

FELINE INFECTIOUS PERITONITIS (FIP): Update 2007

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Extensive research efforts worldwide has led to a new understanding of Feline Coronavirus (FCoV) infection and FIP but has produced an even greater number of questions that remain unanswered. Currently there is no effective prevention or treatment for FIP. Equally, there is no method of accurately predicting which cats are at risk of developing the disease. The invariably fatal consequences, lack of predictable disease patterns, ineffective treatment regimes and the significant emotional and financial impact of FIP makes it a formidable disease.

Background

FIP is a fatal immune mediated disease of wild and domesticated cats (*Felidae*) caused by mutant strains of Feline Coronavirus (FCoV). It is one of the most important causes of death in young cats. It occurs in cats of all ages but most commonly those under 3 years.

The disease was first described in 1963 by Holzworth as a syndrome known as "chronic fibrinous peritonitis" but the name, along with the current name of FIP, is limiting in its description of this incredibly variable disease. FIP is now known to manifest as varying degrees of

- 1) **systemic serositis** (inflammation of the serous membranes eg. the superficial surfaces of the abdominal or thoracic organs leading to wet FIP),
- 2) **vasculitis** (inflammation of the blood vessels) and
- 3) **disseminated pyogranulomas** (many areas of inflammation in body organs, consisting of the white blood cells called macrophages and neutrophils).

The first reported appearance of FIP in Australia was in 1974^{1, 2} but despite the anecdotal evidence of its frequent occurrence in Australia, there has been a conspicuous absence of peer-reviewed reports until a recently review of 42 cases.³

Viruses within the family *Coronaviridae*, are known for their tendency to mutate frequently during viral replication (reproduction). Feline coronaviruses are typical in this regard. The exact nature of

the FIP inducing mutations are still unknown but are likely to be complex. The 3C, 7B and spike genes are now considered to be most important in the development of FIP-causing mutant FCoV although the mutation occurs at various points along these genes. **A key feature of the mutant FCoV is the ability to replicate in large numbers in a type of white blood cell known as the macrophage** (also known as monocytes when circulating in the bloodstream). It is on this principle that the only reliable diagnostic tests for FIP are based.

To complicate matters further, the role of the immune system in protecting against disease in some animals, while contributing to the disease in others, is another poorly defined issue in the development of FIP.

Genetic susceptibility

FIP is reported to occur more frequently in cats from catteries, boarding facilities and multicat households.⁴ While no breed predisposition has been firmly established, certain bloodlines and matings within a breed may be at greater risk.⁵ **The incidence of FIP in purebred catteries increases in proportion to the number of animals kept in that facility. Environmental factors, however, are not the sole contributor to FIP susceptibility.** Foley and Pedersen⁶ determined that FIP susceptibility was a partially heritable trait, with close relatives of affected cats within four Persian and one Birman catteries being significantly more likely to die of FIP than unrelated cats.

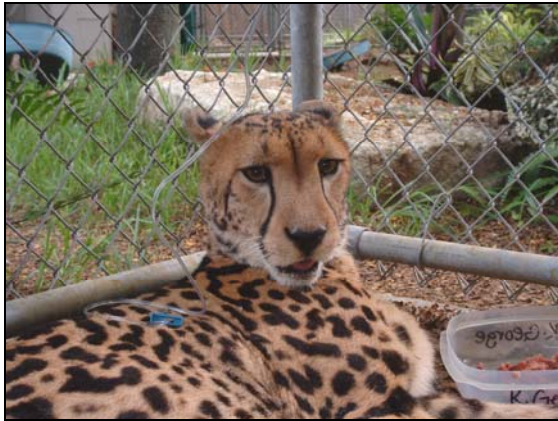


Figure 1: Inbreeding in cheetahs has led to an increased susceptibility to infectious diseases including feline infectious peritonitis.

