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Feline Infectious Peritonitis (FIP). What Happened, Why It Happened. What Will Happen to My Cat and What Are My Options?

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A long time ago, a Latin teacher at Mount Holyoke College who loved cats decided to change professions. She chose the premier American veterinary school of the time, <u>Cornell</u>, and sought a position at the best American veterinary hospital of the time, <u>Angell</u>. She became the first feline medicine specialist. In 1962, she reported her observations on a perplexing and always fatal disease of cats, which she called "chronic fibrinous peritonitis". Two years later, a veterinarian at <u>PennVet</u> reported on a cat with a similar disease. You

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can read the articles here: & Humans have lived with house cats for thousands of years and written about them for centuries. It is unlikely that a disease as serious as FIP would have gone unnoticed and unrecorded that long. I believe that an important coronavirus virus mutation occurred in the late 1950s. Some propose that the common intestinal forms of coronavirus of dogs and the one of cats met and combined. (read here)

Today veterinarians call the widespread and rarely dangerous intestinal (enteric) coronavirus of cats FCoV (=feline enteric coronavirus aka FECV) and its dangerous mutated form, FIPV (feline infectious peritonitis virus). When coronavirus mutation events occur, it is often the virus's cell-seeking <u>spike proteins</u> that change their choice in the cells they prefer to attack. (<u>read here</u>) That something like that had occurred in cats was proposed in 1996 by a group including Dr. Niels Pedersen at Davis. (<u>read here</u>) In 2009 he confirmed it. (<u>read here</u>)

When a virus accomplishes a mutation that is in its interest, this new mutated form becomes the prevailing form. That is not the case with FIP coronavirus. The mild FCoV form of cat coronavirus is still the prevailing form. It is never in a virus's interest to kill the host it inhabits. Most veterinarians and research scientist currently believed that the mutated FIPV form of cat coronavirus must arise anew from the mild intestinal FCoV form in every new cat that becomes ill with FIP (or succeeds in overcoming it). In most cats that mutation probably never occurs. We currently believe that in perhaps 8-10% of cats it does. Of those cats, some overcome the virus on their own and survive and some do not. Until recent discoveries at the veterinary school in Davis, California, all cats that began to exhibit ill health perished. Genetic factors unique to your cat undoubtedly are another factor in which cat does and which cat doesn't develop FIP. It is also known that experimentally transferring the mutated FIPV corona virus from an ill cat to a health cat produces FIP in the majority of cats that receive it. (<u>read here</u>

How Common Is the Ordinarily Mild Intestinal Form of Feline Coronavirus?

The ordinary, mild, feline coronavirus (FCoV) is quite common in cats throughout the world. Some studies suggest that almost half of the world's house cats have been exposed to it. In some urban areas, up to nine out of ten cats have encountered the virus. However, which cats get sampled is quite important. (read here, here, here & here) In those studies the number of FCoV-positive cats living in group situations is much higher than in those living in individual homes. Cats in remote isolated areas apparently live their lives free of coronavirus. (read here & here)

Detection of prior exposure to the FCoV virus through the common antibody-based tests do not necessarily mean that the virus is still present in your cat. And lack of antibody can also occur early in a true FCoV infection. Whatever the true numbers, the virus is considerably more common than veterinarians would like it to be. When cats are not concentrated closer together than Nature intended them to be, both the mild form of feline coronavirus and the mutated FIP form are not significant problems. Only 4% of your cat's wild European ancestors show evidence of ever having met coronavirus – and that was probably through a chance encounter with a domestic cat. (<u>read here</u>)

Does The Ordinarily Mild Intestinal Form of Feline Coronavirus (FCoV) Cause Illness?

This mild form of coronavirus is most common in cats less than two years of age. Many cats (probably most) show no health-related signs due to this infection. In those that do, a few days of mild diarrhea is generally all that occurs. Most cats eventually eliminate the active virus from their body – although some are uncertain if virus might linger dormant in a replication-defective, inactive <u>provirus</u> form. We all carry provirus in our bodies.

Is My Cat's Age Important When Ordinary Coronavirus Mutates to FIP?

Yes.

Most cats that contract FIP are young – usually between three and sixteen months of age. Over half are less than one year old. In one California study, laboratory-bred cats developed an increased resistance to FIP infections between 6 and 12 months of age. That said, FIP occasionally develops in older cats as well. Veterinarians do not know if the immune systems of older cats is more likely to nip coronavirus mutants in the bud (destroy them before they can proliferate) or if the virus is less likely to mutate in older cats or if other unknown factors are involved. (<u>read here</u>)

How Does An Ordinary Unimportant Coronavirus Infection Become A Case of FIP?

