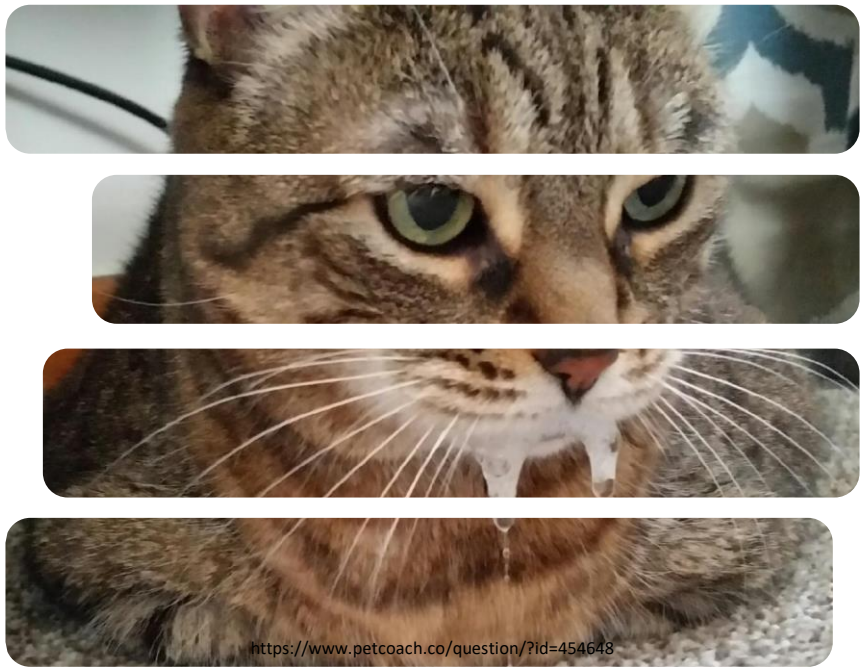
Sphynx Cat Breed Information Purina

Presumptive Diagnosis

Disease History

The median duration of clinical signs before diagnosis is approximately 10 days (Range: 1–210 days) (Coggins, SJ. et al. 2023)

Clinical signs are variable → depending on whether the patient has effusive or non-effusive disease



Presumptive Diagnosis

Retrospective study and outcome of 307 cats with feline infectious peritonitis treated with legally sourced veterinary compounded preparations of remdesivir and GS-441524 (2020-2022)

Samantha S Taylor, Sally Coggins, Emi N Barker, Danièlle Gunn-Moore, Kamalan Jeevaratnam, Jacqueline M Norris, David Hughes, Emily Stacey, Laura MacFarlane, Carolyn O'Brien, Rachel Korman, Gerard McLauchlan, Xavier Salord Torres, Aimee Taylor, Jos Bongers, Laura Espada Castro, Max Foreman, James McMurrough, Bethany Thomas, Emilie Royaux, Isabel Calvo Saiz, Guido Bertoldi, Caroline Harlos, Megan Work, Cameron Prior, Stephanie Sorrell, Richard Malik, Séverine Tasker

Clinical History:

Findings are variable and depend on whether the patient has wet or dry disease.

The findings to the left are based on BOTH presentations combined

Original Article

Clinical Sign	Percentage
Lethargy	93.8
Inappetence	75.5
Weight loss	42.8
Abdominal distension	28.1
Neurological Signs	20.3
Diarrhoea	15
Ocular Signs	13.1
Respiratory Signs	12.1
Vomiting	7.8

Presumptive Diagnosis

Retrospective study and outcome of 307 cats with feline infectious peritonitis treated with legally sourced veterinary compounded preparations of remdesivir and GS-441524 (2020-2022)

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Original Article

jfms Journal of Feline Medicine and Surgery

Physical Examination:

Findings are variable and depend on whether the patient has the wet or dry manifestation of the disease.

The findings to the left are based on BOTH presentations combined

Physical Exam Finding	Percentage
Pyrexia	57.2
Abdominal Effusion	38.9
Poor BCS (<3/9)	38.1
Jaundice	19
Neurologic Deficits	17
Tachypnoea	13.7
Ocular Abnormalities	13.1
Abdominal Mass	10.5
Dyspnoea	5.2
Dull Heart Sounds	5.2

Presumptive Diagnosis

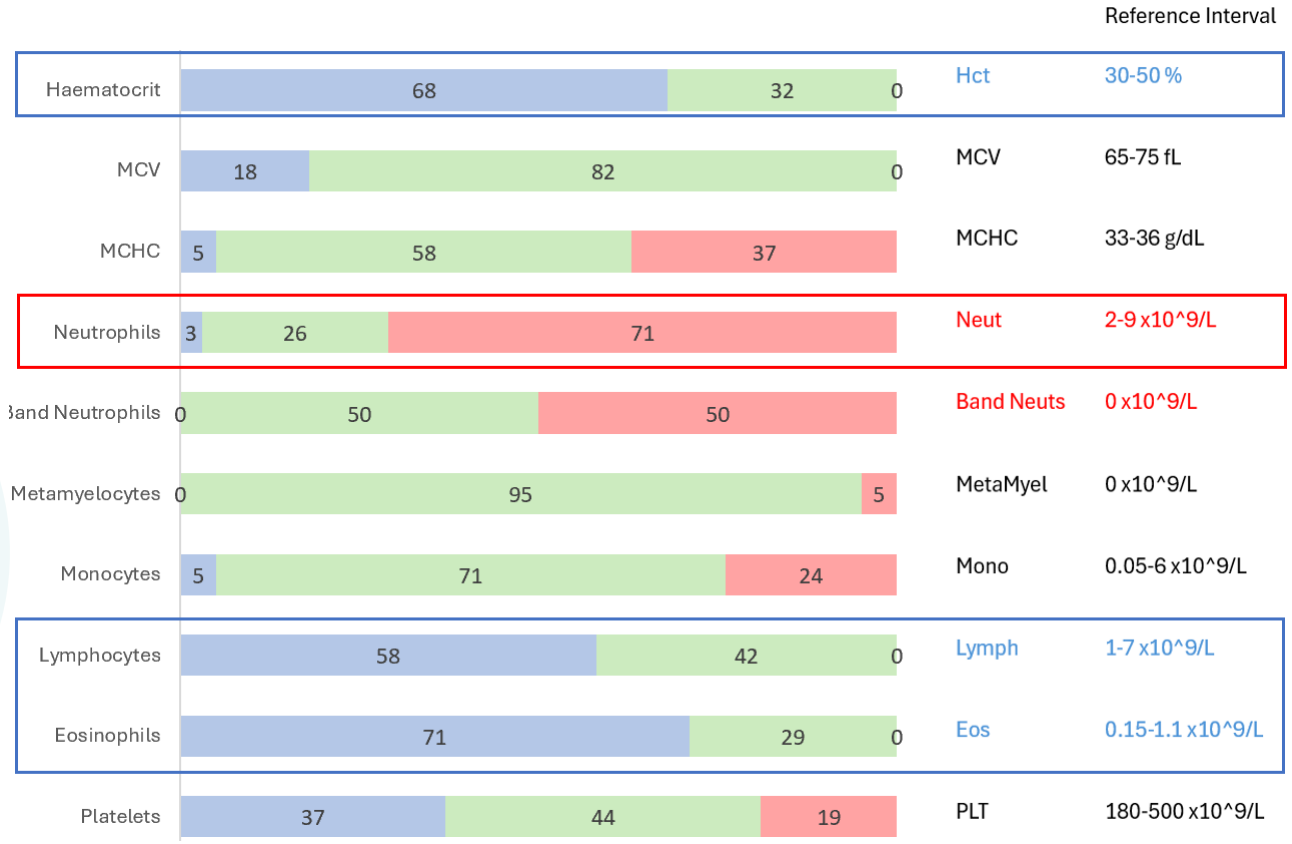
Variability in Clinical Signs of Effusive and Non-Effusive FIP

	Anatomic Location of Disease				% of Cats	
	Peritoneal Cavity	Pleural Cavity	Ocular	Neurological	Effusive	Non-Effusive
One Region	✓				58	30
		✓			11	1
			✓		-	14
				✓	-	22
Two Regions	✓	✓			22	4
	✓		✓		2.8	7
	✓			✓	1.9	-
			✓	✓	-	8
Three Regions	✓	✓	✓		-	2
	✓	✓		✓	<1	3
	✓		✓	✓	<1	2
		✓	✓	✓	<1	-

