

Biogal Laboratories, MediCare and Catvirus.com present:
**Diagnosing and treating feline coronavirus and
infectious peritonitis (FIP)**

Prof. Nilufer Aytug & Dr Diane D Addie

26th May 2021



The banner features a close-up image of a fluffy orange and white cat on the left. On the right, there are two circular portraits of the speakers: Dr. Diane D. Addie and Prof. Dr. Nilüfer Aytug. The text is in white and blue on a dark blue background. Logos for Biogal Galed Labs., ACADAMY Canlı Webinar, and MediCare Sağlık Hizmetleri are visible at the top.

Biogal Galed Labs. | **ACADAMY**
• Canlı Webinar

mediCare
MediCare Sağlık Hizmetleri

Dr. Diane D. Addie | Prof. Dr. Nilüfer Aytug

Haydi! FIP ile ilgili tüm konuları masaya
yatıralım...

26 Mayıs | 20:00 İstanbul >> LCV <<

Türkçe İngilizce Simültane Çeviri Yapılacaktır.

**This webinar data and information was develop according with
Turkey applications and is not applicable for other regions.**



These are the notes from the Addie lecture: Prof. Aytug's lecture notes are given separately.

Amongst the many irregularities surrounding the SARS-CoV2 pandemic, Dr Scott Jensen testified that doctors in the USA had been instructed to put COVID as the cause of death on certificates regardless of the actual cause. And as always there was a cartoonist who made light of the situation.

Unfortunately there are vets who diagnose FIP without good evidence, and there is a tendency to assume FIP if a cat or cattery has once had it and is presented again with some other condition. **No matter how good an FIP treatment is, it won't work if the cat does not have FIP.**



Key message:
Get the correct diagnosis
 40% of cats diagnosed with FIP turn out to have some other condition

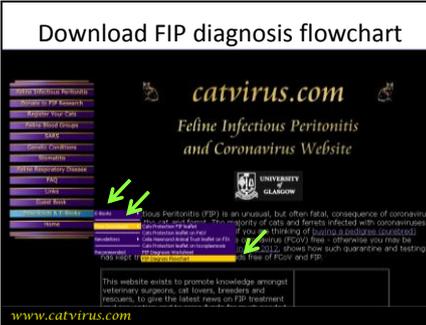


"A wrong diagnosis can be far more devastating than no diagnosis."

Prof. Mike Willard

Feedback from Turkish veterinary surgeons on my webinars on [FIP Diagnosis in 2020](#) and [FIP Treatment in 2021](#) was that some of the FCoV RT-PCR diagnostics that we have easily in the UK aren't available in Turkey. This was good feedback, because in fact there is a delay even in the UK between submitting a sample and obtaining a result: therefore when a cat needs treatment urgently, one has to use diagnostics which can be performed more quickly and in your clinic. To this end, in this webinar, I am going back to my FIP diagnosis algorithm for a guide on how to diagnose FIP using your clinical skills, your microscope and in house biochemistry machine. It is relatively easy to rule out FIP in many cases quite simply.

To access the free FIP diagnosis algorithm in Turkish log on to my website: www.catvirus.com and go to the [Downloads page](#).

<p>go to the Downloads tab on the left (green arrow) ...</p> 	<p>... select FIP Diagnosis algorithm in English and other languages.</p> 	<p>Countries are listed alphabetically, so Turkey is near the end (green arrow).</p> 
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You will obtain a pdf which may open in another tab, or in Firefox browser it may simply download.

The effusive FIP diagnosis algorithm

The effusive FIP diagnosis algorithm

FCoV diarrhoea diagnosis flowchart

I know these look daunting, with all the arrows, but if you just follow the steps, it soon becomes obvious.

Interpreting FCoV antibody test results

The 4th algorithm is about interpretation of FCoV antibody and RT-PCR test results.

FIP diagnosis: FCoV antibody test

FCoV antibody test

Negative

NOT FIP

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A negative FCoV antibody test rules out a diagnosis of FIP or FCoV-related chronic diarrhoea. It doesn't rule out acute FCoV diarrhoea in kittens under 7 weeks of age because seroconversion takes 18-21 days post-infection, whereas virus shedding begins 2 days post-infection.

FIP diagnosis: FCoV antibody test

FCoV antibody test

Negative

Positive

True negative?

False negative?

You need a test with excellent sensitivity to rule out FIP with absolute confidence

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The predictive value negative (PVN) of a FCoV antibody test depends on the sensitivity of the test used.

Sensitivity = the ability to detect a small amount of something

Specificity = the ability to detect something correctly

Ruling out FIP

Sensitivity = the ability to detect a small amount of something

You want a sensitive test because you do NOT want false negatives

Low or negative FCoV antibody titre rules out FIP and FCoV infection*

... provided the FCoV antibody test is sensitive enough

* provided >3 weeks post-infection



Addie DD, le Poder S, Burr P, Decaro N, Graham E, Hofmann-Lehmann R, Jarrett O, McDonald M, Meli ML. 2015. Utility of feline coronavirus antibody tests J Feline Med Surg 17(2):152-62.

A really good, sensitive, FCoV antibody test is essential for both ruling out a diagnosis of FIP or FCoV-associated diarrhoea and also for confirming that a cat has fully recovered from FCoV infection / FIP.

In a comparison of various FCoV antibody tests, the FCoV ImmunoComb (Biogal, Israel) was shown to be the most sensitive, Addie et al, 2015 even in the presence of large amounts of virus. Meli et al 2013

Using blood rather than effusion can reduce the incidence of false negative results.

The utility of feline coronavirus antibody tests

Diane D Addie¹, Sophie le Poder², Paul Burr³, Nicola Decaro⁴, Elizabeth Graham¹, Regina Hofmann-Lehmann⁵, Oswald Jarrett¹, Michael McDonald¹ and Martin L. Meli¹

Abstract
Eight different tests for antibodies to feline coronavirus (FCoV) were evaluated for attributes that are important in situations in veterinary practice. We compared four indirect immunofluorescent antibody tests (IFAT), one enzyme-linked immunosorbent assay (ELISA) (FCoV ImmunoComb; Biogal) and three rapid immunochromatographic (RIM) tests against a panel of samples designated by consensus as positive or negative. Specificity was 100% for all but the two IFATs based on transmissible gastroenteritis virus (TGEV), at 83.3% and 97.5%. The IFAT and ELISA tests were best for obtaining an antibody titre and for working in the presence of virus. The RIM tests were the best for obtaining a result quickly (10–15 mins); of these, the Speed F-Corona was the most sensitive, at 92.4%, followed by FCoV ImmunoComb (92.4%) and Anigen Rapid FCoV antibody test (84.6%). Sensitivity was 100% for the ELISA, one FCoV IFAT and one TGEV IFAT, and 88.2% for a second TGEV IFAT and 96.1% for a second FCoV IFAT. All tests worked with effusions, even when only blood products were diluted in the instruction manual. The ELISA and Anigen RIM tests were best for small quantities of sample. The most appropriate FCoV antibody test to use depends on the reason for testing; in excluding a diagnosis of FIP, sensitivity, specifically, small sample quantity, rapidly and ability to work in the presence of virus all matter. For FCoV screening, speed and sensitivity are important, and for FCoV elimination antibody titre is essential.

Accepted: 14 May 2014

Introduction
There are several reasons for testing cats for antibodies to feline coronavirus (FCoV), and a number of different tests may be used for this purpose. The choice of which test to use depends on the reason for testing. In excluding a diagnosis of FIP, sensitivity, specifically, small sample quantity, rapidly and ability to work in the presence of virus all matter. For FCoV screening, speed and sensitivity are important, and for FCoV elimination antibody titre is essential.

FCoV antibody test

	IFA FCoV		IFA TGEV		ELISA	Rapid Immunomigration		
	Biobest	VDS	EVNA	Zurich	FCoV ImmunoComb	Speed F-Corona	FASTest FIP	Anigen Rapid FCoV
Sensitivity %	96.1	100	96.2	100	100	92.4	84.6	64.1
Specificity %	100	100	97.5	83.3	100	100	100	100

Addie DD, le Poder S, Burr P, Decaro N, Graham E, Hofmann-Lehmann R, Jarrett O, McDonald M, Meli ML. 2015. Utility of feline coronavirus antibody tests J Feline Med Surg 17(2):152-62.



Contact:
info@biogal.com
www.biogal.com

To obtain FCoV ImmunoComb: contact info@biogal.com.

References

Addie DD, le Poder S, Burr P, Decaro N, Graham E, Hofmann-Lehmann R, Jarrett O, McDonald M, Meli ML. 2015. Utility of feline coronavirus antibody tests. J Feline Med Surg 17(2):152-62.

Meli ML, Burr P, Decaro N, Graham E, Jarrett O, Lutz H, McDonald M, Addie DD. 2013. Samples with high virus loads cause a trend toward lower signal in feline coronavirus antibody tests. J Feline Med Surg. 15 4 295 – 299.

FCoV antibody test

Excellent sensitivity is essential for ruling out FCoV/FIP: no false negatives. Starting dilution <1:25.