Nature designed viruses to randomly change their structure in a never-ending battle to defeat the immune system and move on to invade a new susceptible host. It is a hit or miss, but very effective approach. Most of these random genetic changes in virus composition (mutations) are unsuccessful. The viruses that carry those unsuccessful mutations are destroyed and never heard from again. But occasionally by sheer chance, a mutation occurs that give the virus certain advantages. When that occurs, that mutated virus becomes the predominant variety. Coronaviruses are notorious for the frequent mutations that allow them to jump between species or a ttack new areas of the body that they previously could not. Attacking a new species or a new area of the body often involves changes in the virus's surface <u>spike proteins</u> that I mentioned earlier. In the case of the FCoV to FIPV mutation, it allows the virus to invade a new cell type, your cat's <u>macrophages</u> and <u>monocytes</u>. This transformation or change in the virus's preference (tropism) causes the cat's immune system to run amuck, producing severe inflammation as it immune system cells attack the cat's cells that harbor the virus (liberation of <u>pro-inflammatory cytokines</u>). (read here, here & here)

I do not believe that the mild feline enteric coronavirus' (FCoV) mutation into the highly pathogenic (dangerous) feline infectious peritonitis virus (FIPV) offers any advantages to the coronavirus. Killing your host is never an advantage to a virus. I believe that is why FIP only occurs in a few cats that carry FCoV. FIPV mutations probably occurs in many more cats than those that develop FIP disease. But in those cats, their body recognizes and destroys these mutants soon after they appear. Some sources say that FIP develops in 5-10% of FCoV-infected cats. But the actual numbers are probably much lower than that among the general cat population. That is because a large portion of healthy cats never visit a veterinarian or, if they do it is only to receive periodic vaccinations. If you check patients arriving at a hospital, the majority of them are ill.

Is There More Than One Form Of FIP?

Yes.

Veterinarians generally recognize two forms of FIP, wet and dry. In the "Wet" form, inflammatory fluids are produced on the surface of the cat's abdominal and/or chest organs. In the "Dry" form, inflammation occurs within body organs without the production of excess fluids. Occasionally signs of both forms are present in the same cat.

The "Wet" or Effusive Form Of FIP

This was the first form of FIP that veterinarians like Jean Holzworth recognized. In the effusive or wet form of FIP, fluid buildup in your cat's chest or abdomen or both. This leaked fluid is primarily the result of the cat's immune system attacking what it perceives as a threat from a foreign invader (the presence of proteins that do not belong in the cat's body = antigens). Most veterinarians believe that this fluid buildup (an exudate) is not due to any direct damage that the virus causes to the cat's body cells that it inhabits. It is the cat's own cytokine-driven inflammatory response that liberates a mixture of fluid (blood serum) and proteins (globulin & fibrin) as well as white blood cells that would normally be confined to your cat's blood stream. This fluid has a characteristic thick ("fibrinous") consistency with a yellow-tinged appearance that always makes my heart sink when I see it aspirating slowly into my syringe.

Your veterinarian will probably tap (withdraw) and examine the fluid to confirm suspicions and then run tests to confirm that the liquid is indeed an exudate. On X-rays, this liquid has a characteristic granular appearance (a "ground glass" look). When fluid is found in your cat's abdomen, causes other than FIP that might pass through your veterinarian's mind. Lymphoma tumors, heart, or liver disease or even a ruptured bladder are occasionally the underlying cause of abdominal fluid. Additional laboratory tests can rule those causes out. When the fluid is in a cat's chest (a pleural effusion) other tests distinguish inflammatory fluid (exudate) from <u>lymphatic chyle</u>. When cats have fluid accumulations in their chest your veterinarian might remark that your cat's heart sounds are muffled and difficult to hear through his/her stethoscope (difficult to auscultate). When the cat's liver is involved, its gums, besides being pale from anemia, might have a slightly yellowish tinge (<u>jaundiced</u>). When effusive FIP occurs in a kitten, the youngster may just appear to fade away or have ceased to grow satisfactorily.

The Dry Form Of FIP aka The Non-effusive, Pyogranulomatous Form

Granulomas are composed of immune system cells that gather around objects and disease organisms that the body is attempting to wall off or eliminate. When FIP coronavirus-infected cells are primarily located within organs, this is the way a cat attacks them. It might be in your cat's liver, kidneys, lymph node(s), eye(s) or nervous system where these events occur, or it might be in a combination of any of those locations. The clinical signs cat owners and veterinarians see are highly variable. Veterinarians call it the "dry" form of FIP because unlike the effusive form, excess fluid does not accumulate – or at least it does not predominate. The dry form is sometimes called the "parenchymatous" form. The functional cells of various organs are called its <u>parenchyma</u>.