Table adapted from Greene's Infectious Diseases of the Dog and Cat

Presumptive Diagnosis

Haematological changes in cats with FIP



Anaemia of chronic inflammation

Inflammatory leukogram

% of Cats Below RI

% of Cats Within RI

% of Cats Above RI

Information adapted from Greene's Infectious Diseases of the Dog and Cat

Presumptive Diagnosis

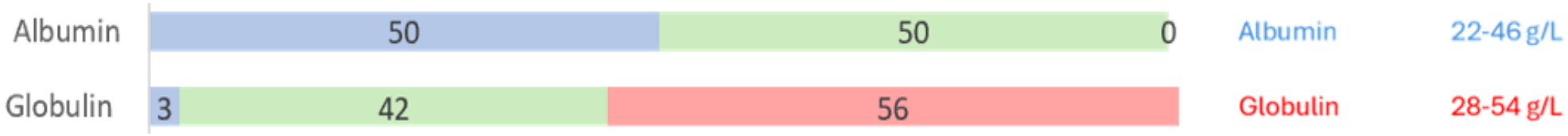
Serum Biochemical changes in cats with FIP

Increased bilirubin

Alb:Glob Ratio

Information adapted from Greene's Infectious Diseases of the Dog and Cat

Presumptive Diagnosis



Albumin : Globulin Ratio

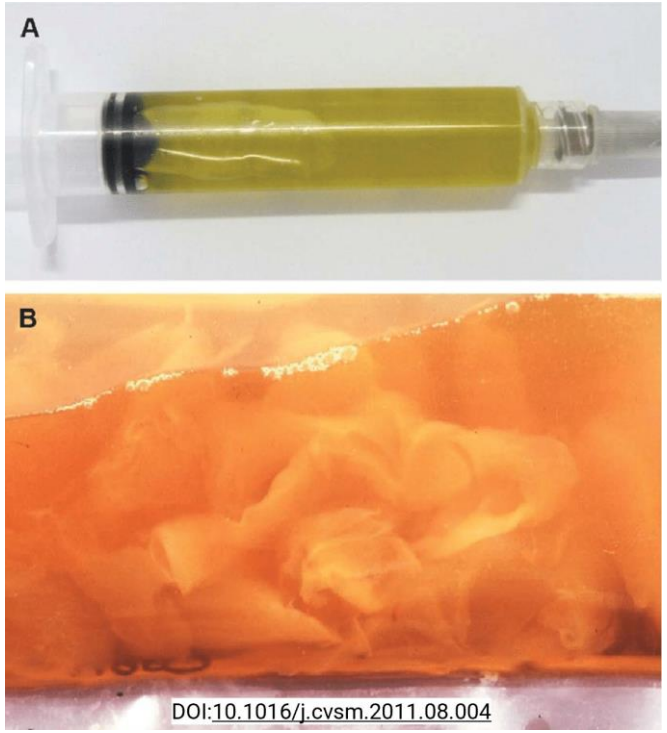
The A:G ratio in FIP cats is frequently below normal (<0.6)

Serum A:G ratio >0.6 → FIP is <u>less likely</u>.
Serum A:G ratio <0.6 → FIP is <u>more likely</u> but not definitive.

The predictive value of the A:G ratio is only dependent on the presence of other clinical findings associated with FIP.

Presumptive Diagnosis

Effusion Analysis:



Free peritoneal or pleural fluid is one of the most diagnostic clinical features in cats with FIP (effusive form).

Classic effusions are:

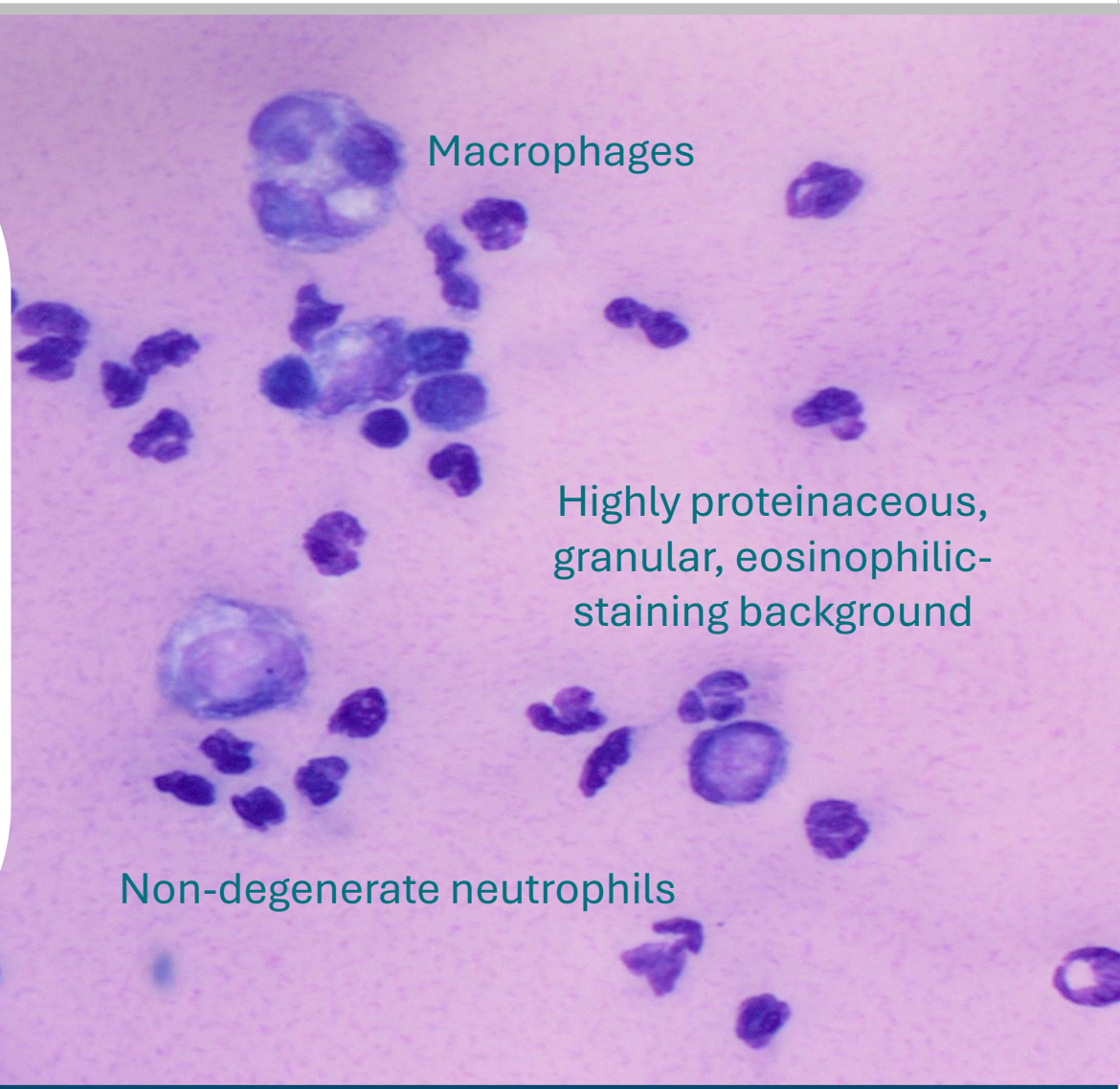
- Yellow tinged (or blue-green)
- Cloudy
- High protein
- WBCC >3000 cells/µL (>3 x 10^9/L)
- Viscous (egg white-like consistency), contains fibrin tags, and frequently forms partial clots when in a serum tube.

Presumptive Diagnosis

Effusion Analysis: Cytology

Typical findings on cytological evaluation of FIP effusion include:

1. A highly proteinaceous, granular, eosinophilic-staining background
2. Non-septic pyogranulomatous inflammation
    1. Macrophages
    2. Non-degenerate neutrophils
    3. Very few lymphocytes



Cytology courtesy of NovaVet Diagnostics

Presumptive Diagnosis

Effusion fluid

Acetic Acid

Image from Green's Infectious Diseases of the Dog and Cat

Adobe Stock Image

Effusion Analysis: Rivalta Test

What is the Rivalta Test?

Rivalta test for the diagnosis of FIP were lower than previously reported except when used in young cats <2 years of age.

- Se 91.3%
- Sp 65.5%
- NPV 93.4%
- PPV 58.4%

Values from Fischer Y, et al. Diagnostic accuracy of the Rivalta test for feline infectious peritonitis. Vet Clin Pathol. 2012 Dec; 41(4): 558–567.

The components in effusions that lead to a positive Rivalta test are unknown (suspect proteins), with positive test results also occurring in cats with bacterial peritonitis or lymphoma.