Use blood (serum/plasma) rather than effusion.

FCoV antibody titre useful for monitoring recovery from infection.

FIP diagnosis: FCoV antibody test

FCoV antibody test

Positive



Both cats were presented for FIP treatment advice, but only 1 cat had FIP

1. Skywise: 5yo NFC: uveitis 5 cat hh
FCoV titre >10,240

2. Frank: stray Greek cat: uveitis. FCoV titre 160.



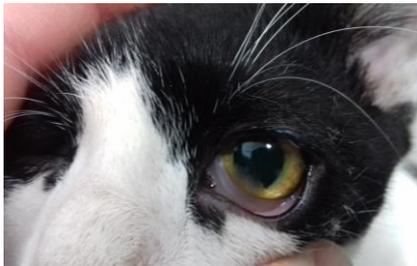
Cats with non-effusive FIP usually have a very high FCoV antibody titre

It is more difficult to interpret a positive FCoV antibody titre in a sick cat: does the cat really have FIP or is the antibody titre merely because the cat was previous exposed to FCoV, or is currently co-incidentally infected with FCoV?

Both cats shown here had uveitis - you can see the keratic precipitates – both had FCoV antibody titres, both were presented to my online clinic for FIP treatment advice ... but only one cat had FIP.

In Frank's case the diagnosis of FIP was more suspect because his FCoV antibody titre was only 160: cats with non-effusive FIP tend to have high FCoV antibody titres.

Frank had toxoplasmosis: he was cured with one month of clindamycin ...



...Frank is alive and well 2 years on



Key message:

The presence of FCoV antibodies does NOT equate to a diagnosis of FIP!

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The first step of the FIP Diagnosis Flowchart is the history ...

History

The cat MUST have had an opportunity to become infected with FCoV

Other cats / animals in household?

Is the cat a hunter?

Food ... infection? toxicity? deficiency?

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ISLAK FIP TANISI

1. ANEMNEZ: YAŞ VE İRK
FCoV enfeksiyon geçmişi esastır
FIP olan kedilerin %70'i saf kan kedilerdir.
Her yaşta görürse de kedilerin %50'sinden fazlası 2 yaşın altındadır
Genellikle hastalık görümeden önceki haftalar içinde bir stres hikayesi vardır.

2. ABDOMİNAL GENİŞLEMİ VEYA DİSPNE (SOLUNUM GÜÇLÜĞÜ) ŞİKAYETİ
Klinik muayenede effüzyon tespit edilmişse: abdominal, pleural, perikardial, skrotal
Islak FIP'te kedilerde genelde ateş, bazen iştahsızlık vardır, hareketli veya durgun olabilirler.

3. EFÜZYONUN KLİNİKTE İNCELENMESİ
Görünüm: Sıvı, berrak, kokusuz, nadiren şilöz
Protein seviyesi: <35g/litre
Albumin:globulin oranı: <0.8
Neutrofiller ve makrofajlar: Pozitif
PPV 58%: Pozitif
Rivalta testi: Negatif
FCoV antikor testi KANDAN: Negatif

4. EFÜZYONU DIŞ LABORATUVARA GÖNDERME
Normal FIP'i ekarte eder (<500µg/ml) AGP Yüksek (>1000µg/ml)
Negatif FCoV RT-PCR Pozitif

5. SONUÇ FIP (96% SPESİFİKİTİR)
TEDAVİ: Mutian veya feline interferon omega: 1 MU/kg s/c veya effüzyonun olduğu bölgeye 2 günde bir, artı meloxicam. Vit B12 enjeksiyonu. Eğer lenfopenikse Pl.
Bakınız: FIP tedavi sayfası www.catvirus.com.

Yaş (Yılı)	Safkan Kedi	Ev Kedisi
<1	95	79
1	70	42
2-3	53	41
4-5	60	33
6-7	20	21
8-9	23	34
≥10	11	14

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The second step is the clinical examination, and if the cat has an effusion, the 3rd step is to draw off the effusion and examine it.

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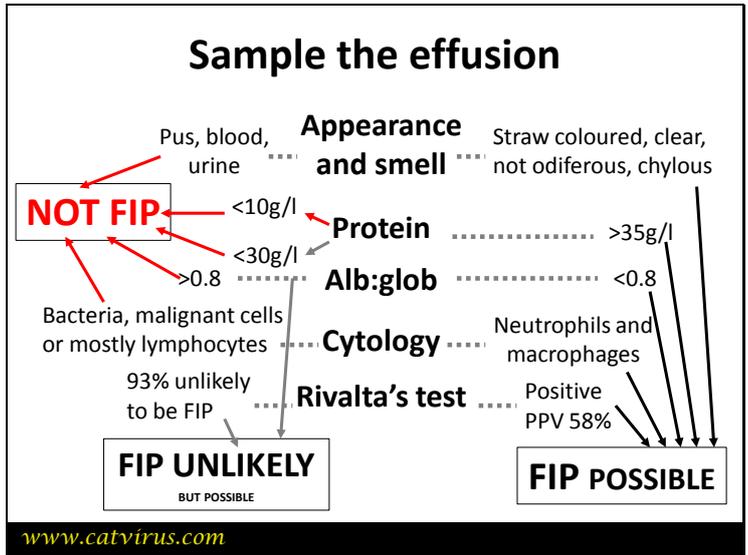
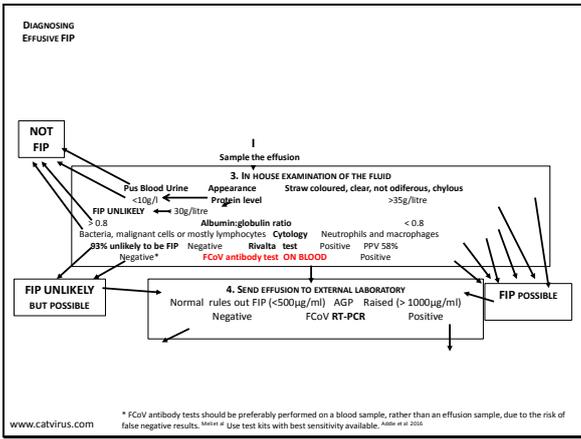
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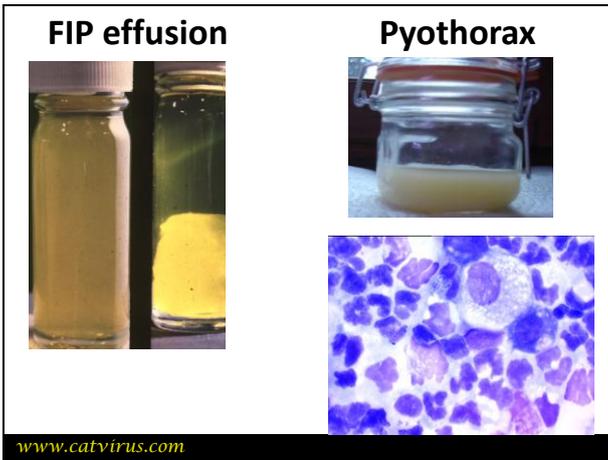
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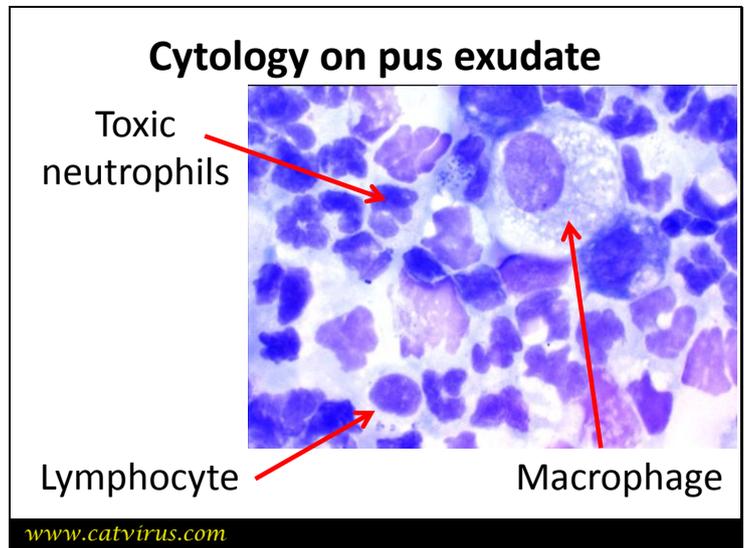
Visual examination of the effusion can tell you whether FIP should be on your list of differential diagnoses or not.

On the left is an FIP effusion: you can see that it clotted when left standing. On the right is a pyothorax effusion – much more cloudy and smelly than the FIP modified transudate.