Of the non-domestic felids, cheetahs have been found to be especially susceptible to FIP. Inbreeding in this species has predisposed them to diseases involving a variety of infectious agents, including FCoV.⁷ Conversely, cats from some Abyssinian bloodlines have been reported to have significantly longer survival times after experimental challenge with virulent FIP strains than other breeds, suggesting an inherited resistance to FIP.^{6, 8}

A retrospective study in Australia⁹ found that purebred cats were over represented in the FIP cohort while DSH were under represented. Within the purebred cats, **Burmese, Australian Mist, British Shorthair and Cornish Rex cats were significantly over-represented**, while Persian cats were under-represented, dispelling the explanation of husbandry practices being the only contributor to the incidence of FIP. The overrepresentation of certain purebreds, most notably the Burmese and BSH cats has been mirrored in the demographics of confirmed cases of FIP received via clinical samples (tissues and effusions) submitted to our diagnostic lab over the past 3 years from all over Australia (Veterinary Diagnostic Pathology Services, The University of Sydney). In our observations, other breeds or at least breed lines have also been noted as 'breeds of interest' due to an increase number of cases of FIP. These breeds include the Birman and Ragdoll. Conversely we now rarely see cases of FIP in Australian Mists. Our research team is currently investigating the differences in the immune response between different breeds of cattery-confined cats to gain an

understanding of factors that make some cats more susceptible to FCoV infection and the disease FIP.

While FCoV antibody titres are unable to predict which cats will go on to develop FIP, it is widely accepted that the magnitude of the FCoV antibody titre broadly reflects the viral load within a given cat.^{10, 11} In other words, a cat with a high antibody titre to FCoV will have a high FCoV load in its body and is likely to be shedding virus in the faeces. Although this is not a direct predictive relationship, some researchers have speculated that certain cats with persistent and/or high FCoV antibody titres, **given the right host (cat) susceptibility**, are at a greater risk of developing FIP due to the greater risk of viral mutations occurring.^{12, 13} The exact titre that constitutes a 'high' titre varies markedly depending on the test used. Kummrow and colleagues suggested the guideline listed in the table below.¹⁴

Recent studies in Australia¹⁵⁻¹⁷ have further highlighted a possible role of genetics in the development of this immune mediated viral disease. In serum antibody surveys conducted in household and cattery confined cats it was found that certain cat breeds had significantly higher antibody titres than other breeds.¹⁷ In an Australia wide retrospective study of 637 cats,¹⁶ the FCoV antibody titres of Siamese, Persians, DSH and Bengal cats were significantly lower than that of British Shorthair, Cornish Rex and Burmese cats. In a Sydney based serum antibody study of household pet cats,¹⁷ the antibody titres of DSH, Persian, Siamese and Devon Rex cats were significantly lower than that of Burmese, BSH, Abyssinian, Birman, Ragdoll, and Russian Blue. The significant relationship between the breed of the cat and the FCoV antibody titre, especially in those breeds identified to be at greater risk of developing FIP, further supports the notion that breed (genetic) related differences exist in the immunological response to FCoV infection.

Considerable work into the differing immune responses to FCoV and the role of genetics in controlling these immune responses is required if we are to have any chance of controlling this disease.

Transmission

FCoV infection is common in cattery-confined cats (80-100%) and pet cats (20-35%) worldwide due to faeco-oral transmission and environmental resistance of the virus. While it is endemic in many cat populations, the outcomes of infection are variable. Understanding the modes of transmission of Feline Coronaviruses requires knowledge of the virus location and its ability to infect tissues within the body.

FCoV is a fairly fragile virus that is destroyed by most household disinfectants and detergents. It can however survive up to 7 weeks in dry conditions eg dried faeces, carpet etc. The most common method of FCoV transmission is via virus-infected faeces, although in the first few hours to days of infection it can be shed in the saliva and respiratory droplets. Usually kittens are infected with FCoV from their mother or other FCoV excreting cats, at the age of 6 to 8 weeks, when their maternal antibodies wane. Maternal antibodies are thought to protect kittens from FCoV infection until this time, as most kittens that are removed from an environment of FCoV shedding cats at 5 to 6 weeks do not become infected.¹⁰



Figure 2: Faeco-oral transmission of feline coronaviruses is facilitated by the use of communal litter trays.

Replication of the feline coronaviruses in clinically normal cats occurs mainly in the intestinal lining (enterocytes). However these viruses are known to infect monocyctic cells, circulate in the blood and spread systemically even in clinically normal cats,^{18, 19} although their ability to

reproduce within monocyctic cells is limited. Shedding of infected enterocytes from the intestinal villi means that virus is shed in the faeces and cycles through the feline household via faeco-oral route. Testament to this is the finding in Australia (and many other parts of the world) that 98% of cats within catteries are infected with FCoV, and only 34% of pet cats are infected, with cats in single cat households significantly less likely to be infected.^{15, 17} The interesting finding in our studies has been the variation in antibody titres and likely viral loads between cats in the same cattery environment. For example, in one cattery the antibody titres ranged from 1:400 to 1:25,600 and this variation was not related to the age of the cat.