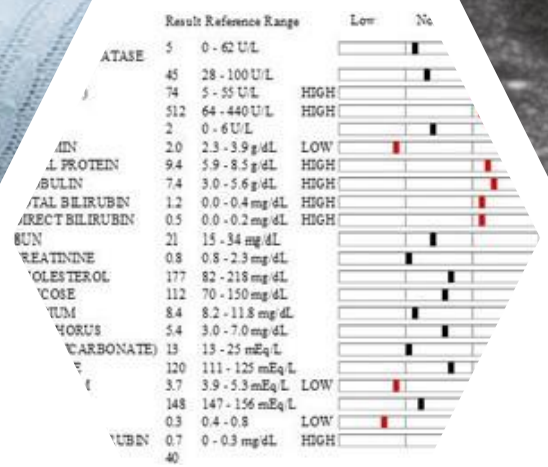
Presumptive Diagnosis

All of these consistent findings are required to make a presumptive diagnosis

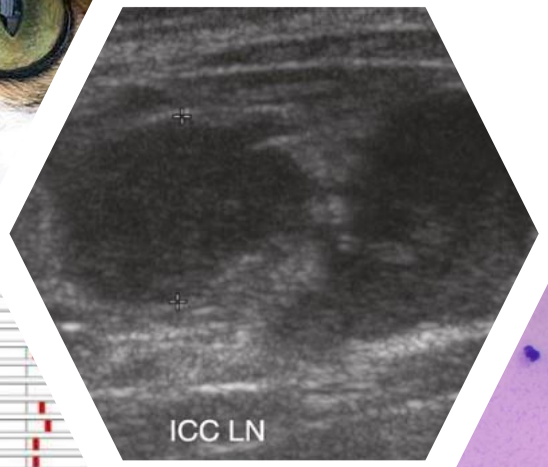
Signalment

Clinical Signs

Physical Exam

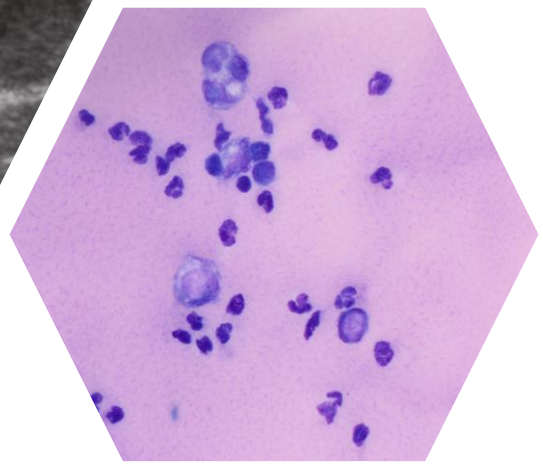


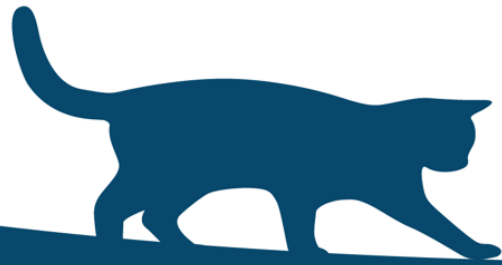
Blood Findings



Imaging Findings

Cytology



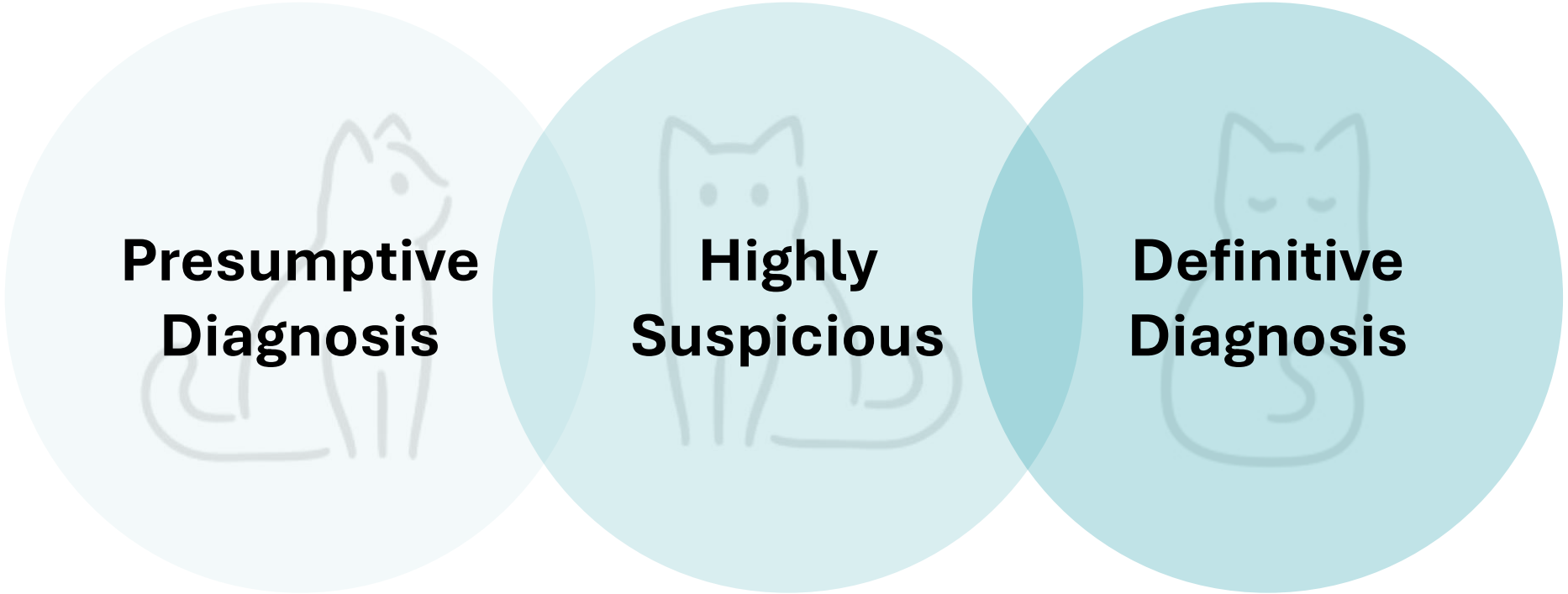


https://cattime.com/cat-breeds/sphynx-cat

History of Feline infectious Peritonitis 1963-2022 – First description to Successful Treatment Niels C. Pedersen
https://www.zoetispetcare.com/blog/article/cat-drooling-a-lot

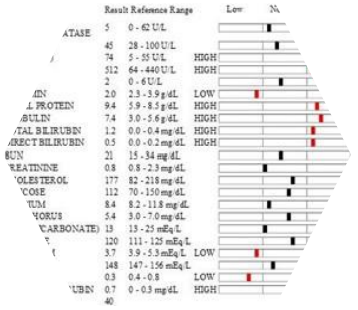
https://allscience.substack.com/p/navigating-fip-diagnostics
Greene's textbook: infectious diseases of the dog and cat

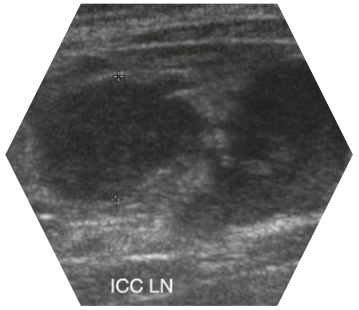
How is FIP Diagnosed?

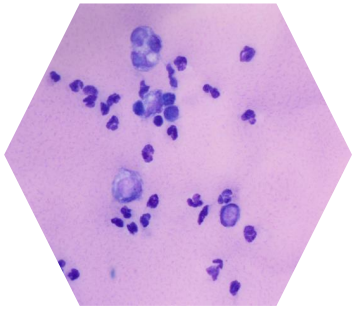


HIGHLY SUSPICIOUS OF FIP







All the factors that make up a presumptive diagnosis
+ “indirect tests” increase the odds that the patient’s clinical signs are due to FIP

HIGHLY SUSPICIOUS OF FIP

FCoV RNA Detection by RT-PCR

REMEMBER: Cats with FIP + healthy cats can intermittently shed FECoV antigen.

PCR testing of faeces for FCoV shedding is of limited value (= FECoV biotype).

Most PCR tests do not differentiate between virulent and avirulent FCoV strains

Recent studies show FCoV RNA in tissues outside the gastrointestinal tract ≠ FIPV
→ avirulent strains may be found in tissues and blood.