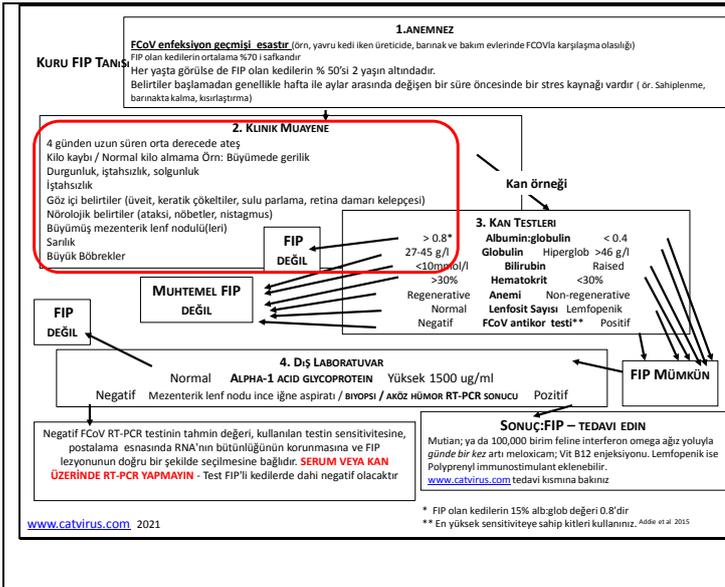


You can simply stain effusions with something like DiffQuik and examine the cells: if there are too few cells then centrifuge them (1000 rpm for 1 minute) and resuspend the pellet. FIP effusions typically have a very low cellularity unlike the purulent exudate shown below. FIP effusions have neutrophils and macrophages: if you see many lymphocytes, then the cat does not have FIP. FCoV-infected macrophages release tumour necrosis factor-alpha which causes apoptosis of lymphocytes, which is why around half of FIP cases are lymphopenic.

In bacterial peritonitis and pleurisy you can also often see movement of the tiny bacteria, even after staining.



Tips for differentiating non-effusive FIP from other conditions using your clinical skills



1st – take the temperature of the cat: cats with FIP almost always have a low grade pyrexia which doesn't usually respond to antibiotics.

2nd - abdominal palpation: cats with FIP tend to have palpably enlarged mesenteric lymph nodes (whereas cats with feline infectious anaemia tend instead to have a large spleen).

3rd - I can almost always find some kind of intra-ocular signs such as I'm showing you below.

Keratic precipitates: these can be hidden under the third eyelid, which can be prominent in cats with FIP, so try to get the cat to look upwards and watch the eyes carefully.

Non-effusive FIP diagnosis

Raised mesenteric lymph nodes

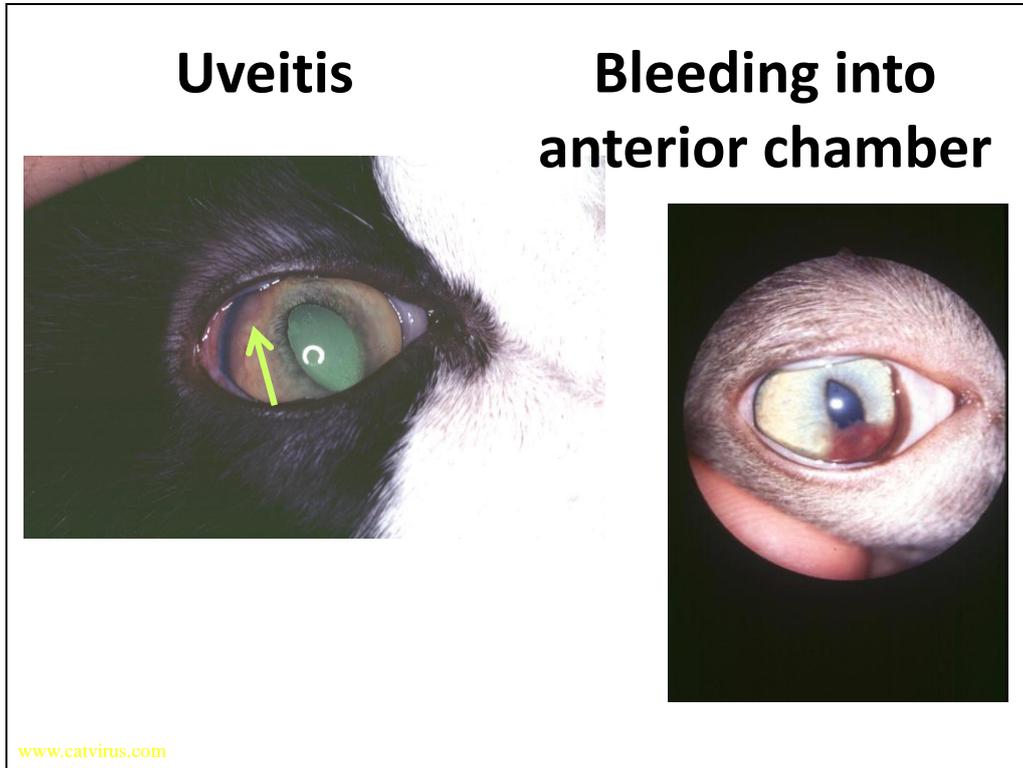
Intra-ocular signs:

- uveitis
- keratic precipitates
- aqueous flare



Uveitis: in the photograph on the left (below), you can just see the edge of my thumb pulling the upper eyelid up and there underneath was a small area of uveitis.

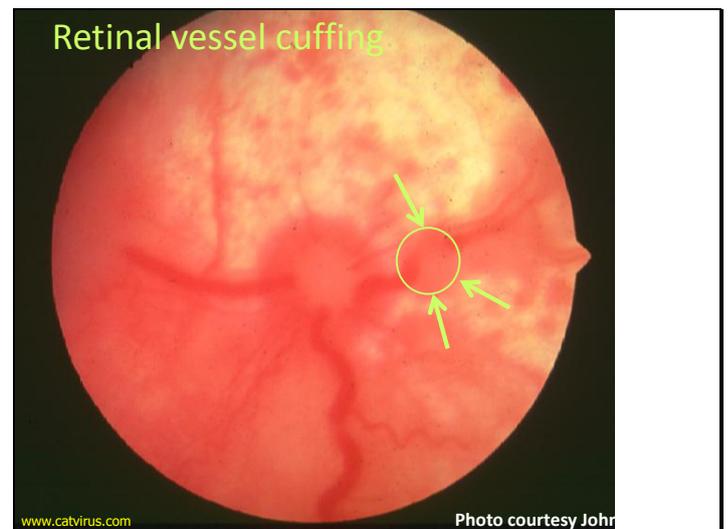
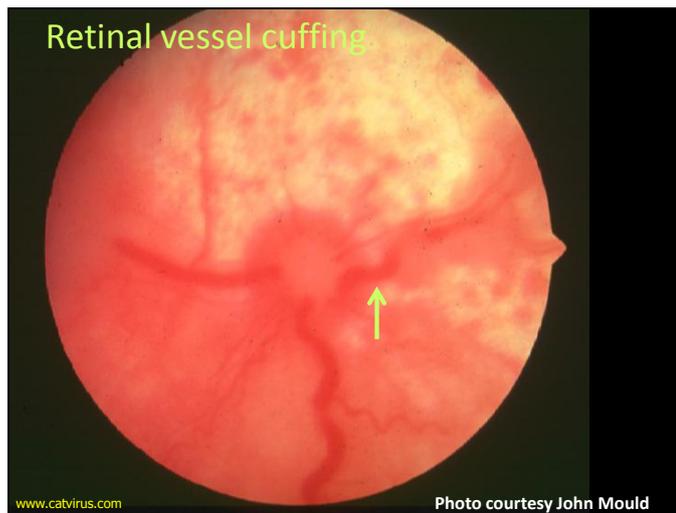
Bleeding into the anterior chamber – shown right – is less common, but can still occur (obviously check the blood pressure, thyroid and urine specific gravity of a cat with intraocular haemorrhage and check for frayed claws / trauma).



The retina is the one place in the body where you can actually see an FIP lesion without doing an exploratory laparotomy.

Look at the blood vessel to the right of the optic papilla, where the small arrow is.

Follow that blood vessel to the right and you can see it going into and emerging from an FIP pyogranuloma. The greyish fuzzy lines either side of the blood vessel are also FIP lesions: we call that retinal vessel cuffing.



Anisocoria

2008



2010

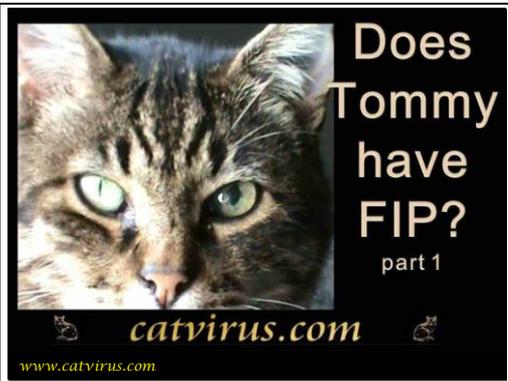


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Anisocoria is remarkably frequent in cats with non-effusive FIP, but of course also other conditions.

Tommy, shown here, had evenly sized pupils in 2008 but his pupils were obviously different sizes in 2010.

Differential diagnosis of feline uveitis.