Many apparently healthy cats who are persistently infected with FCoV play an important role in recycling FCoV in multicat environments. FCoV shedding cats produce many millions/billions of virus particles in their faeces, some of which can be spread to the environment during digging of litter (Figure 2).

There is considerable debate over how a persistently FCoV infected cat develops FIP. One theory is that a mutation of the virus occurs within an individual cat. The formation of mutant strains is thought to confer the ability to infect large numbers of macrophages and reproduce large volumes of the virus. This theory is substantiated by recent work of Kipar and colleagues²⁰ which showed (using real time RT-PCR) that cats with FIP have considerably larger viral loads in the areas of the body that produce blood cells (eg spleen, lymph nodes) than healthy FCoV infected cats. These mutant forms of FCoV are thought NOT to shed faecally but are contained within the internal structures of an infected animal. Greater than 40% of cats with FIP will shed the enteric based FCoV, however the mutant forms of the virus (previously called FIPV) has **not** been found in the secretions or faeces from cats with FIP to date. Therefore transmission of mutated FCoV from one cat to the next is considered unlikely under natural conditions. It is theoretically possible, although not substantiated by current research, that cats with FIP lesions in the

kidneys or intestines may shed virus. This theory has been put forward to explain some reported “outbreaks” of FIP. Alternatively, the existence of immunocompetent carriers of the mutant virulent form of FCoV may explain these infrequent occurrences. Neither of these theories have been substantiated. When dealing with FIP within litters of kittens it is important to also consider the role of cat's susceptibility in the development of disease as frequently only certain kittens within a litter are affected. It is important NOT to condemn litter mates of kittens affected by FIP. We have many examples of litter mates who have lived long healthy lives despite the demise of their litter mate and in many cases while cohabitating with the affected kittens.

One final important point about transmission is that veterinarians when dealing with the **effusions of cats with wet FIP or performing post-mortems** within the clinic should be aware that these fluids and tissues are **highly contagious to other cats and pose a significant threat for the subsequent development of FIP if hospital cats are exposed to the virus.**

Development of Disease

The development of FIP is still a poorly understood disease process. Most of the pathology seen is caused by the cat's immune response to the virus. Two theories have been proposed to explain subsequent events. One theory is that mutant FCoV infected macrophages exit the blood vessels and enter the tissue. The virus attracts antibodies and certain proteins known as complement. More macrophages and neutrophils (two types of white blood cells) are attracted to the tissue, leading to the development of pyogranulomatous lesions. An alternative theory suggests that circulating immune complexes deposit on the blood vessel walls, leading to the release of substances that cause the lining of the blood vessels to leak fluid. This allows FCoV infected monocytes to enter the tissue. Release of further substances from infected and dying monocytes stimulates further blood vessel leakage and the development of high protein fluids into the abdominal/chest

cavities in some cases. The immune mediated vasculitis and the formation of pyogranulomas are the key features of FIP seen in microscopic sections.

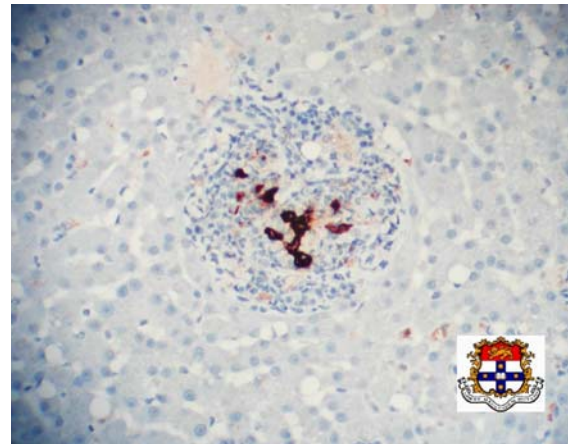


Figure 3: This section of liver has been stained using the specialised technique known as immunohistochemistry. On the outside of the picture are normal liver cells, while the concentration of cells in the centre shows a typical pyogranuloma. The brown staining cells are FCoV infected macrophages.