These changes brought on by the dry form of FIP tend to begin gradually. They are so nonspecific that they could have many non-FIP-related explanations. Inflammatory changes in an eye(s) (<u>uveitis</u>) is a textbook symptom of the non-effusive form of FIP Because of that, it will probably set off FIP alarm bells earlier than most. That is particularly true when it is accompanied by other nervous system or eye changes. Those neurological problems might include lameness, seizures, or just a tipsy unstable rear end gait (ataxia). In both forms of FIP, it is not unusual for the cat's owner to tell me that their pet experienced a major life stress event within the previous few months. Events such as boarding, the addition of a new cat(s) to the family, a move, a rival cat in the neighborhood, or some other issue that was thought to have been resolved. Another typical history is that the cat was recently obtained from an animal shelter, a cat group home or a private cattery. (<u>read here</u> & <u>here</u>)

How Is the Common Milder Coronavirus (FECV) Transmitted Between Cats?

The more common, milder, non-mutated FCoV form of cat coronavirus lives in the cells that line your cat's intestine. When released, this virus passes out through the cat's feces in large numbers. (read here) Cats grooming each other or sharing a litter box are thought to be the most common ways this virus transfers to another cat. Although no one has documented the survival time of the coronavirus of cats in the environment, coronavirus in general survive in the environment for only a few days at the most. So, most veterinarians do not believe that contaminated objects in your cat's environment are a source of many (if any) infections. That said, frequently changing the litter boxes in multi-cat households is always a good idea. When you contemplate introducing a new cat into your household, a <u>PCR test</u> (FCoV RT-PCR) of its feces can tell your veterinarian if there are FCoV virus in its stool at the time. However, FCoV virus shedding is often intermittent. And early in infections the test results might be negative even when the virus are already present in the cat's stool – but in numbers too low for the PCR test to detect.

How Is the Dangerous FIP-Mutated Coronavirus Transmitted Between Cats?

Veterinarians do not believe that natural transmission of FIP virus from cat to cat frequently occurs. FIV-infected cats are known to shed little or no mutated virus in their stools. (<u>read here</u>) Most veterinarians currently believe that every case of FIP requires a new mutation of the common FCoV virus after it infects a new cat. One article disputed that. However, no one was able to duplicate those results. (<u>read here</u>)

When a new mutation creates the dangerous feline infectious peritonitis virus (FIPV), a percentage of cats go on to develop FIP. But not all of them do. Experimentally, scientists can extract the FIP virus from an ill cat and inject it directly into another cat. That often produces FIP in the second cat. However, that is not something that we think occurs in the real world. Yet the complex interactions between the virus and a cat's immune system, the innumerable ways a virus can mutate and all cat's unique genetics make absolute statements unwise. (read here) Few things in medicine are absolute.

How Long After This Mutation Occurs Might My Cat Become ill?

I mentioned earlier that most cats that are exposed to ordinary feline coronavirus never become seriously ill. When the virus stays in your cat's intestines where it belongs, the most you might see is a short period of soft stools or diarrhea. Infection of the cat's intestinal lining (its <u>enterocytes</u>) is most likely immediate after a cat ingests the coronavirus. But it can take a few days before sufficient virus numbers are present for them to be detected in laboratory tests. (<u>read here</u>) After that initial infection, most cats appear to eliminate the virus from their bodies rather rapidly. However, some cats become intermittent or persistent shedders of the non-mutated form of the virus, and a few will go on to develop FIP. (<u>read here</u>)

The time it takes from infection with the mild form of coronavirus until a mutation might occur and the possible development of FIP begins is highly variable. It would be extremely difficult to design valid studies to look into that. In the laboratory, FIP-related illness can begin within a matter of weeks. But that is when the already mutated FIP virus is experimentally transferred from cat to cat. Besides laboratory environments and "purpose bred" cats tell us little about what occurs in the real world. Veterinarians really do not know what the dynamics of FIP is in a home or cattery situation when "wild" strains of the virus and genetically diverse cats are present. Long lag-times often occur between the time a cat was likely exposed to the "wild" coronavirus and the time it begins to show illness – months or even years. As I mentioned, many veterinarians associate FIP emergence with a stress or trauma. Things like overcrowding, frequent pregnancies, genetic predisposition, inbreeding and surgical procedures have all been discussed as triggers that might tip the balance in the FIP virus' favor. This is particularly sad for me to witness because by the time the cat becomes ill my clients are already so emotionally attached to it.

What Are the Clinical Signs Of FIP?

I mentioned that the early signs of FIP are often subtle and easily missed. Lethargy, a rough hair coat, little interest in grooming or playing, more sleep time, picky eating and weight loss are often the first reasons these cats are brought to animal hospitals. But those signs could be due to so many other things.

During a veterinary exam it's common for FIP cats to run low-grade fevers. But please remember that normal cats often run a Fahrenheit degree or so hotter due to travel, stress, fear or manipulation by strangers. You might have mentioned to the receptionist that your cat is having more litter box accidents. Under-the-weather cats are less careful about their hygiene. So perhaps your vet might suspect a bacterial infection and treat the cat with antibiotics. But antibiotics do not make these fevers go away. When these cats have struggled with the FIP virus longer, it is common for them to become anemic (a non-regenerative anemia = too few reticulocytes present in their blood).