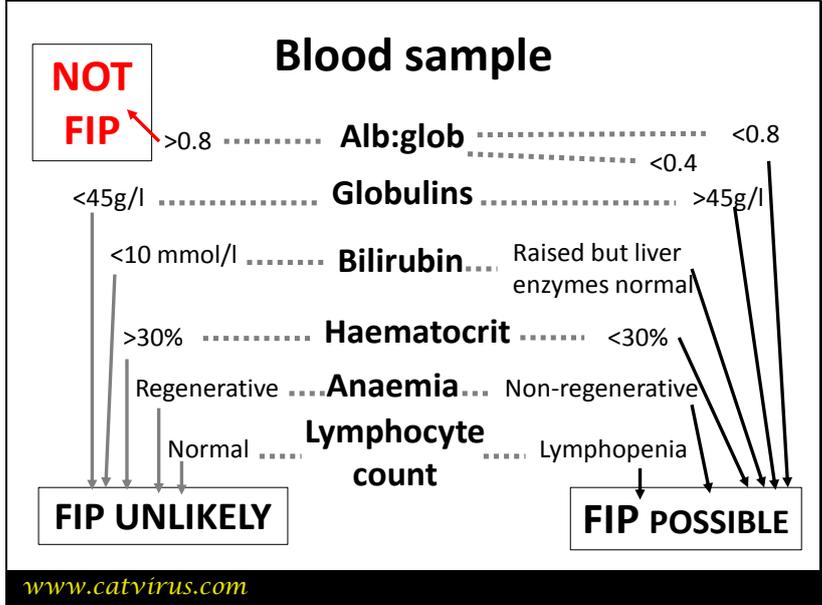
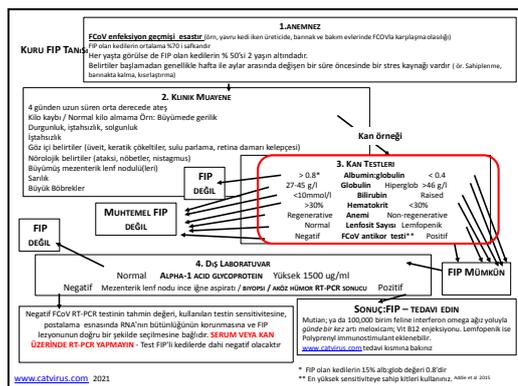
There is not time to convey all the information that would be useful to feline veterinarians, therefore I am providing links to some of my educational videos.

To see a five part continuing education series on differential diagnosis of uveitis and anisocoria in the cat, called "Does Tommy Have FIP?" please copy and paste this YouTube link: https://youtu.be/F_rR6pZ1RE or this either of these links:

<https://www.bitchute.com/video/z06chepJrPZ5/>

<https://odysee.com/@Catvirus:3/FelineInfectiousPeritonitisTommy1:a>

Step 3 of the dry FIP algorithm: in house blood results



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FCoV RT-PCR has replaced biopsy for FIP confirmation in the living cat (but histopathology remains the diagnostic method of choice post mortem)

1. Correct diagnosis

Effusive FIP: confirm by FCoV RT-PCR on effusion

Non-effusive FIP: confirm by FCoV RT-PCR on ultrasound guided fine needle aspirate of mesenteric lymph node

FCoV diarrhoea: FCoV RT-PCR of cat litter free faecal sample

Dunbar D, Kwok W, Graham E, Armitage A, Irvine R, Johnston P, McDonald M, Montgomery D, Nicolson L, Robertson E, Weir W, Addie DD. 2019. Diagnosis of non-effusive feline infectious peritonitis by reverse transcriptase quantitative polymerase chain reaction from mesenteric lymph node fine needle aspirates. *J Feline Med Surg.* 21(10):910-921.

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FCoV RT-qPCR

Test the CORRECT sample for the condition – **i.e. NOT BLOOD**

Sensitivity is vital: no false negatives. 3' UTR primers are recommended

Include a control for PCR inhibitor in faecal samples

Report virus quantity, even just the C_T

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Key message: Use the right samples for FCoV RT-PCR testing

- DO NOT SEND BLOOD FOR FCoV RT-PCR TESTING and don't use a laboratory that asks you to
- effusion to diagnose wet FIP
- mesenteric lymph node ultrasound guided fine needle aspirate (FNA) to diagnose dry FIP
- faeces (without cat litter) for diagnosing FCoV-enteritis or subclinical FCoV shedding

It's useful if a laboratory reports virus quantity, not just "positive or negative" especially for monitoring virus shedding.

Just as in FCoV antibody testing: sensitivity of the test is vital: the best primers and probe will target the 3' end of the genome.

Make sure your laboratory has the proper controls in place:

- a control for faecal PCR inhibitors for every sample, not just a batch
- to avoid false negative results: an RNA control (e.g. GAPDH) for every sample, not just a batch Dunbar et al, 2018

Reference

Dunbar D, Kwok W, Graham E, Armitage A, Irvine R, Johnston P, McDonald M, Montgomery D, Nicolson L, Robertson E, Weir W, Addie DD. 2019. Diagnosis of non-effusive feline infectious peritonitis by reverse transcriptase quantitative polymerase chain reaction from mesenteric lymph node fine needle aspirates. *J Feline Med Surg.* 21(10):910-921.

Acute phase proteins

Alpha-1 acid glycoprotein (AGP)
Serum Amyloid A (SAA)

100% sensitive, but not specific

Rise in any infection / inflammation

Normal AGP / SAA differentiates FIP from cardiomyopathy, tumour, non-infectious liver disease.

Giori et al 2011 stated "... histopathology was not a sensitive diagnostic test as it failed to confirm FIP in most affected cases."

Duthie S, Eckersall PD, Addie DD, Lawrence CE, Jarrett O. 1997. Value of alpha-1-acid glycoprotein in the diagnosis of feline infectious peritonitis. *Veterinary Record* 141 12 299-303.
Giori L, Giordano A, Giudice C, Grieco V, Paltrinieri S. Performances of different diagnostic tests for feline infectious peritonitis in challenging clinical cases. *J. Small Anim. Pract.* 2011, 52, 152-157.

www.catvirus.com

References

Duthie S, Eckersall PD, Addie DD, Lawrence CE, Jarrett O. 1997. Value of alpha-1-acid glycoprotein in the diagnosis of feline infectious peritonitis. *Veterinary Record* 141 12 299-303.

Giori L, Giordano A, Giudice C, Grieco V, Paltrinieri S. 2011. Performances of different diagnostic tests for feline infectious peritonitis in challenging clinical cases. *J Small Anim Pract.* 52(3):152-7.

Yin Y, Li T, Wang C, Liu X, Ouyang H, Ji W, Liu J, Liao X, Li J, Hu C. A retrospective study of clinical and laboratory features and treatment on cats highly suspected of feline infectious peritonitis in Wuhan, China. *Sci Rep.* 2021;11(1):5208.

There is an unusual presentation of FCoV infection where only the brain is affected. This is Hamish in Glasgow Veterinary School Hospital as an emergency case, on the left. And one year later, on the right. His emergency treatment with mannitol and dexamethasone reversed his blindness and circling. We then gave him Mutian to clear coronavirus from his brain. His bloods looked normal other than a high FCoV antibody titre.

FCoV hydrocephalus without systemic FIP

March 2020



April 2021



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FCoV hydrocephalus without systemic FIP

Clinical signs: sudden onset painful tail, ataxia, circling, blindness.

Bloods: appear normal except for high FCoV antibody titre.

Treatment: 8mg/kg Mutian pills q24 hours. If unavailable: Mannitol infusion over 20 mins; dexamethasone.

www.catvirus.com

I believe that FCoV was causing leakage of plasma into the CSF, causing build up of thick CSF which couldn't drain properly – i.e. hydrocephalus – which caused the clinical signs.

FCoV as cause of GIT signs

Transient infection (2-3 months)
Can be associated with diarrhoea ± vomiting

Persistent infection
Can cause chronic diarrhoea

FCoV Infection

Resistant
Healthy

FIP
Can cause chronic diarrhoea or constipation



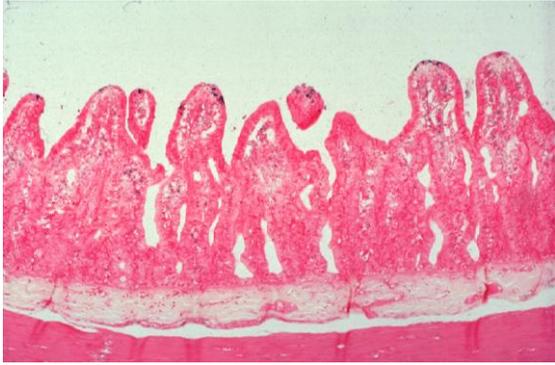
www.catvirus.com

In recent years I have stopped referring to FCoV-infected cats who do not have FIP as “healthy” and now refer to them as subclinically infected.