Clinical Presentation

The clinical presentations of FIP are variable and often complex, reflecting variations in the virus itself, the nature of the cat's immune response and the influence of environmental stresses. Approximately 50% of all cats diagnosed worldwide are less than two years old and purebred cats are generally over represented. Two broad forms of the disease have been described across all ages and breeds: “effusive” (wet) or “non-effusive” (dry). Despite this apparent division, these are not distinct disease entities. Cats with non-effusive FIP may develop effusions in the terminal stages of disease and conversely, there are reports of non-effusive FIP being preceded by a subtle effusive form of the disease.

Typically, patients with effusive FIP have high protein abdominal, pericardial (around heart) and/or thoracic (chest) effusion(s), fever, weight loss, anaemia and elevated serum globulin levels, although not all cats adhere to this stereotype. The non-effusive form of FIP is often more vague in its presentation with non-specific signs including fever, weight loss, and inappetance. Clinical signs, beyond the non-specific, relate to the

tissues affected. Possibilities include liver, kidney, pancreas, spleen, abdominal lymph nodes, central nervous system (CNS), gastrointestinal tract (GIT), eyes, skin and heart. Usually more than one body system is involved but occasionally only one is affected e.g. CNS or GIT, and clinical signs are restricted to this particular system.

Studies in Australia⁹ compared the clinical presentations of FIP in Australia's geographically isolated cat population with overseas reports. Significant features of this study were i) the over-representation of certain breeds (Burmese, Australian Mist, British Shorthair, and Cornish Rex) and the under-representation of other breeds (Domestic Shorthair, Persian); ii) the overrepresentation of males (2 to 1); iii) the even age distribution of disease seen in cats older than 2 years-of-age; and iv) the presence of immune-mediated haemolytic anaemia (red blood cell destruction) in two cats in that study plus three cats subsequent to the study.

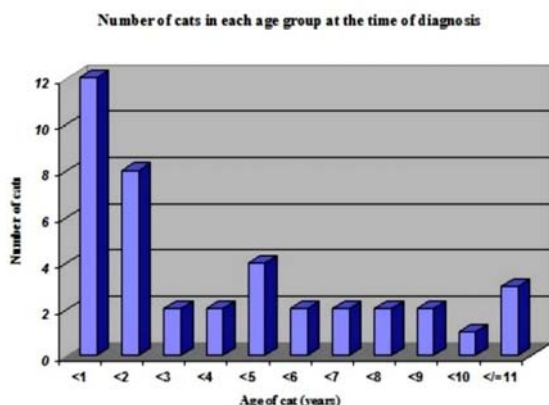


Figure 4: The age distribution of cats presented with feline infectious peritonitis in the study by Norris et al 2005.

Diagnosis

The difficulties in diagnosing FIP have been a hot topic in feline medicine for many years. Adopting traditional instruments of infectious disease diagnosis (eg PCR, serology) for FIP diagnosis and FCoV infection control has led to ongoing confusion for vets and unwarranted euthanasia of cats. This has stemmed from an incomplete understanding of the dynamics of FCoV infection in cats and the development of FIP. **Diagnostic tests for FIP must therefore rely on the biological behaviour of the virus. A key feature of the**

nasty mutant FCoV is the ability to reproduce in large numbers in macrophages and monocytes and it is on this premise that the only reliable diagnostic tests for FIP are based.

The clinical similarity between FIP and many other feline diseases, coupled with the non-specific nature of many of the tests available, makes the definitive diagnosis of FIP difficult even when the diagnostic approach is broad and thorough. While a cat presented with elevated blood globulin (type of protein), fever, and high protein abdominal and/or thoracic effusion may be highly suggestive of FIP, the variation in clinical manifestations beyond this stereotype is remarkable.

The advent of FCoV antibody titres and RT-PCR (reverse transcription polymerase chain reaction) has added to the complexity due to the indistinct differentiation between mutant FIP-causing FCoV and those FCoV that are unlikely to cause disease. **While these tests were first met with enthusiasm, it is now known that it is not possible to differentiate between the harmless and mutant forms of the virus by RT-PCR or any FCoV antibody test to date.** This severely limits their use in the diagnosis of FIP. Of greater concern is the finding by several researches of FCoV infection in the tissues of healthy cats without clinical signs, highlighting the need to exercise care to avoid over interpretation. In other words, performing RT-PCR, a technique that detects tiny amounts of virus in tissue or blood cannot be used for the diagnosis of FIP as many normal cats have small amounts of FCoV at these sites. Recent developments in the detection of replicating FCoV within circulating monocytes by RT-PCR however look more promising.²¹ This is now available in the USA but must be interpreted with great caution and should not be used in isolation.