Extraintestinal tissues with:

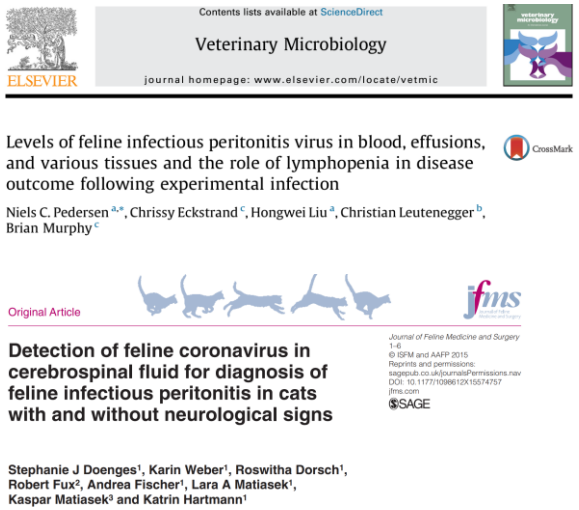
1. High copy numbers = FIP more likely
2. Low copy numbers = FIP less likely

Highly Suspicious of FIP

FCoV RNA Detection by RT-PCR

Sample Type	Sensitivity	Specificity
Peripheral blood mononuclear cells	29%	100%
Serum	15%	86-100%
Cell-free body cavity effusions	89%	89%–100%
CSF	41.5 - 85.7%*	100%

* Sensitivity of cats showing ocular and/or neurological signs – Sensitivity was only 41.5% when considering all cats regardless of clinical presentation.



Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Levels of feline infectious peritonitis virus in blood, effusions, and various tissues and the role of lymphopenia in disease outcome following experimental infection

Niels C. Pedersen [a,*], Chrissy Eckstrand [c], Hongwei Liu [a], Christian Leutenegger [b], Brian Murphy [c]

Original Article

Detection of feline coronavirus in cerebrospinal fluid for diagnosis of feline infectious peritonitis in cats with and without neurological signs

Stephanie J Doenges[1], Karin Weber[1], Roswitha Dorsch[1], Robert Fux[2], Andrea Fischer[1], Lara A Matiasek[1], Kaspar Matiasek[3] and Katrin Hartmann[1]

These sensitivities and specificities are only in association with cats definitively diagnosed with FIP **via other means**.

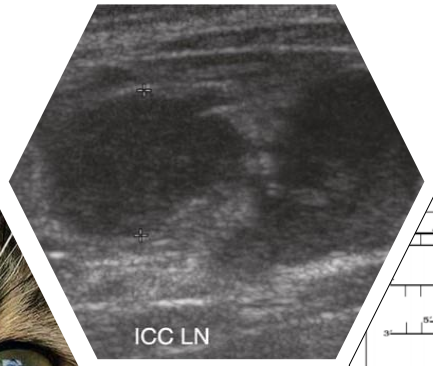
Highly Suspicious of FIP

All of these findings are required to be highly suspicious of FIP

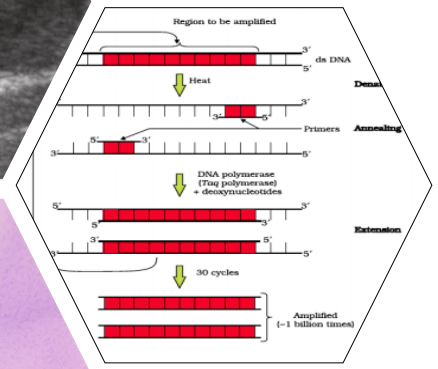
Signalment

Physical Exam

Imaging Findings

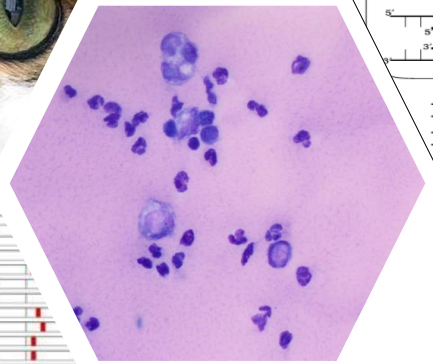


RT-PCR

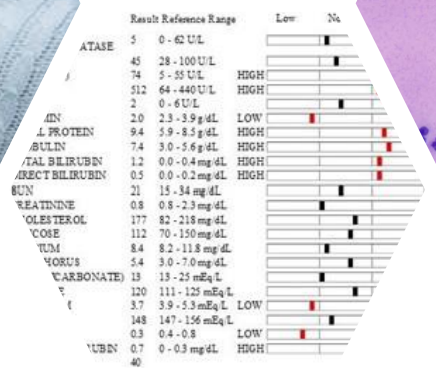


Clinical Signs

Cytology



Blood Findings



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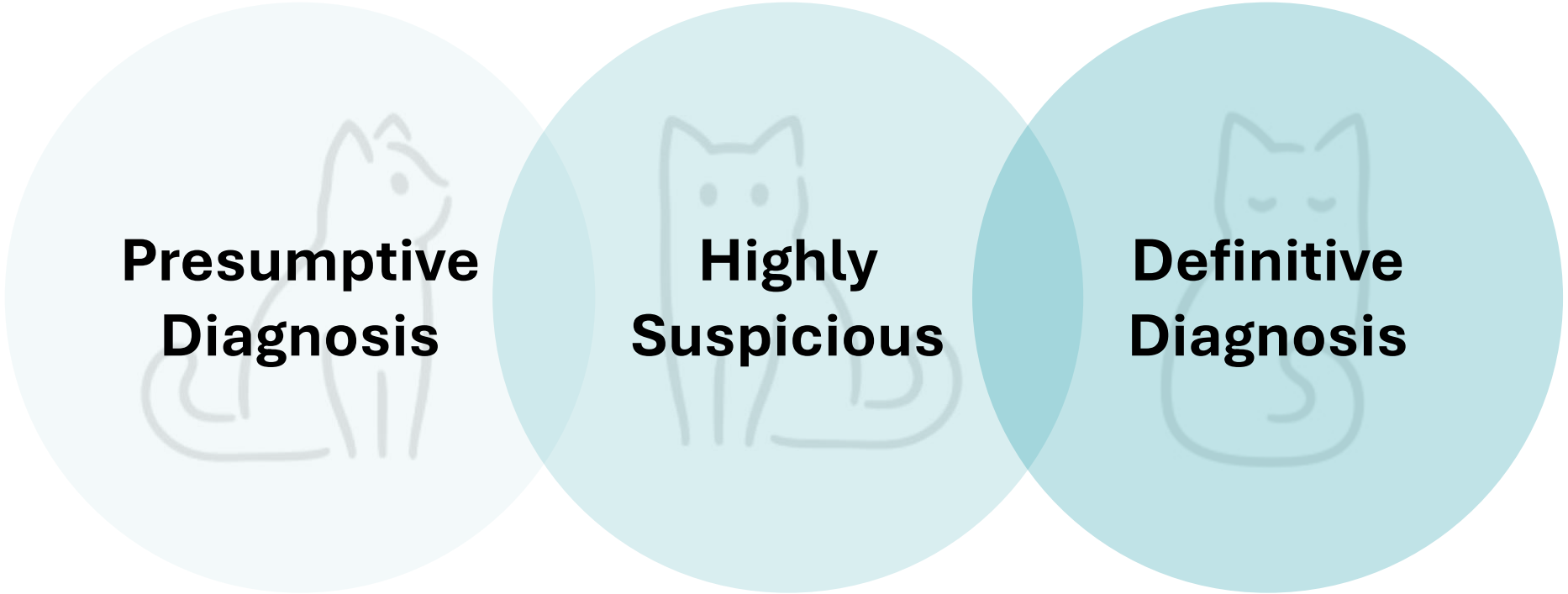
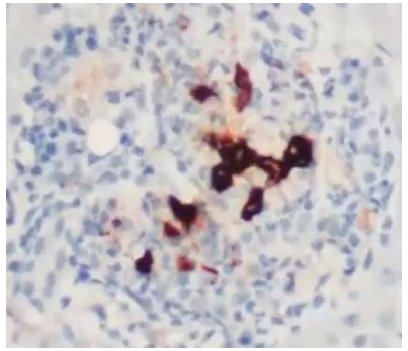
https://allscience.substack.com/p/navigating-fip-diagnostics
Greene's textbook: infectious diseases of the dog and cat

How is FIP Diagnosed?

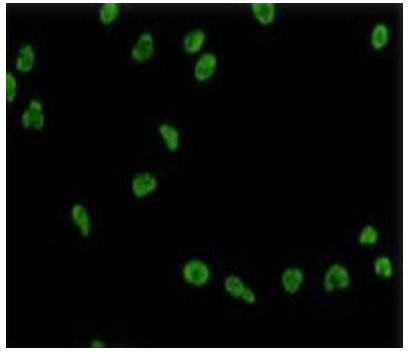


Definitive Diagnosis of FIP

FIP Diagnosis IFA and IHC tests: Veterinary Pathology Diagnostic Services, University of Sydney



Immunohistochemistry



Immunocytochemistry

Tests performed thus far have been “indirect tests” which do not provide a definitive diagnosis.