The Clinical signs Of The Effusive Form Of FIP

When a cat has already progressed to the effusive wet form of FIP, mediator compounds (<u>inflammatory cytokines</u>) released by the cat's immune system result in blood vessel

inflammation on the outer surfaces of body organs (polyserositis). (<u>read here</u>) When that occurs in the abdomen, the cats develop a fluid-filled, enlarged, pear-shaped belly. When it occurs in the thorax (chest) breathing becomes labored. When it is your cat's abdomen that accumulates the fluid, its weight may not change even though it is, at best, a picky eater. That is because of the weight of the excess fluid in its abdomen. However, if you run your fingers along the cat's spine you will note that it is bony and many have lost leg muscle mass as well. <u>Malaise</u> and <u>cachexia</u> accompany this condition.

The Clinical signs Of the Non-Effusive Dry Form Of FIP

In this less common non-effusive (= granulomatous FIP) fluids do not tend to accumulate in your cat's chest or abdomen. This form of FIP also tends to develop slower. The non-effusive, dry form of FIP is also more likely than the wet form to be initially confused with non-FIP diseases that produce similar signs. Neurological health issues such as epilepsy, seizures, tremors, balance problems, personality changes or increased sensitivity to touch resulting from underlying FIP could easily be confused with other causes. So could vision problems. It is common for the dry form of FIP to affect nerves and the brain. But other organs can be affected as well: the eye(s) (read here), the liver the kidneys, respiratory tract (read here) the intestinal tract, the skin. (read here)

What Is There Other Disease That Could Be Mistaken For FIP?

Diseases that might be mistaken for FIP include <u>toxoplasmosis</u>, <u>cryptococcosis</u>, <u>hemobartonella</u>, middle ear infections, trauma, drug toxicities, <u>lymphoma</u>, <u>FeLV</u>, <u>FIV</u> and tumors. Occasional cats show cllinical signs of both the effusive and non-effusive forms. (<u>read here</u>)

How Will My Veterinarian Confirm That My Cat Has FIP?

The wet form of FIP is relatively straightforward for your veterinarian to diagnose. Young cats arriving with low-grade fevers and fluid accumulations in their chest or abdomen or both are likely to have the disease. Blood samples your veterinarian obtains usually show mild to moderate <u>anemia</u>. Blood <u>albumin</u> levels are often low, <u>A:G ratios</u> are off, blood <u>globulin</u> levels high giving an albumin to globulin ratio of <0.6. However, this test serves better as a rule-out test than a rule-in test. (<u>read here</u>) Total <u>lymphocyte</u> counts are often low and <u>neutrophil</u> counts elevated. Examination of the <u>specific gravity</u> of the fluid confirms that it is an exudate (> 1.030).

When a cat has developed the dry form of FIP diagnosis is much more challenging. High blood globulin levels (hyperglobulinemia) – often combined with low blood albumen levels are suggestive of FIP. Tissue biopsies can confirm the disease with certainty, but they can

be challenging or impossible to safely obtain. Advanced centers have found MRI imaging and spinal fluid analysis useful tools. (<u>read here</u> & <u>here</u>)

Most veterinarians make a dry-form FIP diagnosis based on a preponderance of evidence – not 100% certainty. *Preponderance* is a very relative term and probably accounts for the miracle FIP cures that are sometimes reported. Just because a cat is coronavirus positive and has some of the common cllinical signs of dry form FIP does not mean that it has FIP. None of the more common tests taken alone can confirm that a cat has dry form FIP. But several, taken together with the cllinical signs your cat is experiencing are usually sufficient for your veterinarian to make a reasonable diagnosis. Even the presence or absence of corona virus antibody or the virus themselves is insufficient since so many healthy cats harbor that virus and anti-coronavirus antibody levels do not correlate well with FIP disease.

Some, including Idexx Laboratories, believe that high FCoV antibody titers add to an FIP suspicion. In 2014, the Company introduced their FIP Virus RealPCRTM test that claimed to be able to tell (differentiate) the mild FCoV coronavirus from the mutated FIP coronavirus. The test was designed based on some German studies. (<u>read</u> <u>here</u>, <u>here</u> & <u>here</u>) However more recent studies not sponsored by the Company have cast considerable doubt on the value of their patented test. (<u>read here</u>)

What Treatment Can Veterinarians Offer My Cat?