Despite these limitations, FCoV antibody titres are still used indiscriminately for the diagnosis of FIP. A clinician must carefully consider the environment and age of the cat in question. For example a high antibody titre from a young cat or a cat

from a multicat household is impossible to interpret and is in no way helpful for the diagnosis of FIP. Incorrect interpretation can lead to incorrect diagnosis and unnecessary euthanasia. To use the words of Neils Pederen, an eminent researcher in FIP, "more cats have died from the misdiagnosis of FIP than from FIP itself".

The detection of characteristic microscopic changes within affected tissue (biopsy or post mortem) has been considered the **only conclusive test for FIP** for a considerable time and detecting virus within macrophages in the areas of pathology using immunohistochemistry allows definitive confirmation of the diagnosis. In a disease process where the treatment of choice is often euthanasia, diagnostic accuracy is essential.

a) Serum biochemistry and haematology

The results of routine blood tests (biochemistry and red and white blood cell counts = haematology) found in association with FIP are **non-specific and non-diagnostic**. They may include elevated serum protein due to elevated globulin, increase bilirubin (may appear as jaundice clinically), anaemia, and white blood cell changes traditionally seen with stress. These are found in many other diseases. In addition, blood tests specific to affected organs (eg kidney, liver) MAY be elevated. Hartman and colleagues²² compared the value of certain diagnostic tests in the largest study of FIP cases to date and found that elevations of total serum proteins above 80g/L was only 60% specific for FIP. This highlights the need to view elevated serum protein as being supportive of a diagnosis of FIP and several other diseases, but of limited diagnostic value when in the normal range. In cases in which total serum protein is elevated, additional supportive evidence for FIP can be gleaned from measurement of albumin-globulin ratios, γ -globulin concentrations and α 1-acid glycoprotein. **None of these tests are conclusive and are considered merely supportive or circumstantial evidence (not enough to convict a cat of FIP).**

While blood profiles can provide essential baseline information in the investigation of sick cats, clinicians cannot exclude

disease in certain body organs simply due to the absence of abnormal findings. In our retrospective study of cases, some cats with extensive pathology in the kidney or liver had normal serum biochemical test results.

b) Measuring FCoV antibody titres

The difficulties in interpreting antibody titres of FCoV have led to widespread acceptance that **diagnosis of FIP by antibody titres is neither possible nor appropriate**. Despite this, antibody titres continue to be given undue emphasis in the diagnosis of FIP. The antibody titre to FCoV in cats with FIP varies according to the nature of the clinical syndrome. There is considerable variation in the reported magnitude of anti-FCoV antibody titres in cats with confirmed FIP, with considerable overlap with healthy patients, making interpretation difficult. Indeed, a negative antibody titre alone cannot rule out a diagnosis of FIP, while a high FCoV antibody titre certainly does NOT confirm a diagnosis of FIP. The emergence of tests that claimed to measure antibodies against mutant FCoV alone became popular but their validity was NEVER supported by peer reviewed publications and they are now considered of no greater value than other antibody tests.

The gold standard for measuring antibody levels to FCoV is by indirect immunofluorescence (IFA), a test that is now available in several diagnostic laboratories in Australia. Hartmann²² has reported that cats with antibody titres of 1:1600 had a very high probability (94%) of having FIP, however it is noteworthy that this study compared cats with FIP to sick cats with diseases clinically similar to FIP. Healthy cats from multicat environments were not included in that study and the authors of that paper comment that a **high titre from a cat in a multicat environment is not predictive of FIP due to the high level of FCoV in those environments**.²³ In addition, the method used in that paper is different to those used in Australia. Currently all labs in Australia use a method of indirect immunofluorescence that involves feline cells infected with a FCoV (type not always specified). Studies in Switzerland by

Kummrow and colleagues¹⁴ have shown that **measuring the antibody titre using different cell lines and coronavirus types produces markedly different antibody levels.**