1. “Indirect Tests” → Increase the odds that the CSx are due to FIP, or
2. “Direct Tests” → attempt to provide a definitive diagnosis

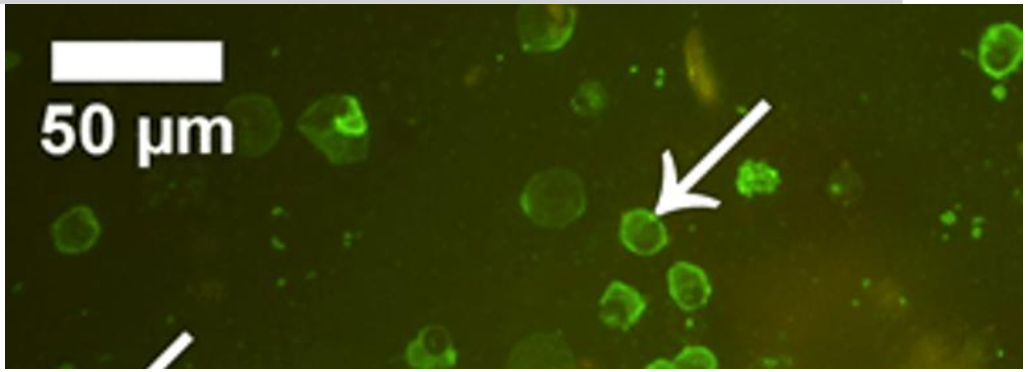
Definitive Diagnosis of FIP

Immunocytochemistry

University of Sydney uses direct immunofluorescence (IFA) of effusion fluid or fine needle aspirates to detect the virus within the cytoplasm of macrophages.

Based on studies performed with the university of Sydney:

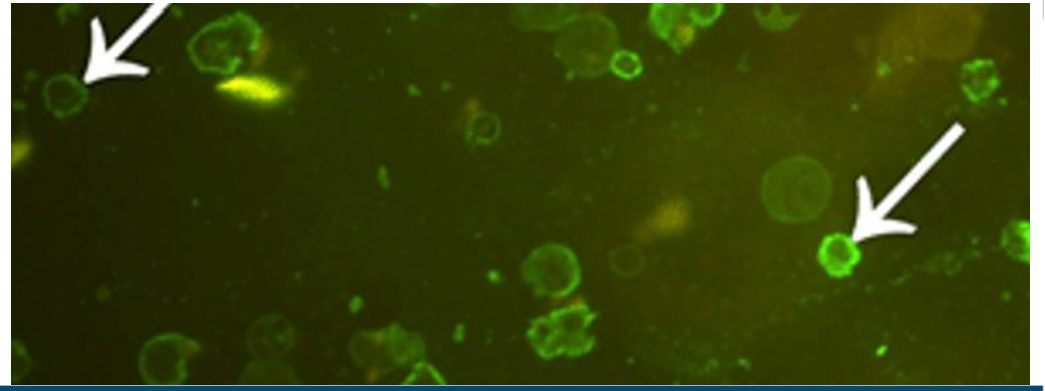
- Specificity: >99%
- Sensitivity: 75%



Immunohistochemical Methods to Diagnose Atraumatic Spleen Rupture in Feline Infectious Peritonitis of Tiger (*Panthera tigris*)

CRISTINA HORHOGEA, VIOREL FLORISTEAN*, MIRCEA LAZAR, CARMEN CRETU, CARMEN SOLCAN
University of Agricultural Sciences and Veterinary Medicine, Faculty of Veterinary Medicine, 8 M. Sadoveanu Alley, 700489, Iasi, Romania

Macrophages and lymphocytes positive for FCoV antibodies (arrows) in pericardial fluid. Direct immunofluorescence test



Definitive Diagnosis of FIP

Example Report

SCHOOL OF VETERINARY SCIENCE
VETERINARY PATHOLOGY DIAGNOSTIC SERVICES

THE UNIVERSITY OF SYDNEY

Direct Immunofluorescence Report

Several cell preparations (cytospins) were made from the fluid submitted. Using a fluorescin labelled antibody against Feline Coronavirus (types I and II), immunofluorescence was performed to identify the presence of the virus within macrophages seen in the fluid. This was **POSITIVE** for feline coronavirus infected macrophages in the fluid.

Protein Level & Albumin/Globulin Ratios

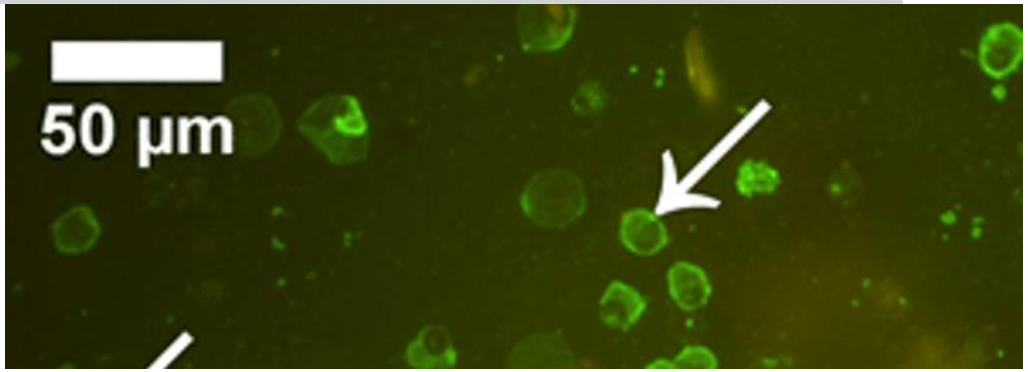
Protein = 73 g/L, Albumin = 16.9 g/L, Globulin = 55.8 g/L. Albumin/globulin ratio = 0.30

CONCLUSION

A diagnosis of FIP is supported by the results of the direct immunofluorescence (IFA) test.

Protein level – a protein level of less than 30g/L is highly unlikely to be FIP. A protein level above 30 g/L can be seen in many diseases including FIP and so is non-specific.

Albumin/globulin ratios in effusion can be useful in the diagnosis of FIP but are not specific for FIP, so must be interpreted in light of all other evidence. Reports of useful cut-off values for A:G ratios in the diagnosis of FIP vary, but in general an A:G ratio of <0.4 makes FIP very likely.



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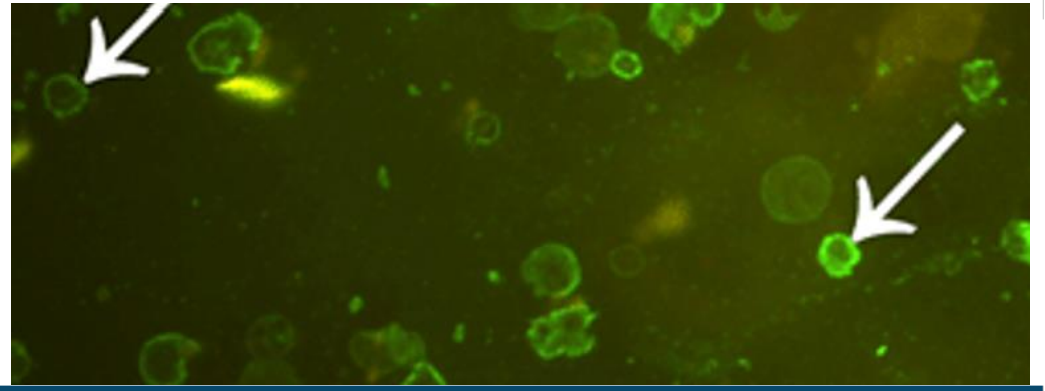


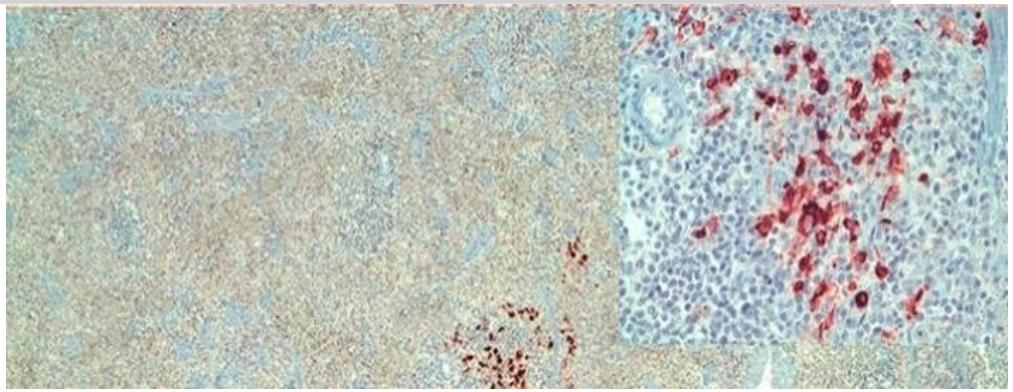
Definitive Diagnosis of FIP

Immunohistochemistry

IHC of tissue samples is considered the gold standard for diagnosing FIP

IHC is recommended when histology is consistent with FIP:

- Sensitivity: 46.2 - 76.9%
- Specificity: 100%



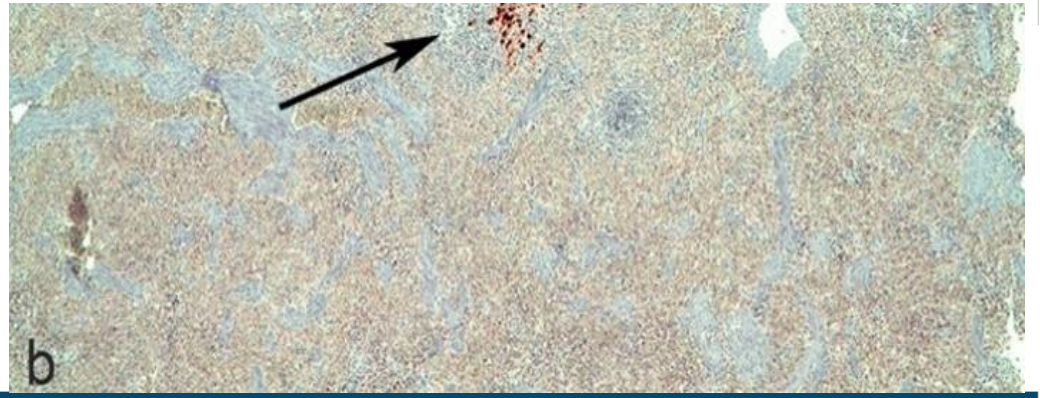
pathogens

MDPI

Article

Concordance between Histology, Immunohistochemistry, and RT-PCR in the Diagnosis of Feline Infectious Peritonitis

Angelica Stranieri [1,2], Donatella Scavone [1,2], Saverio Paltrinieri [1,2,*], Alessia Giordano [1,2], Federico Bonsembiante [3,4], Silvia Ferro [3], Maria Elena Gelain [3], Sara Meazzi [1,2] and Stefania Lauzi [1,2]



Definitive Diagnosis of FIP

IDEXX FIP Virus RealPCR™?

Specific PCR Test
= FIP Virus RealPCR™
= Detects Feline Coronavirus 7b gene and may detect mutations M1058L and S1060A of the spike gene.

The detection of these mutations in a feline tissue sample is strongly supportive of FIP in a cat with consistent clinical history / other diagnostic tests supportive of FIP.

Sensitivity is higher in tissues from inflamed organs and lower in organs not histologically involved

Some examples include:

	Sensitivity	Specificity
Effusion	68.6 - 88.9 %	95.8 – 100 %
Whole Blood	0 – 30 %	100 %

i.e. it cannot be used to exclude FIP

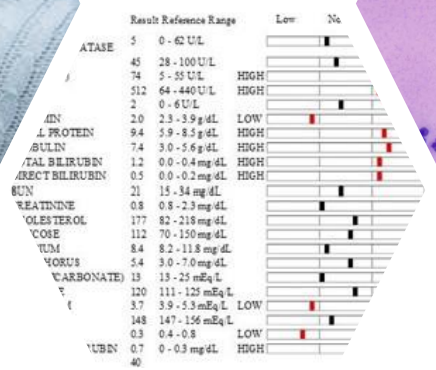
Definitive Diagnosis of FIP

Signalment

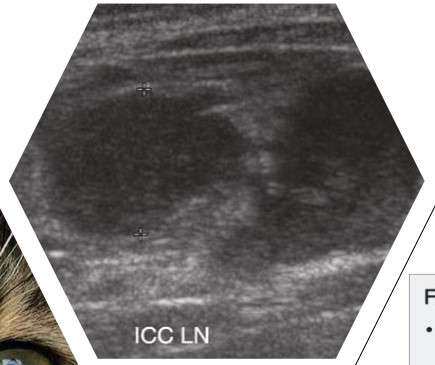
Physical Exam

Clinical Signs

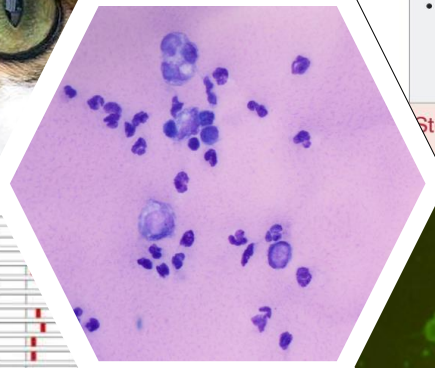
Blood Findings



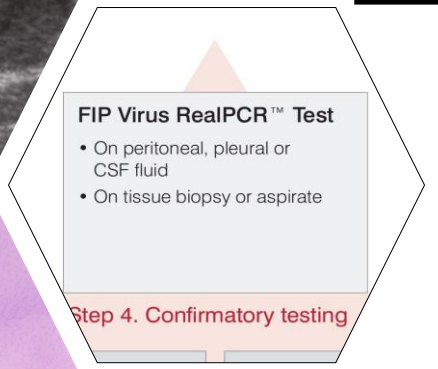
Imaging Findings



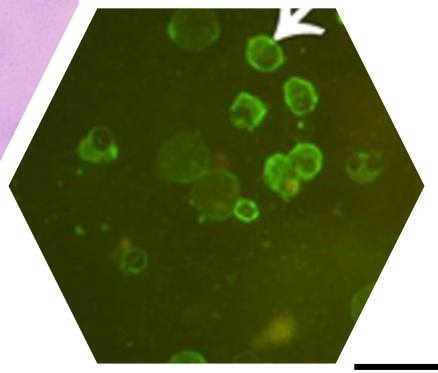
Cytology



FIP RT-PCR



ICC / IHC



The addition of a positive FIP specific PCR **OR** ICC / IHC is needed to make a definitive diagnosis

https://cattime.com/cat-breeds/sphynx-cat

History of Feline infectious Peritonitis 1963-2022 – First description to Successful Treatment Niels C. Pedersen
https://www.zoetispetcare.com/blog/article/cat-drooling-a-lot

https://allscience.substack.com/p/navigating-fip-diagnostics
Greene's textbook: infectious diseases of the dog and cat

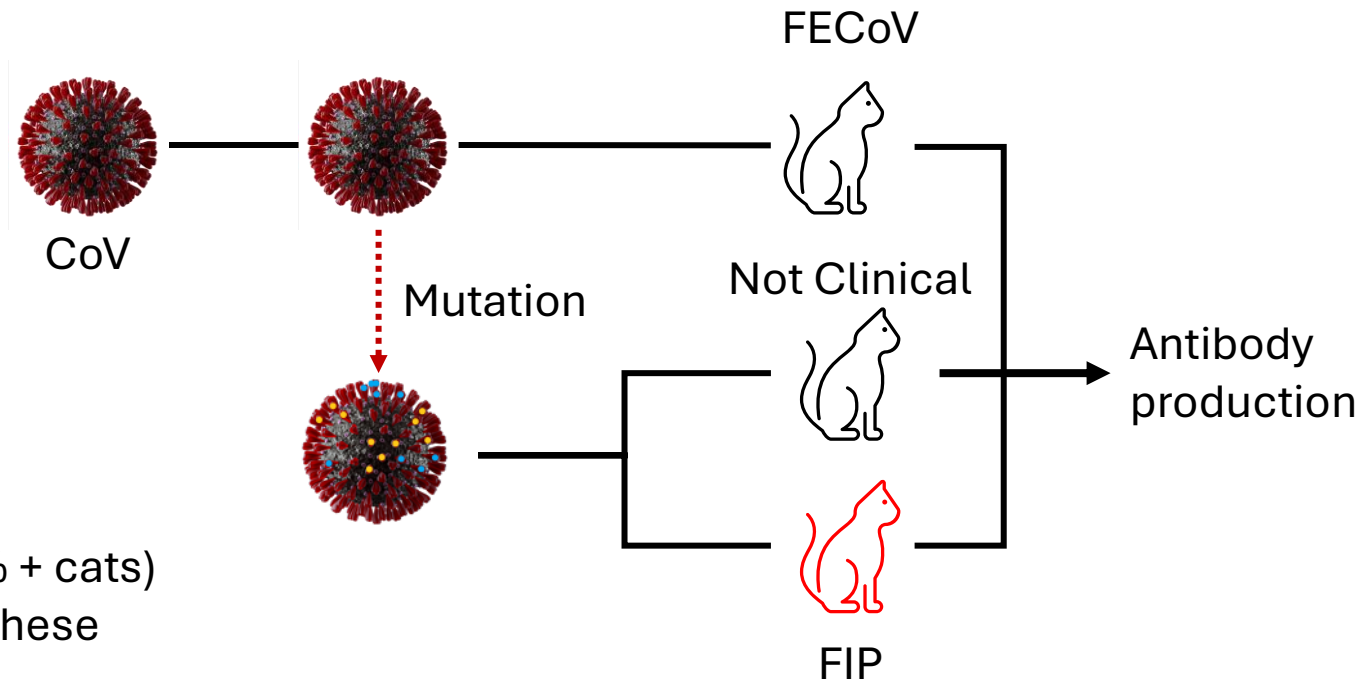
CORONAVIRUS ANTIBODY (AB) TESTING?