Although most cats throw off the infection with only mild diarrhoea, one of the cardinal signs of early FCoV infection is stunting and uneven litter sizes, with protruding third eyelids (membrana nictitans). In some cases the intestinal FCoV infection can be life threatening. Kipar et al, 1998

There is also a particular form of dry FIP which manifests as thickening of the colon.

FCoV infection of the small intestine



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On the left is the small intestine of a Persian kitten called Poppy, showing FCoV (stained black by immunohistochemistry) in the epithelial cells at the tips of the intestinal villi. This kitten presented with vomiting and diarrhoea and died of her intestinal FCoV infection. You can also see that the intestinal villi were stunted and fused, similar to transmissible gastroenteritis virus infection in piglets.



FCoV enteritis

Diarrhoea and third eyelid syndrome

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One of the biggest tell-tale signs of FCoV infection is protrusion of the third eyelid (nictitans / nictitating membrane) as shown in the two grey kittens at the top of this slide: contrast their appearance with that of the healthy, FCoV-free black kitten below.

Any gastrointestinal infection can cause this, but especially in a pedigree kitten, or kitten from a shelter, 3rd eyelid protrusion should be a red flag and possible indicator for FCoV infection.

FCoV enteritis



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This anus is very inflamed, painful and leaky.

FCoV enteritis



This is the cat to whom this anus belongs: Tessa, a Sphynx kitten.

She has had problems with faecal incontinence since she was adopted from her breeder in February 2021 at about 4 months of age.

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FCoV enteritis



In April her diarrhoea became even worse and on occasions had streaks of blood.

Her guardian, Lindsey, said *"She is in pain due to the constant anal grooming and she even cries out in pain."*

Tessa's guardian said:
"She is in pain due to the constant anal grooming"

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FCoV enteritis is a diagnosis of exclusion: all other possible infectious or dietary causes must be ruled out.

Medical records documented faecal leaking and that the cat was "super hungry."
On other occasions she was off her food and slept all day.
Severely underweight at 3.9 lbs (1.9kg) at 6 m.o.
Parasites were ruled out: FCoV enteritis is a diagnosis of exclusion.

www.catvirus.com

FCoV enteritis: a diagnosis of exclusion

Date samples received: 20apr21				
Initials <u> </u> <u> </u>			Page 1 of 1	
Client sample ID	Zoologix accession ID	Sample type	Assay	Assay result
Tessa Young Blue Point Sphynx Kitten	2104200020	3 fecal swabs	POO28	Positive for feline enteric coronavirus; negative for other panel components

Assay descriptions and notes

Panel P0028: Feline diarrhea panel -- qualitative detection and differentiation of feline enteric coronavirus, feline panleukopenia virus/canine parvovirus, *Campylobacter*, *Clostridium*, *Cryptosporidium*, *Giardia*, *Salmonella*, *Toxoplasma gondii* and *Trichomonas* by PCR.

Feline panleukopenia virus	<i>Cryptosporidium</i>	
<i>Campylobacter</i>	<i>Giardia</i>	<i>Tritrichomonas</i>
<i>Clostridium</i>	<i>Salmonella</i>	
	<i>Toxoplasma gondii</i>	

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(I found it amusing that the test code was POO 28!)

All other parasitic, viral, and bacterial causes of chronic diarrhoea were ruled out in Tessa's case (the negative parasite results are not shown here).

Tessa's guardian spent literally thousands of dollars trying to help her kitten, trying different treatments and diets. Below, you can see how the diarrhoea began to become less watery, more formed.

FCoV enteritis



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FCoV enteritis



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FCoV enteritis



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FCoV enteritis



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Tessa's bottom became less inflamed.

What caused this miracle? Quite simply – probiotics (Fortiflora for now – but the best probiotics, which are Protexin pro-kolin enterogenic and on order) and chicken and pumpkin canned food (Applaws or Almo Nature brands: I buy those online from Zooplus).

Tessa's guardian, Lindsey, wrote:

"It has only been a few days and the Applaws and Almo Nature Chicken and Pumpkin (along with probiotics and fiber supplement) have stopped the diarrhea completely. It's incredible!

Her demeanor has also changed: she is now lively, wants to play and has gained new confidence"

www.catvirus.com

Applaws & Almo Nature chicken and pumpkin are good for controlling diarrhoea



However please remember that real meat based foods do not have enough calcium for growing kittens

Purchase online from Zooplus

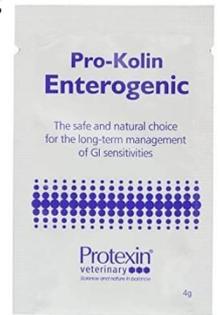
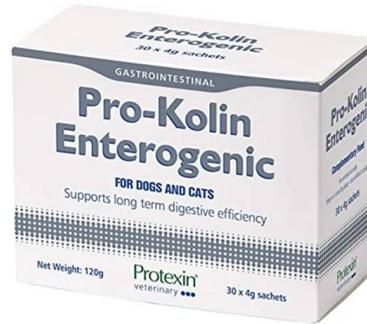
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Signs of FCoV in a cattery



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Best probiotics: Pro-kolin Enterogenic



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FCoV enteritis



Many thanks to Lindsey Young for photography and permission to tell Tessa's story

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FCoV-infected litters of kittens tend to be of uneven sizes

Two of this litter of 3 Oriental kittens died of FIP: the largest one (on the left) died first - she developed wet FIP at 6 months old. The little runty one in the middle developed dry FIP at 10 months of age.

In addition to diarrhoea beginning usually around 5-7 weeks of age, another big tell-tale sign of FCoV infection in a litter of kittens is uneven sizes of the littermates:

Contrast these three purebred kittens with the more even sizes of the FCoV negative littermates from a different breeder in the small photo in the corner.

Mutian pills stop FCoV shedding and it is my belief that a brief (5-7 day) course of Mutian pills can prevent FIP although I have yet to prove this. A short course of Mutian pills are the absolute cure for FCoV-associated diarrhoea unless the cat actually has FIP of the intestine (colonic FIP) when they will need a longer course than one week. If Mutian is unavailable, try ivermectin – see further on in these notes.

Dose of Mutian pills to stop FCoV shedding in faeces / cure FCoV-related diarrhoea



One Mutian 200/2kg q24 hrs for 4-7 days stops FCoV shedding in faeces

Since the publication of our paper, Mutian has slightly increased their recommended dose: in the paper we used one Mutian 200 per 2.5kg of bodyweight q24 hours.

This paper is free to read thanks to all the donors who responded to a crowdfunding set up by Kristina Macaulay to help pay the high publishing fees of the journal. You can download it here: <https://www.sciencedirect.com/science/article/pii/S0034528819312056>

FIP Treatment: first remove the effusion, if it is present

When effusive FIP is suspected, it is more useful to analyse the effusion than the blood to diagnose or rule out FIP, and removing the effusion also physically reduces the amount of virus in the cat; importantly easing clinical signs, especially in a cat with a thoracic effusion, struggling to breathe.

Treating FIP: draw off the effusion – best for diagnosis, and alleviates clinical signs



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After thoracentesis, the cat was able to sleep comfortably and eat

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The cat shown here was only restrained by clips placed on the scruff: Pozza et al, 2008 he had not been given any sedative.

Rules of FIP Treatment

1. Remove the effusion
2. Don't use corticosteroids: use meloxicam instead

www.catvirus.com

Corticosteroids reduce the lifespan of cats with FIP: Legendre et al, 2017 use meloxicam instead (provided kidney function and blood pressure are OK).

References

Legendre AM, Kuritz T, Galyon G, Baylor VM, Heidel RE. 2017. Polyprenyl Immunostimulant Treatment of Cats with Presumptive Non-Effusive Feline Infectious Peritonitis In a Field Study. Front Vet Sci. 4:7.

Pozza ME, Stella JL, Chappuis-Gagnon AC, Wagner SO, Buffington CA. 2008. Pinch-induced behavioral inhibition ('clipnosis') in domestic cats. J Feline Med Surg. 10(1):82-7.

FCoV and FIP treatment options

3. Which treatment is best?

GC376

GS-441524

Remdesivir



Mutian pills /-injectable

Online various brands e.g. Spark, Aura

Interferon: Virbagen Omega

Polyprenyl immunostimulant

Anti-SARS-CoV2 treatments

www.catvirus.com

In my experience Mutian pills—but not Mutian injection—are the best FIP and FCoV treatment.

I have to confess that I haven't got experience of many online brands, but I do get horror stories of people who have had cats on various GS concoctions for months: we switch them to Mutian and they recover rapidly, or we find that they didn't actually have FIP. I had two bad reports about Spark in the days prior to the webinar and Aura causes SDMA to rise.

Prof. Malik in Australia is using Remdesivir with some success: but I have grave reservations about using that drug based on reports of side effects and resistant viruses emerging following its use in humans.