Treatments That Often Work:

Antiviral Medications

AKA / Protease Inhibitors, Polymerase Inhibitors, Nucleoside Analogues

Protease inhibitors and similar compounds are the only medications that currently offer hope to cats dealing with FIP. Their existence dates back to studies conducted in the early 1990s to screen drugs for their ability to cure human hepatitis C and suppress human AIDS. Later it was the 2003 <u>SARS</u> coronavirus epidemic that spurred the research. The general interest in antiviral medications, motivated the Veterinary School in Manhattan, Kansas to examine some of these compounds. (<u>read here</u>) Some were already known to be active against coronavirus. Being veterinary school-based, their interest naturally turned to the until then untreatable FIP coronavirus of cats as well as <u>feline calicivirus</u>. In 2015 they confirmed that of the 13 compounds studied, several were active against feline coronavirus. Among them was GC-376. (<u>read here</u>) That information made its way to the veterinary school in Davis, California where a veterinary virologist, Dr. Niels Pedersen, began trials administering GC376 to client-owned cats with either the wet or the dry form of FIP. (<u>read</u> <u>here</u>) Results were very promising, although the medication appeared to be more effective treating the wet than the dry form of the disease. In another 2018 study, that group in Davis, working with <u>Gilead Sciences</u> identified another closely related compound, GS-441524, that was also effective against FIP. (<u>read here</u> & <u>here</u>) A colleague in the vet school department led a similar study – this time on purpose-bred cats using GS-441524 to determine a suitable feline dose. (<u>read here</u>) Gilead holds the patent on both GC376 and GS-441524. That particular compound is formed from a <u>prodrug</u>, <u>remdesivir</u> (aka GS-5734) which the Company currently markets as a treatment for human <u>Covid-19</u>. Much of the information on the use of Remdesivir in cats is word of mouth over the Internet. So, both valid and mistaken advice probably exist online. For further information you might wish to contact Bova Australia.

GS-441524

Dr. Petersen documented that this drug is, in many cases, effective. The problem has been in obtaining it. Gilead is a publicly traded company. Stockholders demand maximum profits. The Company's valid opinion is that there is vastly more money to be made selling products like Remdesivir/Veklury® for human use than for veterinary use. As I mentioned, remdesivir is the protide or prodrug that the body later converts into GS-441524. Furnishing the drug in its protide or prodrug form helps it enter the correct immune system cells where immunosuppressive coronaviruses reside. In Dr. Pedersen's drug's trials in cats, GS-441524 was administered in its unaltered form with successful FIP cure rates never encountered. Gilead's refusal to release GS-441524 for use in cats quickly led to desperate cat owners turning to black market Chinese chemical laboratories that operate in defiance of international patent law.

GC-376

In other studies, at the Kansas State and California veterinary schools, another similar protease inhibitor compound, GC376, also appeared to help cats infected with the FIP virus. A compound with similar potential is GC373 (<u>read here</u> & <u>here</u>) GC376 was initially licensed by a company called Anivive Lifesciences. I do not know what their marketing plans for the drug are but maximizing profits generally comes into play.

One of the Chinese pharmaceutical suppliers, MUTIAN Biotechnology Co. Ltd., located in Nantong, markets a drug they call Mutian® xraphconn. When I last checked their website, it was not available in capsular form anymore. But when it was, the FDA's unapproved drug list listed its active ingredients as: inonotus obliquus fruiting body, nicotinamide ribotide, crocin, S-adenosylmethionine, and milk thistle/silymarin inotodiol. Nothing likely to cure FIP. I am told that at one time the product was marketed as "a 'dietary supplement exclusively designed for cats with FIP, by "boosting their immune system and overall wellbeing". Mutian is also available in an injectable form. As to what either of those brews is likely to contain, you will have to go to the <u>Sock FIP</u> and the <u>FIP Warriors</u> websites not the Mutian website to find that out. Word has it that<u>Gilead</u> has their suspicions.

I was told that Mutian's injectable compound was at one time being sold for about \$4,000 for a 6.6/3 kg cat. Friends in Russia tell me the price there in 2021 has dropped to \$1,000. That is probably due to competing suppliers in China, but I have no special knowledge. A

veterinarian friend in China tells me they get a considerably better deal: Sock FIP and FIP Warriors would be much better sources of that sort of information. At one point, the Company claimed that their product's contents were a proprietary secret. But I also read that Gilead, the makers of remdesivir, sued them for patent infringement. Cat owners need to remain aware of the type of individuals they are dealing with as well as the possibility that these drugs might be seized by US Customs agents if discovered.

More anti-viral compounds helpful in treating FIP-positive cats are almost certain to be discovered soon. (<u>read here</u> & <u>here</u>) I believe that some will be found among the <u>3CLpro</u> inhibitors. Pfizer already has two of these in human trials. So, treatment options for owners of FIP+ cats should soon be much greater and above board. I don't believe that any of these future medications will be low in cost. But the cost will hopefully come down substantially as one drug competes with another for the human coronavirus treatment market.

Davis had also considered Merck's MK-4482/EIDD-2801 (<u>Molnupiravir®</u>), an oral anticorona virus medication in development, as a candidate drug to treat FIP. However, I do not believe that Merck, the patent owner, made any of that drug available to them. I could be wrong. But in April of 2021 one of the two human <u>Title 21</u> clinical trials of that compound, Molnupiravir®, in Covid-19 patients was halted as being ineffective in aiding seriously ill hospitalized patients. I see online that human trials in less serious cases of Covid-19 might be continuing. Drug companies tend to be quite circumspect when it comes to releasing data – particularly when it is negative and might affect their stock prices.