The short answer is NO

It's well-accepted that Ab tests <u>cannot</u> differentiate between FECoV and FIPV Abs

Even very high Ab titres in blood are not specific for FIP.

A large proportion of the cat population (80% + cats) have serum **Abs against FCoV**, but most of these cats **never develop FIP**



THE PRESENCE OF ANTIBODIES FOR DIAGNOSING FIP HAS VERY LIMITED SIGNIFICANCE

How is FIP Treated?

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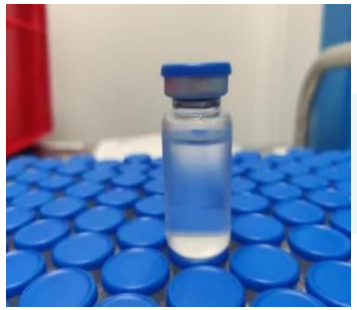
How is FIP Treated?



BOVA: Remdesivir for IV or SC injection

Remdesivir is a protide (nucleotide prodrug) able to diffuse into cells, where it is converted to GS-441524 monophosphate

BOVA: Oral GS-441524 tablets

The basics:

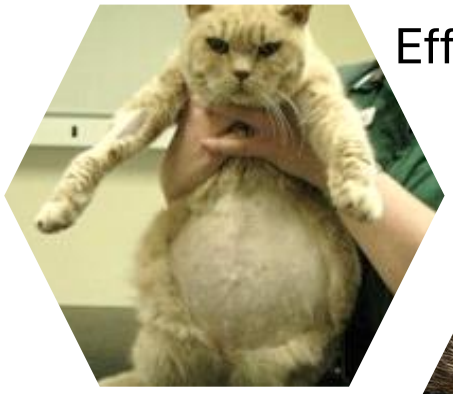
- Drainage of fluid (when necessary)
- Reduction of stress
- Treatment of specific comorbidities (i.e. anti-epileptic medication if seizuring, ocular medications if uveitis is present, etc.).

Antiviral drug therapy:

1. Viral Protease Inhibitor such as GC376
2. Nucleoside Analogues (RNA Transcription Inhibitors)
   → GS-441524 or Remdesivir

How is FIP Treated?

GS-441524 & Remdesivir



Effusive

Ocular

Neurological

An update on treatment of FIP in the UK

Dr. Sam Taylor BVetMed(Hons) CertSAM DipECVIM-CA MANZCVS FRCVS
Prof. Séverine Tasker BVSc BSc DSAM PhD DipECVIM-CA FHEA FRCVS
Prof. Danielle Gunn-Moore BSc(Hon), BVM&S, PhD, MANZCVS, FHEA, FRSB, FRCVS
Dr. Emi Barker BSc BVSc PhD PGCertTLHE DipECVIM-CA MRCVS
Dr. Stephanie Sorrell BVetMed(Hons) MANZCVS DipECVIM-CA MRCVS

Table 1: Summary of dosage recommendations for remdesivir and GS-441524

Clinical presentation	Remdesivir – by injection	GS-441524 – oral
Cats with effusions and without ocular or neurological signs	10 mg/kg once daily	10-12 mg/kg once daily
No effusion and without ocular or neurological signs	12 mg/kg once daily	10-12 mg/kg once daily
Ocular signs present (effusive and non-effusive)	15 mg/kg once daily	15 mg/kg once daily
Neurological signs present (effusive and non-effusive)	20 mg/kg once daily	10 mg/kg **twice** daily (i.e. 20 mg/kg given as a divided dose)

https://www.rochfordvets.co.uk/feline-infectious-peritonitis-a-new-option-for-treatment/ https://sevneurology.com/blog/vestibular-disease-in-cats

How is FIP Treated?

GS-441524 & Remdesivir

Treatment Phase (Weeks 0-12)					
	PEx / Weight	CBC / Chem	UA	Centesis	Retroviral Testing
0	✓	✓	✓	✓ *	✓
2	✓			*	
4	✓			*	
6	✓			*	
8	✓			*	
10	✓			*	
12	✓	✓	✓	*	
Monitoring Phase (Weeks 13-52) – Owner / Patient / Vet Dependent					
14	✓				
18	✓				
22	✓				
26	✓				
38	✓				
52	✓				

* Centesis to be performed only if necessary

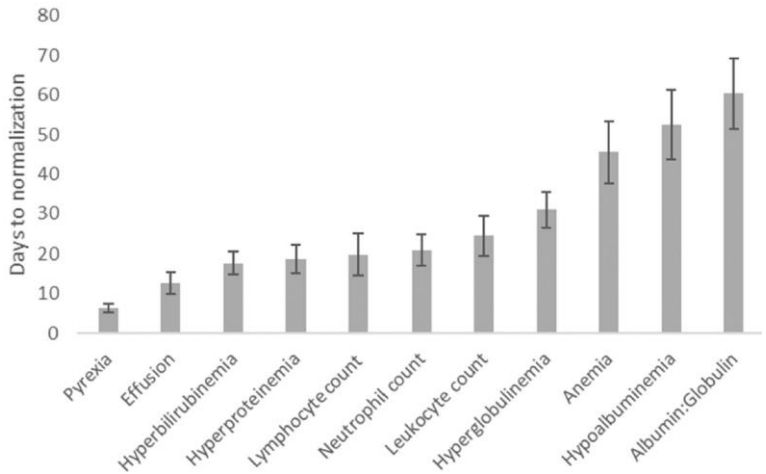
DOI: 10.1111/jvim.16803

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM Open Access

Outcomes of treatment of cats with feline infectious peritonitis using parenterally administered remdesivir, with or without transition to orally administered GS-441524

Sally J. Coggins[1] | Jacqui M. Norris[1] | Richard Malik[2,3] | Merran Govendir[1] | Evelyn J. Hall[1] | Benjamin Kimble[1] | Mary F. Thompson[1]



Days to normalisation for key clinical and clinicopathologic parameters in 25 cats with FIP that survived to complete 84 days of treatment

ANTIVIRAL RESISTANCE?

“in the face of cost and emergence of viral drug resistance, the aim should still be to be as confident as possible that a cat is truly suffering from FIP before starting antiviral treatment, and this can only be done by veterinarians”

- Daniela Krentz et al. Viruses. 2021 Nov; 13(11): 2228.
- Curing Cats with Feline Infectious Peritonitis with an Oral Multi-Component Drug Containing GS-441524

Resistance to GS-441524 has been confirmed over the last 3 years (Pedersen NC. 2021)

The rapid mutation of RNA viruses promotes resistance to drugs directly targeting viral proteins.

Antiviral Resistance?

Drug resistance can only be overcome in two manners:

1. By progressively increasing the antiviral dosage to achieve drug levels in body fluids that exceed the level of resistance), or
2. By using another antiviral drug that has a different resistance mechanism, either by itself or in combination.

With the rise of COVID-19, effective anti-viral drugs have only recently become readily available for veterinary use.

Resistance to this is likely to cause FIP mortality to increase, as few other options are available

Prognosis

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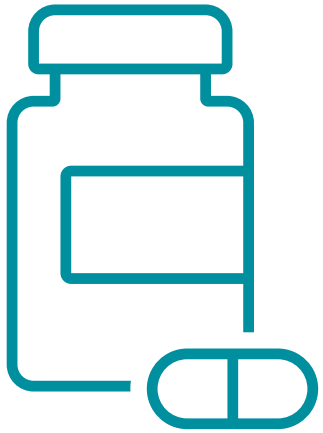
PROGNOSIS

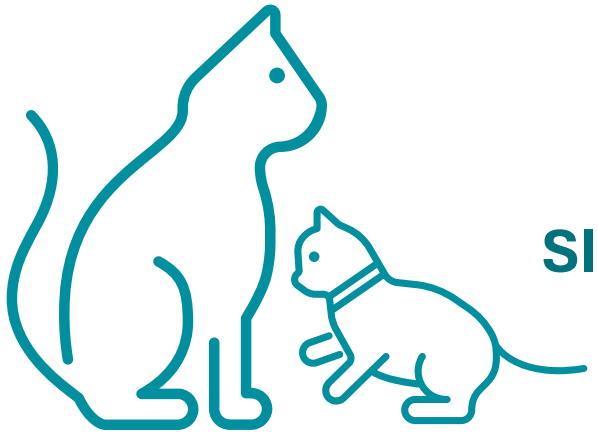
TREATMENT



Non-virus specific medications only
95% mortality within 12 months.