Mutian doses for treating FIP

FIP Treatment: Mutian pill doses

FIP treatment: one Mutian 200 per 2.0kg bodyweight q24hrs

Intra-ocular signs: 1½ Mutian 200 per 2.0kg till resolution of signs, then one per 2.0kg q24hrs

Neurological signs: 2 Mutian 200 per 2.0kg till resolution of signs, then one per 2.0kg q24hrs

Duration of treatment: until AGP normalises on two consecutive tests, or 12 weeks if unable to measure AGP

www.mutianstore.com

www.catvirus.com

This slide shows you the dosage as recommended by the Mutian company, but the advice about the duration of treatment is my own recommendation based on my as yet unpublished data. The Mutian company recommends a 12 week course for all cats with FIP, but I have found that when cats have had two normal alpha-1 acid glycoprotein (AGP) tests in a row, at least one week apart, they can stop Mutian and go on to 100,000 units of Virbagen Omega by mouth instead. The Mutian company warns that they won't honour their guarantee if the cat receives less than a 12 week course.

The dose for effusive or non-effusive FIP is one Mutian 200 per 2kg bodyweight daily in divided doses but I recommend a 7 to 10 day period of double dose to clear the virus from the brain: this is best done early on in treatment because as the cat gains weight, he or she will require more Mutian.

In cats with **intra-ocular or neurologic signs**, the increased dose (1.5 and 2 Mutian 200/kg q24hrs respectively) may be required for longer, until clinical signs abate, carefully monitoring symmetric dimethyl arginine (SDMA) (see following page).

Where to buy Mutian pills: www.mutianstore.com

FIP Treatment support

Vitamin B12: e.g. Protexin Cobalplex

S-adenosyl-L-methionine (SAME): e.g. Denamarin, Hepatosyl

Nutrition: real meat daily, omega-3

Mirtazapine: if required

Erythropoietin, PI: if required

Duration of treatment: until normal AGP levels or 12 weeks

www.catvirus.com

Vitamin B12 has three benefits for cats with FIP:

- it stimulates appetite
- it supports red blood cell production (cats with FIP often have a non-regenerative anaemia)
- it is anti-inflammatory

Give vitamin B12 injections once a week (but they sting, so rub the site before and after the injection to release endorphins). Alternatively use Protexin Cobalplex orally.

Cats are obligate carnivores: arginine is an essential amino acid for them (unlike in humans), and arginine is essential for immune function, as well as the urea cycle. Therefore it is advisable to give cats with FIP one tablespoon of real meat every day (most cat foods, despite looking meaty, are cereal based). The meat can be cooked or raw although the latter carries the risk of infections such as *Toxoplasma gondii*.

FIP Treatment: follow Mutian course with Virbagen Omega

Dose: 100,000 units per cat per day by mouth

Duration of treatment: until FCoV antibody titre reduces significantly

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The Mutian company recommends a 12 week course of their pills. However, we stopped Skywise's Mutian treatment at 50 days because his SDMA levels were increasing and his AGP levels had returned to normal, indicating that there were no active FIP lesions at a blood vessel level. It is my experience that it is safe to discontinue Mutian pills when two consecutive AGP tests are 500 µg/ml or under: most cases seem to be cured by 7-8 weeks.

Following the Mutian course, put the cat onto 100,000 units of Virbagen Omega by mouth: the instructions for diluting Virbagen Omega can be downloaded at www.catvirus.com from the FIP Treatment page.

The length of the feline interferon treatment varies from cat to cat but will usually take some months. It is safe to discontinue when the FCoV antibody titre has reduced at least three-fold: that is to say more than three dilutions, for example, from 10,240, via 5,120, 2,560, to 1,280. Actually I prefer the FCoV antibody titre to be below 100 before stopping the interferon, but if at least 6 months have elapsed, or the cat has reached and maintained their optimum weight, stopping the Virbagen may be OK (I don't have enough data yet to be sure).

Are there side effects of Mutian pills?

- some vomiting
- give S-adenosyl-L-methionine (SAME, e.g. Denamarin) to protect liver
- possible kidney damage at higher doses: monitor symmetric dimethylarginine (SDMA)

Contraindicated for cats in IRIS stage 3 chronic kidney disease or liver disease

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Adverse drug reactions / side effects

Cats are great vomiters—especially of pills—and so occasional vomited pills has been reported to me: this is more a problem in the short course of treatment for clearing FCoV from subclinically infected virus shedders, because missing a pill during a 4 day course can result in only partial virus clearance. Therefore although most virus shedding stops within 4 days, for guaranteed virus clearance amongst in-contact cats, it's a good idea to give 5-7 days of treatment.

The active anti-viral component of Mutian is an adenosine nucleoside analogue and such drugs are notorious for being hepatotoxic and renotoxic, therefore a supplement with S-adenosyl-L-methionine (SAME) is recommended to protect the liver, although I actually have never seen worrying liver enzyme levels in Mutian treated cats.

For cats on higher doses of Mutian I recommend monitoring SDMA.

GS-441524, drug resistance and side effects

1. Correct diagnosis
2. Do NOT use systemic corticosteroids
3. Which treatment is best?
4. **Faecal samples from patient AND in-contact cats for FCoV RT-PCR test**
5. Monitor weight
6. Monitor treatment
7. Secondary diseases
8. Post-FIP syndrome

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In Pedersen's study on GS-441524 anti-viral, one of the cats was found to be resistant to the drug. ^{Pedersen et al, 2019} What I recommend is taking a cat litter free* faecal sample before beginning the antiviral, then one week after, to check that the anti-viral works against the virus strain infecting my patient. The only problem is that around 25% of cats with FIP are no longer shedding FCoV in the faeces. ^{Addie et al, 1996}

*cat litter can inhibit the PCR test

References:

Addie DD, Toth S, Herrewegh AAPM, Jarrett O. 1996. Feline coronavirus in the intestinal contents of cats with feline infectious peritonitis. *The Veterinary Record*. **139**: 522-523

Pedersen NC, Perron M, Bannasch M, Montgomery E, Murakami E, Liepnieks M, Liu H. 2019. Efficacy and safety of the nucleoside analog GS-441524 for treatment of cats with naturally occurring feline infectious peritonitis. *J Feline Med Surg*. 21(4):271-281.

Side effects: GS-441524

Painful injections
Severe
inflammatory skin
reactions at
injection site



Prof. Pedersen's paper documented that the side effects of GS-441524 included that the injections were very painful and resulted in severe inflammatory skin reactions (which of course are a risk for feline injection site sarcoma).

www.catvirus.com

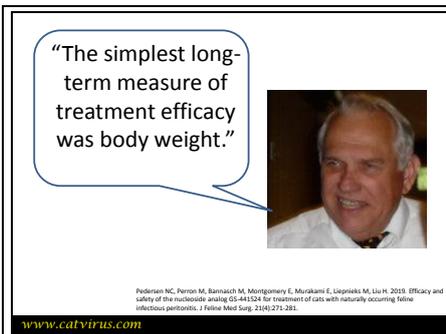
Markers of recovery from FIP

Clinical signs, e.g. effusion, uveitis, weight loss	Resolution of clinical signs, e.g. weight gain
AGP raised	AGP \leq 500 μ g/ml
Anaemia	Hct / PCV >30%
Lymphopenia	Lymphocytes >1500/ml
Hypergammaglobulinaemia	Normal globulin
Raised bilirubin	Normal bilirubin
High FCoV antibody titre	Reducing FCoV antibody titre

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The diagnostic criteria for FIP are shown on the slide above; therefore it makes sense that recovery from FIP is marked by reversal of these abnormalities.

Monitoring weight is a simple way to monitor FIP treatment



In Prof. Pedersen's 2019 JFMS paper on the nucleoside analogue GS-441524, he said,

"The simplest long-term measure of treatment efficacy was body weight."

The paper stated, "Weight gains of 20-120% occurred during and following treatment, even in cats 1 year of age and older at disease onset."

This showed that even in cats who would normally be considered to be adult and finished growing, treatment was able to at least partially reverse the stunting that FCoV/ FIP had caused.

Monitor weight

Expect about 25g/day (1 oz/day) weight gain during Mutian pill (not injection) treatment

Effusive FIP cases may appear to lose weight for the first 7-10 days

Around 10g/day (1/2 oz/day) weight gain during Virbagen Omega treatment

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Cats should gain about 1 ounce (25g) of weight per day while on Mutian pills, although cats with effusive FIP may initially appear to lose weight for the first 7-10 days due to the effusion resolving.

When they stop Mutian and start Virbagen Omega by mouth weight gain usually decreases to around half an ounce per day on average (about 10 grams).