None of these drugs are completely without risk. Occasional skin reactions, sensitivity and sores occur at their injection sites. Infrequently they have been severe. Much of that could be due to errors in injection technique. Minor kidney damage was once attributed to one of the Chinese knockoffs. The severity of your cat's condition at the time that these drugs are begun also affects success rates. Some of these cats require fluid therapy. When secondary infections are present, they need to be addressed with antibiotics and nutritional support. Those and heroic measures that might even include a blood transfusion might give your cat the best chances for survival. A complete blood analysis (CBC & blood chemistry including an A:G ratio) shortly before the treatment begins and periodically as treatment progresses is always wise. They allow your veterinarian to keep track of your pet's general health in a scientific way as treatment proceeds. But a good appetite, progress in returning to your cat's traditional weight and a slow return of its old cheerful self is always the best sign. If the cat won't eat, a few days of corticosteroid (eg prednisolone) is permissible. Nonsteroid appetite stimulants such as **Entyce®** are available, but we have no idea if they interact negatively with any of these drugs. If you have given it or mirtazapine to FIP cats, let me know the result. The only time removal of effusion fluid is desirable is when it is affecting your cat's ability to breath. Some cat owners throw in liver or kidney tonics such

as <u>SAMe</u>, <u>silymarin</u>/=milk thistle, S-Adenosylmethionine, probiotics, <u>vitamin B3</u>, etc. But none of those products affect outcomes.

According to Dr. Pedersen and others, young cats less than seven years old are more likely to be cured than cats that develop FIP at an older age. And as I mentioned earlier, cats with the wet form of FIP are more likely to benefit than cats with the dry form – particularly those who are already experiencing neurological and/or eye problems. Relapses of FIP after the 12-wk course of GS-441524 have also been reported. Sometimes an additional 8 weeks on the drug has been beneficial and sometimes it hasn't. Occasional cats that develop the neurological form (dry form) of FIP that have been successfully treated with authentic or Chinese GS-441524 to eliminate the FIPV virus do not fully recover from their disabilities. That is particularly true when it includes paralysis and leg weakness due to <u>central nervous system</u> damage. Some believe that a higher drug dose might prevent that. But the general belief in medicine is that peripheral nerves (arms, legs, etc.) often slowly regenerate: but <u>neurons</u> of the central nervous system once destroyed, never do. (<u>read here</u>) But most cats recover – if not completely, sufficiently to lead future happy lives.

Medications of Unproven Value

I mentioned earlier that the cytidine nucleoside analog Molnupiravir (EIDD-2801) that is or was being developed by Merck for severe coronavirus disease in humans might prove helpful to cats with FIP. We do not know, at least I do not know.

Japanese veterinarians, generally publish quality veterinary studies. One veterinarian in Japan thought that a combination of the anti-rheumatoid arthritis drug, <u>Humira®</u> combined with an anti-fungus drug, <u>itraconazole</u>, might be of some benefit to FIP cats. (<u>read here</u>) Perhaps that will prove to be useful, perhaps it won't. No controlled studies that I know of have been performed. Itraconazole's primary use in cats is to treat stubborn cases of ringworm.

Curcumin

<u>Curcumin</u> is obtained from the spice, <u>turmeric</u>. It is sold in health food stores with various health benefit claims. One 2020 study reported that curcumin had suppressive effects on the FIP virus when grown in their laboratory. But they never got around to trying it in FIP+ cats. (<u>read here</u>) Curcumin gets a lot of notoriety. But far as I know it has never been found to be beneficial or curative for any human disease. (<u>read here</u>) We really have no idea what, if anything, it might offer to FIP-positive cats.

Mefloquine

In 2020, four University of Sidney's veterinarians looking for FIP treatment options examined how cats metabolize a compound, <u>mefloquine</u> used to treat human malaria. (<u>read here</u>) In the USA it is sold as Lariam®. They had an interest in the drug because a previous study appeared to show that it was active against the feline coronavirus. (<u>read</u> <u>here</u>) I do not know if those studies continue. Clinical trials were also begun in Russia to see if the drug might be beneficial to Covid-19 patients. No results have been announced.

Treatments I Have No Faith In

For many year I have believe that the FIP "cures" that are occasionally reported probably represent cases where cats were carrying only the non-fatal intestinal form of coronavirus but exhibited signs similar to FIP because of some other unrecognized health problem(s). In no report that am aware of was it ever verified that the coronavirus had left the intestine and invaded the cat's body. (monocyte/macrophage tropism). That is something that has to happen before a cat develops FIP.