GS-441524 and remdesivir
Potentially curative, with ~ 80% survival within 16 weeks of diagnosis and commencing treatment.

SIGNALMENT



Younger cats
Often more acute and severe disease
Shorted survival times

Older cats
More chronic, less severe
Longer survival times

Prognosis

Marked pyrexia, lethargy, inappetence, weight loss, and icterus are indications of a poorer prognosis.

Lymphopenia is often associated with more fulminant disease. Higher counts are associated with more localised and less intense inflammation.

Cats that are still active, eating, and maintaining weight are more likely to manifest lower-grade fever, clearer fluid, and less likely to be icteric.

Prevention

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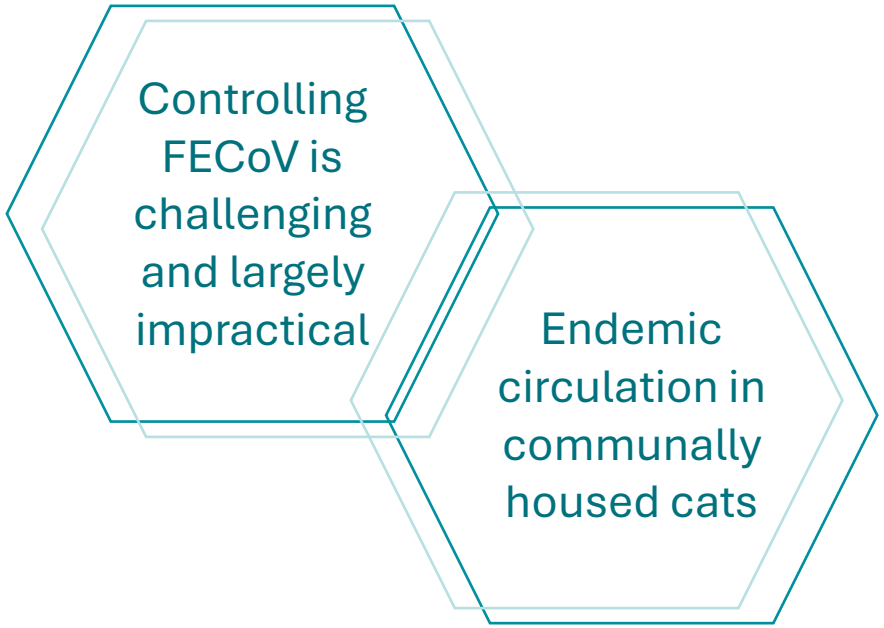
Prevention



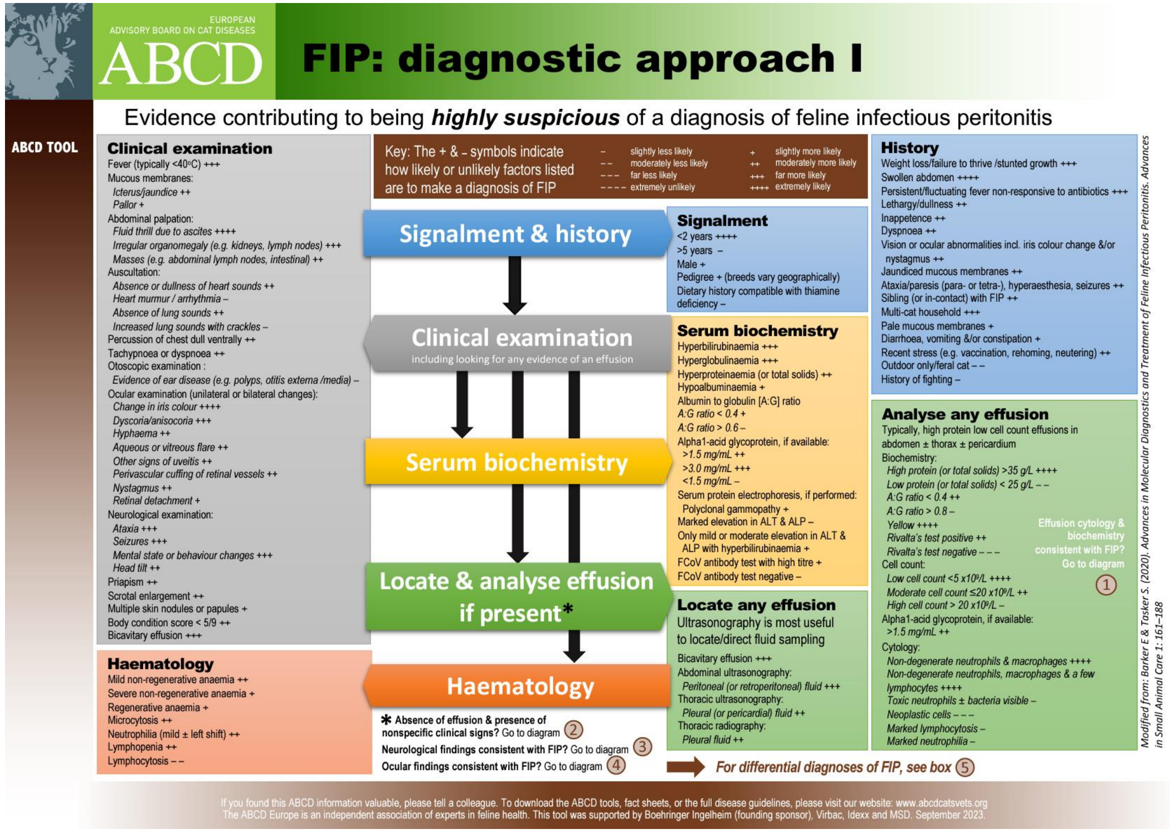
Best prevention methods

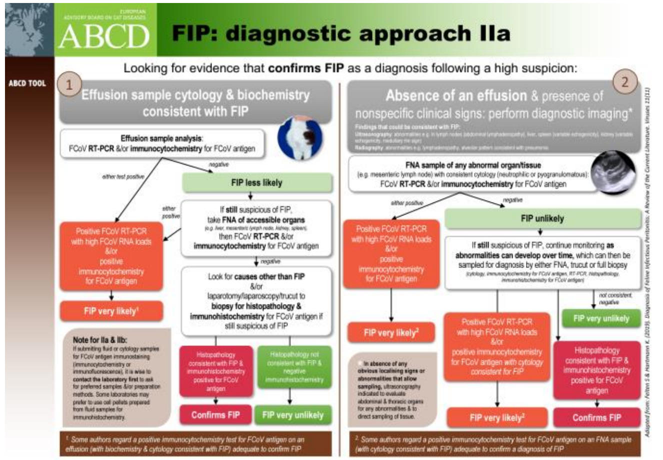
1. Eliminate overcrowding
2. Actively manage litter boxes & litter dust
3. Breed a minimum number of litters
4. Don’t breed from cats with FIP positive kittens

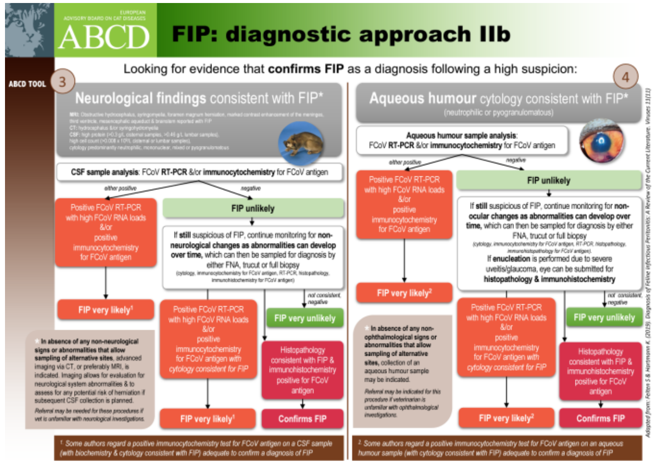
Widespread prophylactic use of anti-viral medications against FECoV is strongly discouraged

- Increases risk of generating antimicrobial-resistant viruses
- Antiviral therapy only temporarily decreases FECoV shedding

Many Available Resources!!







ABCD – European Advisory Board of Cat Diseases

Tiarni Johnston
BVSc (Hons) MANZCVS (SAM)
Resident in Internal Medicine

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QUESTIONS?