To see the full video about using weight to monitor the effectiveness (or otherwise) of FIP treatment, go to: <https://youtu.be/UllpVkJ0Ys5g>

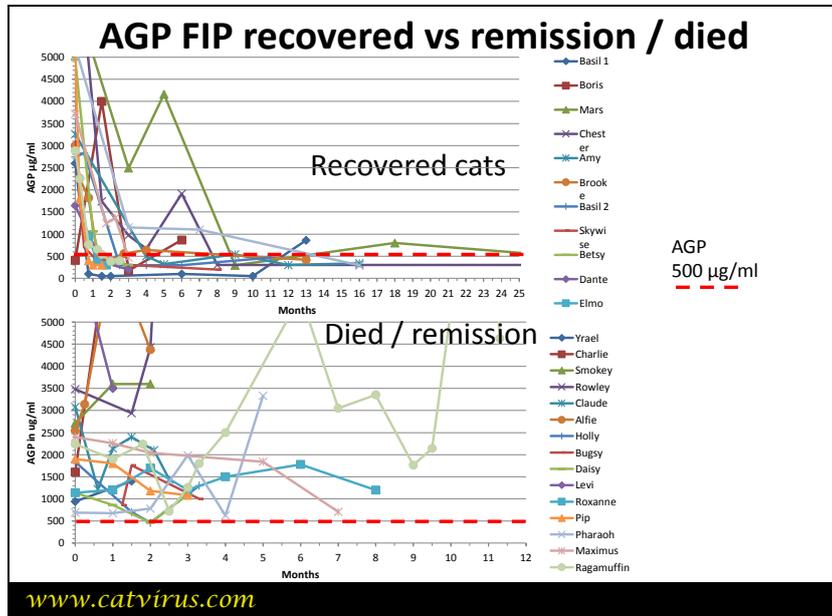
or Bitchute:

<https://www.bitchute.com/video/Vr3wkoW8SkrP/> The photo on the left is of the thumbnail of the video, showing wee Skywise on the scales.

In that video, I also show how weight monitoring can alert you to secondary conditions such as furball or infectious anaemia.

Using acute phase protein level reduction is the most effective and rapid way to distinguish FIP recovery – i.e. cure – from the cat merely being in remission

This is a figure from a paper I am working on. The top graph shows sequential AGP test results from recovered cats: you can see the level reducing to normal – the dotted red line at 500 µg/ml – whereas the AGP levels in the cats who died in the lower graph stayed above that level.



When to stop treatment? Recovery vs Remission?

Consistent reduction of alpha-1 acid glycoprotein (AGP) levels to normal (<500µg/ml) is the single best marker for recovery from FIP

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In my last webinar people asked if serum albumin A (SAA) levels would similarly reduce as FIP resolves? I have not measured that, but since it is also an acute phase protein which rises in FIP, there is every reason to expect that SAA levels would also reduce in cured cats.

When to stop treatment? Recovery vs Remission?

Stop Mutian when you have 2 consecutive AGP results under 500µg/ml (or at 12 weeks)

Stop feline interferon (Virbagen Omega) when the FCoV antibody titre reduces significantly

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AGP reduced to normal levels more quickly than globulins did, but haematocrit (Hct) increased to normal before AGP levels normalised. However, in our study only around half of cats with FIP were anaemic.

After Mutian, I give oral Virbagen Omega until the FCoV antibody titre reduces significantly. Reduction of FCoV antibody titre to zero is evidence that there is no more antigen in the cat's body stimulating an immune response. However, the FCoV antibody titre can stay elevated for many months after FIP.

Zinc Mefloquine and Azithromycin

What if the client can't afford Mutian or Virbagen Omega?

NOTE: I have NOT tried any of the suggestions that I am about to offer

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A common question from Turkish attendees in my last FIP treatment webinar was what could be used if Mutian and Virbagen Omega were not available, or not affordable? Attendees were very much aware of some of the human treatments, such as ivermectin.

Disclaimer: what I am about to suggest has NOT been tried – I am simply speculating here. If you try these suggestions, you assume full responsibility for the consequences.

SARS-CoV2 treatments

Remdesivir / GS-441524

- { Zinc picolinate
- { Hydroxychloroquine (HCQ) ionophore
- { Azithromycin
- Ivermectin
- Vitamin D
- REGN-CoV2
- Ly-CoV2

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The combination of hydroxychloroquine and azithromycin with or without zinc has been used with enormous success by Prof. Didier Raoult's group in their University teaching hospital in Marseille, France, to prevent COVID developing in SARS-CoV2 infected people, and to treat those who are sick.

Zinc has anti-coronavirus effects, but needs an ionophore to get into cells. Zinc picolinate is the form which is best absorbed from the gut, but one has to be wary of zinc toxicity in cats, although short term it should be OK. Zinc is found naturally in oysters and grass fed beef.

In humans with COVID, hydroxychloroquine is the ionophore used to get the zinc into the cells but again toxicity is a concern. Yu et al (2020) published on using mefloquine in cats so I'm wondering about trying a combination of Zinc, mefloquine and azithromycin. However, I have **not** actually tried this in real life so I do not know if it would work (please join my MeWe veterinary group for news of this when I obtain news).

Zinc / mefloquine /azithromycin

Yu et al 2020, "Mefloquine may provide a safe effective treatment for feline coronavirus and feline calicivirus infections in cats."

Yu J, Kimble B, Norris JM, Govendir M. 2020. Pharmacokinetic Profile of Oral Administration of Mefloquine to Clinically Normal Cats: A Preliminary In-Vivo Study of a Potential Treatment for Feline Infectious Peritonitis (FIP). *Animals (Basel)*. 10(6):E1000.

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Zinc / mefloquine /azithromycin

Zinc: from grass-fed meat

Mefloquine: one quarter of a 250 mg mefloquine tablet (Lariam, Roche, Millers Point, NSW, Australia) to an adult cat with food twice a week up to 4 doses. This dose equates to 10-12mg/kg.

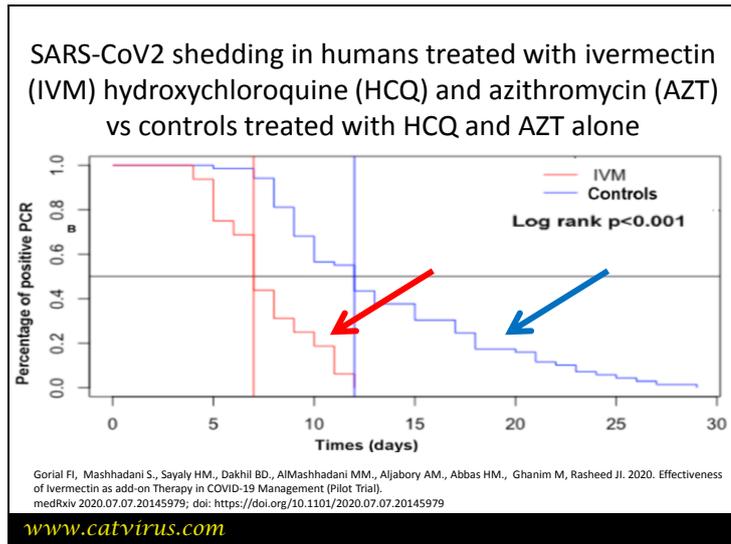
Yu J, Kimble B, Norris JM, Govendir M. 2020. Pharmacokinetic Profile of Oral Administration of Mefloquine to Clinically Normal Cats: A Preliminary In-Vivo Study of a Potential Treatment for Feline Infectious Peritonitis (FIP). *Animals (Basel)*. 10(6):E1000.

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Reference

Yu J, Kimble B, Norris JM, Govendir M. 2020. Pharmacokinetic Profile of Oral Administration of Mefloquine to Clinically Normal Cats: A Preliminary In-Vivo Study of a Potential Treatment for Feline Infectious Peritonitis (FIP). *Animals (Basel)*. 10(6):E1000. doi:10.3390/ani10061000

Ivermectin

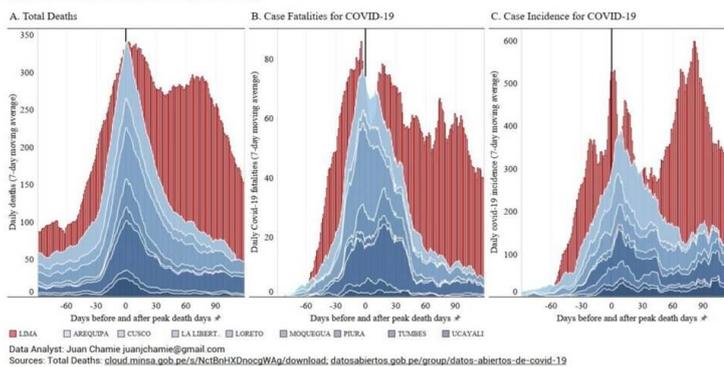


Ivermectin has been giving amazing results in human SARS-CoV2 infection in both curing people with COVID-19 and in reducing the duration of coronavirus shedding, as shown in this Kaplan-Meier curve. The ivermectin results are shown in red, the control group in blue. People on ivermectin stopped shedding virus in up to 12 days (red arrow), whereas some in the control group were still shedding virus for more than twice that time (blue arrow). But it was a small study.

Reference

Gorial FI, Mashhadani S, Sayaly HM, Dakhil BD, AlMashhadani MM, Aljabory AM, Abbas HM, Ghanim M, Rasheed JI. 2020. Effectiveness of Ivermectin as add-on Therapy in COVID-19 Management (Pilot Trial). medRxiv 2020.07.07.20145979; doi: <https://doi.org/10.1101/2020.07.07.20145979>

Total deaths, case incidence and case fatality for COVID-19 in populations older than 60 years old for eight states deploying early mass ivermectin treatments vs Lima in Peru.