Doxycycline

Some suggest that doxycycline antibiotic, with or without prednisolone, is beneficial to FIP+ cats. Doxycycline is a suitable antibiotic for secondary bacterial infections that you FIP cat might experience. It is also a great drug to cure <u>hemobartonella</u> that some FIP-positive cats might carry. But no one has ever confirmed that it has any effect on the FIP virus. If you give doxycycline in capsular or tablet form to your cat for any reason, be sure to follow it with an aliquot of water or morsel of soft foods as they can lodge in your cat's esophagus causing damage. That is a good idea when you give any sort of pill to a cat.

Prednisolone And Other Corticosteroids

It is true that <u>prednisolone</u> and compounds like it (corticosteroids) decreases inflammation. But they have never been shown to affect the downward spiral of FIP. However, corticosteroids are excellent appetite and positive mood stimulants and in some cases, they do give a short burst of energy and motivation to FIP positive cats. Similar effects occur in humans. (<u>read here</u>) So there is no harm in giving them for a few days under your veterinarian's supervision.

Paradoxically while some veterinarians attempt to stimulate your FIP cat's immune system with drugs like interferon and Polyprenyl immunostimulant, others administer corticosteroids like prednisolone or dexamethasone to depress the cat's immune system.

Polyprenyl immunostimulant (PPI) (aka polyprenyl phosphate, Fosprenil®)

In 1996, the founders of a Russian startup company, Micro-plus, published an article on the amazing abilities of their compound, polyprenyl phosphate (phosprenyl, aka fosprenil)

to cure a wide variety of diseases. You can read that study here: ______They claimed its use to be "highly efficient" in the treatment of rabies, cancer, distemper, hepatitis, enteritis (parvo?) and potentially useful in treating human HIV and human herpes too. They obtained a Russian patent on the compound. Polyprenyl immunostimulant (PPI) is still



widely sold in Russian pet stores where it is still billed to cure most anything.

I remain skeptical that polyprenyl immunostimulant is of any value to your cat. The last time I know that a claim that broad was made for a potion was by <u>Mithridates the Great</u> in 100 BC. Read more about the Great Theriac if you wish to <u>here</u>. Nevertheless, in 2009 veterinarians at the University of Tennessee reported that PPI seemed to benefit several cats that were assumed to have the dry form of FIP. (<u>read here</u>) Naturally, everyone was elated and hopeful. Even the Winn Feline Foundation kicked in some money. But since that initial announcement in 2009 I know of no further publications on this medication in human or animal medicine. As a rule of thumb, truly effective medications that are this urgently needed by veterinarians and cat owners catch on considerably faster. Read a Russian veterinarian's 2013 opinion on the questionable value of PPI in the treatment of

FIP here:

Feline Interferon Omega

Interferons play a part in your cat's natural resistance to corona and other virus. (<u>read</u> <u>here</u>) So one might assume that administering interferon to cats with FIP might help them. A Japanese study once suggested that. (<u>read here</u> However, it was a poorly constructed study. Only a few animals were treated and observed and there was never proof offered that any of the cats suffered from FIP. But since veterinarians had so little to offer FIP cats, it caused a lot of excitement at the time.

A more recent German study found that feline interferon administration had no effect on how long the FIP-infected cats that were studied lived or the quality of their lives. (read here) I suppose one can always argue that the Germans didn't give enough interferon, or gave it the wrong way, or gave it at the wrong stage of the disease, etc. So, there are still some veterinarians who administer it or recommend it. Virbac Corporation's European division still markets a recombinant feline interferon product (Virbagen Omega®). It is not currently sold in the United States, but some North American cat owners manage to get their hands on it. A UK veterinarian published an article in 2020 that suggested its use was beneficial in aiding a cat infected with the dry form of FIP. However, besides the interferon omega, the cat received the Chinese brew, Mutian. (read here) My belief, the belief of the <u>NIH</u>, and others is that these commercially available interferon product have no ability to cure coronavirus and probably not the eventual course of FIP, FeLV or FIV either. (read

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Alternative And Complementary Medicine

One person's desperation is another person's opportunity. There have always been and always will be herbalists, naturopaths, practitioners of the obscure arts and even a few dodgy veterinarians who will claim to be able to cure the incurable. They will get your hopes up by telling you what you want to hear; and then, after money changes hands, they will disappoint you. Tragedy and loss are painful for all of us to face. But false expectations do not delay the inevitable. That said, those options do give a sense of comfort, support, and solace to some cat owners facing FIP. Those cat owners should have the right to use them if they wish.

Are You to Be Trusted/ Who Should I Rely on For Information?

If my advice to you can be trusted is something you will have to decide yourself. But I generally take my cues from the Davis, California group led by Dr. Niels Pedersen. Over the years I have learned to trust him and the Davis' School's publications and judgment. Equally trustworthy is information emanating from <u>Cornell</u>. When I judge the quality of a research paper and its conclusions, I always check to see who paid for it and the standing of the Journal in which it was published. I also consider who stands to benefit monetarily from the findings. You can find a scientific journal that will publish most anything these days. Those two USA veterinary colleges and the UK's Royal Veterinary College (<u>RVC</u>) rank as the top three years after year. Another veterinary institution with very high standards is the veterinary college at <u>Utrecht</u>.

At the RVC there is no consensus on what to currently do for cats with FIP. Neither for what constitutes a sufficiently valid diagnosis of dry-form FIP nor on treatment of either form once the diagnosis is accepted. A few on the staff do still suggest a combination of interferon and prednisolone. Others on the staff have no faith in either. Until the results of the Davis studies became known, most veterinarians at the institution would drain pleural (chest) fluids when indicated and do whatever else they thought might make the cat comfortable. They offer solace to the cat's owner(s) as much as treatment to the cats and began the talk of eventual euthanasia and closure early.

Now I am told that most veterinarians at the RVC probably do make cat owners aware of the FIP Warriors website – with the caution that they could spend a lot of money and that the drug they receive might not be what they thought they had paid for. Regulations and mindset in the UK are such that most veterinarians there would be quite hesitant about getting directly involved for fear they might be "struck off the register" (lose their license). So, some of the vets won't even mention China. The ones I have spoken to, as well as the Davis group are dead set against using these Chinese drugs to clean up coronaviruspositive catteries because of the fear of generating drug-resistant strains of FIP that no longer respond to GS-441524 and similar drugs. I agree. Some have less qualms about doing that. (<u>read here</u>)

There are also veterinarians at the RVC who question the likelihood that every common feline coronavirus can mutate to a FIP variant. That is the current theory accepted here in America and the one I presented to you. Those UK vets wonder what the odds are for the same mutation to happen repeatedly in different cats? And they ask, "isn't it much more likely that there are multiple different forms of coronavirus in cats and only one virus (or a group of closely related viruses) have the ability to cause FIP?" I do not know the answer.

Can My Cat Be Vaccinated Against FIP?

Yes.

<u>Zoetis</u> markets an FIP vaccine, Felocell FIP (IN). It is a vaccine that is given in your cats nose. The company suggests that it only be administered to cats 16 weeks old or older as an "*aid*" in preventing the disease. It is composed of a weakened (attenuated) FIP virus. That particular virus strain is believed to not survive at a cat's core (internal) body temperature and to only proliferate in a cat's upper respiratory tract and nose where it hopefully does no harm.

Not enough data exists to decide if this vaccine is worth giving or if it really protects cats in real life settings. For one, many believe that most cats that are exposed to feline coronavirus are exposed before they are 16 weeks old – too young to be given the vaccine. It does produce anti-coronavirus antibodies. But we do not know how long those antibodies last or if they are any more effective in preventing FIP than the antibodies that most coronavirus-exposed cats already carry. There are also veterinarians who worry that antibodies are what are destroying tissue in FIP-infected cats and that stimulating the production of antibodies might be a negative event. Some early studies concluded the vaccine was beneficial (<u>read here</u>) while others did not. (<u>read here</u>) If you elect to have your cat receive this vaccine it would be helpful to know if it already has coronavirus antibodies in its blood due to prior feline coronavirus exposure. In those situations, the vaccine is unlikely to be beneficial. (<u>read here</u>)

I Have Other Cats. What Should I Do to Protect Them When One Of Them Has Developed FIP?

I generally don't suggest that you isolate a cat that is ill from a stable multi-cat family household. Observe it, be sure it is not bullied at feeding time, meet its special needs if they occur but separation from housemates and household geography can be an added stress for many cats. Assuming the the mutation theory is correct, if your cat family has existed for a time, all the cats have already been exposed to feline corona virus and are immune or perhaps healthy carriers of the non-mutated FCoV virus form. Make every attempt to reduce inter-cat conflicts. Catteries ought to consider a pause in breeding and keep in mind that siblings of FIV+ cats are at greater risk of developing the disease. In those situations, avoiding the stress associated with neutering overcrowding, sale or <u>needless vaccinations</u> ought to be considered as well.

The veterinary school of the University of Colorado has on staff a philosopher, Bernard Rollin. He cautions against keeping suffering animals alive too long. He wrote an article that pertained to end-of-life issues in old cats, but a lot applies to an FIP cat's situation too. His belief and mine is that in making end-of-life decisions for your cat, you owe it to your friend to choose what will cause it the least pain and suffering – even if that means more immediate pain and sadness for you. You can read the abstract of his article <u>here</u>. Or you can <u>ask me</u> for <u>oldcatRollin2007</u> and I will send you his full article. If you wish, read my thought on pet loss <u>here</u>. Over the years, many people have written to me expressing guilt that something they did or did not do caused the loss of their cat. That is rarely ever true, and <u>never</u> true when it comes to FIP.

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