Eight states in Peru gave ivermectin to the population for SARS-CoV2 / COVID prevention: Lima did not. In the graphs on the left the 8 ivermectin states are in blue, Lima in red. These graphs speak for themselves: prophylactic ivermectin massively reduced COVID19 deaths and cases.

<https://covid19criticalcare.com>

Source: <https://covid19criticalcare.com>

www.catvirus.com



There exists one ivermectin preparation for cats - Heartgard by Merial / Boehringer - I don't know if it's available in Turkey or not.

Heartgard is recommended to be used once a month for heartworm, but for FIP/FCoV treatment it would need to be used off label q24 -48 hours until recovery. You would need to give 4 times the dose - i.e. 4 of the tablets - to obtain a dose adequate for treating coronavirus. There is precedent for using this kind of dose, but with a different product ...

Dose for CoV
treatment
200µg ivermectin
per kg

MICRO grams

i.e. 0.2mg /kg
ivermectin q48h



Silbermayr K, Joachim A, Litschauer B, Panakova L, Sastre N, Ferrer L, Horvath-Ungerboeck C. 2013. The first case of *Demodex gato* in Austria, detected with fecal flotation. Parasitol Res. 112(8):2805-10

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... A dermatologist simply used Ivomec for cows - orally - at 0.2mg/kg for treating Demodex ^{Silbermayr et al, 2013} - so it can be done, albeit with great caution, because of course an overdose can cause neurological signs. A colleague told me that it's used regularly at 0.2mg/kg to worm big zoo cats. It has a long half life, so possibly could be used every other day, rather than daily.

However, I've got absolutely NO evidence for using ivermectin to treat FIP or FCoV infection, I have not even done the work of faecal testing before and after dosing, like I did with Mutian, so I have no idea if it would decrease FCoV load or not.

Ivermectin can cause neurological toxicity so use only with extreme caution

References

Muhammad G, Abdul J, Khan M Z, Saqib M. 2004. Use of neostigmine in massive ivermectin toxicity in cats. Vet Hum Toxicol. 46(1):28-9.

Silbermayr K, Joachim A, Litschauer B, Panakova L, Sastre N, Ferrer L, Horvath-Ungerboeck C. 2013. The first case of *Demodex gato* in Austria, detected with fecal flotation. Parasitol Res. 112(8):2805-10. doi: 10.1007/s00436-013-3448-6.

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Vitamin D

Use with caution: and no longer than 4-6 weeks

Hospitalised cats have been shown to have low vitamin D levels, and low vitamin D has also been shown in people who get sick with COVID-19.

Therefore, for cats with FIP, it wouldn't hurt to supplement with vitamin D for 4-6 weeks, but NO LONGER, since Vitamin D is toxic to cats if given in excess.

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HUGE THANKS

to my wonderful co-presenter, Prof. Nilufer Aytug, and to Ertan Isletici for excellent chairmanship and to the brilliant Ozge Kaiser for translation

Many thanks to Zohar Shasha of [Biogal](#) and [MediCare](#) for organising this webinar and inviting me to share my observations on FIP and FCoV diagnosis and treatment, and special thanks to my co-presenter Prof. Nilufer Aytug, to Ertan Isletici for doing a great job of chairing, and to the amazing Ozge Kaiser for translating.

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HUGE THANKS

to Zohar Shasha and the staff of Biogal and MediCare for organising and sponsoring this webinar and to Ertan Isletici and the MediCare team for organising translation of the FIP diagnosis algorithm into Turkish



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Medicare: www.medicareint.com

LABOR / ORATORY

Niels Pedersen: discovered that adenosine nucleoside analogues could cure FIP
Tony Xue and colleagues: invented Mutian pills (www.mutianstore.com)
Sheryl Curran: introduced me to Mutian pills

The word 'Laboratory' can be split into Labor and Oratory; I did the oration of this webinar, but all the labor, the hard work, was done by

- Niels Pedersen, who discovered that nucleoside analogues could cure FIP
- Tony Xue and his colleagues at Mutian Biotechnology who invented their miracle Mutian pill
- and Sheryl Curran, who discovered that Mutian could stop FCoV shedding and told me about it

I am beyond grateful to them all.

I am enormously grateful to the cat guardians and veterinarians who make my research possible without use of experimental cats: I simply could not do my studies without the generosity of these amazing people: only a tiny number were named below, just some of those whose cats were mentioned in this webinar.

Huge thanks as always to my friend and mentor Prof. Os Jarrett. Enormous thanks to the donors and subscribers to www.catvirus.com who financed these studies.

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HUGE THANKS to all the cat guardians and veterinary surgeons who made this research possible

Os Jarrett	David Adby
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ENORMOUS THANKS ... to the www.catvirus.com subscribers who supported me in while doing this research and to the donors who paid for laboratory tests and publication fees

Disclaimer
I have absolutely no financial interests in Mutian, Virbac, Royal Canin, VetImmune or any products mentioned in this webinar.

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Contact me: I hope that Turkish veterinary surgeons will feel free to contact me any time over any cases they would like to discuss: email address draddie@catvirus.com – but PLEASE DO NOT share this address with members of the public, although sharing with other veterinarians is fine.

The public can obtain consultations with me if they have their vet’s consent: my consultation packages (single question or one month subscription) are on the home page of catvirus.com.

For more information on FCoV and FIP please visit

catvirus.com

To keep up to date with FCoV and FIP news, please visit

www.catvirus.com

FIP and FCoV treatment has taken a massive leap in the last two years and while some of what I tell you is the result of three decades of research, unfortunately other areas are still under investigation and new information is being added all the time.

Please follow me on social media for my own updates and news of discoveries by others in the field.

ONLINE PRESENCE

Website: www.catvirus.com

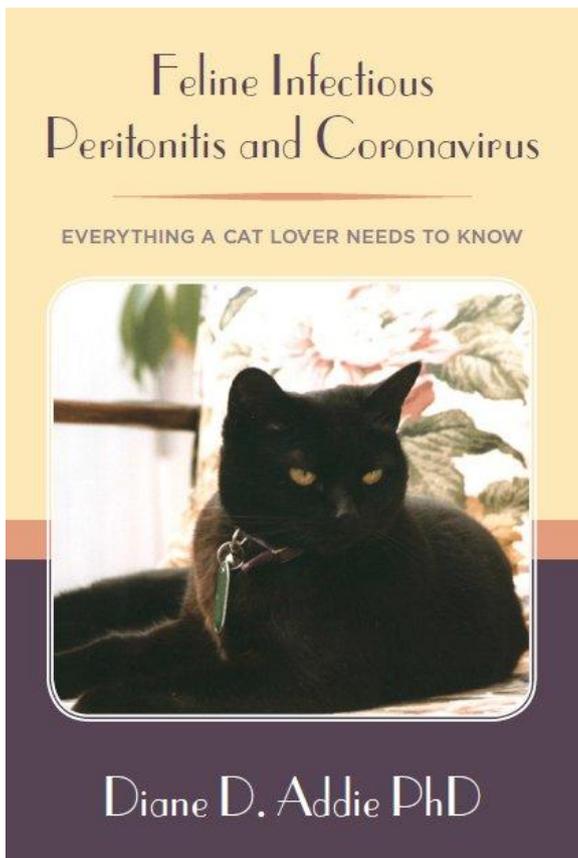
Please follow my work on: Pocketnet (a free speech alternative to Twitter):

<https://pocketnet.app/catvirus?msocialshare=true&ref=PXAY6Ttdx4uZrpyGuyDRktDzm47YZz8jTg>

MeWe (a privacy honouring alternative to Facebook): www.mewe.com/i/catvirus1

Bitchute: www.bitchute.com/channel/ZEk9qdH9iDzm/ (videos uploaded there first in protest against YouTube censorship).

Last but not least, here’s bad ol’ YouTube, who think they have the right to censor free speech and what you and I get to hear about: YouTube: www.youtube.com/user/DrDianeDAddie



Book for cat guardians: Feline Infectious Peritonitis and Coronavirus, written in English and Spanish (but Spanish version has not been updated yet) available from Amazon:

https://www.amazon.com/gp/product/1480208973/ref=ppx_yo_d_t_b_search_asin_title?ie=UTF8&psc=1

Conflict of interest statement: obviously Biogal has paid me for these webinars, but I want to state that at the time of the FCoV antibody comparison study, published in 2015, I had never received any payment from Biogal. Biogal did contribute FCoV Immunocombs – many FCoV antibody test manufacturers contributed their products for my independent assessment.

I have no vested interests in Mutian, Virbac (makers of Virbagen Omega), Applaws or any products mentioned. I was employed at the University of Glasgow Veterinary School where AGP and FCoV antibody testing was available, but am no longer in their employ.

Disclaimer: I am not a lawyer and have absolutely no idea about the legality or otherwise of some of the products I will mention in this webinar. Please consult your own veterinary body for advice in this area. You might also want to contact Niki Ng at Mutian: nikiyu@live.hk for FDA approval updates.

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