In our studies at the Faculty of Veterinary Science, University of Sydney (manuscript in preparation), we measured the FCoV type 1 antibody titres in 306 clinically healthy cattery confined breeding cats throughout NSW. Their antibody titres ranged from zero to 1:102,400. Over two-thirds of cats (213/306) had FCoV type 1 antibody titres of 1:1600 to 1:6400. This is shocking to most cattery owners who are used to the antibody titres reported by Addie and colleagues that have an end titre of 1:1280 and use FCoV type 2 infected cells in their indirect IFA method. **If cats are infected with FCoV type 1 and the titre is measured with FCoV type 1 infected cells, the titres reached may be considerably higher than if measured using another coronavirus.**

While there is a very important role for antibody titres in the management of multicat households and the identification of shedders, its use in the diagnosis of FIP in individual cats is a **dangerous exercise. They can never be used alone to determine a cat's fate.**

c) Fluid analysis and direct immunofluorescence

The analysis of thoracic and abdominal fluid is an essential diagnostic test in effusive FIP. Microscopically, FIP effusion typically consists of low numbers of neutrophils and mononuclear cells (macrophages). The presence of a high protein effusion and low to moderate number of cells as described above is helpful in providing further evidence for the likelihood of FIP, but has been found in other disease processes.

Albumin/globulin ratios in serum and effusion can be useful in the diagnosis of FIP but are not specific for FIP, so must be interpreted in light of all other evidence. Serum albumin/globulin ratio <0.8 has a high probability (92%) of FIP while an effusion albumin/globulin ratio <0.4 also has a high probability of FIP.

Techniques have been devised to detect the presence of FCoV in macrophages within the effusion. The method most commonly used worldwide is **direct immunofluorescence**. This technique uses a fluorescein labelled anti-FCoV antibody to detect large amounts of FCoV within macrophages, an important differentiating factor between FCoV based in the intestines and mutant forms of FCoV. Hartmann and colleagues found that direct immunofluorescence was extremely reliable at diagnosing FIP when positive but can be unreliable when negative due to the high rate of false negatives.²² Immunofluorescence is best done after fluid analysis. In Australia it is available at the Veterinary Diagnostic Pathology Service (The University of Sydney) and VETPATH® a private commercial lab in Perth. **The test relies on the macrophages within the fluid being in good shape, so delays in sampling lead to leakage of FCoV from the macrophages and increases the probability of a false negative result.** Tests are run daily in our laboratory, with results available on the same day the sample arrives to our laboratory.

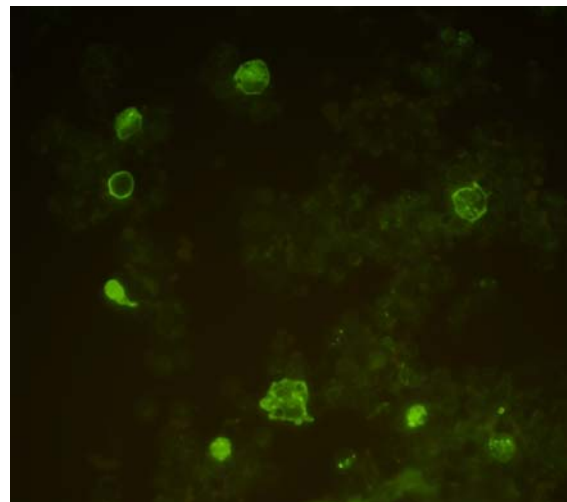


Figure 5: Direct immunofluorescence uses a fluorescein labelled anti FCoV antibody to detect large amounts of FCoV within macrophages

d) Histopathology + immunohistochemistry

The detection of characteristic microscopic changes from biopsy samples has been considered the **only conclusive test for FIP** for a considerable time. Not all cases of FIP have classical microscopic appearance and this has led to the development of more sensitive and

definitive diagnostic tests such as immunohistochemistry.

Immunohistochemistry (IHC) is a sensitive and specific technique used in many infectious and neoplastic (cancer) diseases. In the diagnosis of FIP we use an antibody against FCoV to detect virus within macrophages in formalin fixed tissue sections (biopsy samples). It is used subsequent to histopathology to definitively confirm FIP in those cases when the microscopic findings are inconclusive or in some cases when the diagnosis must be confirmed conclusively (eg for cat breeders due to the implications in breeding). This technique only detects macrophages with sufficiently high numbers of FCoV and allows the macrophage to be viewed in context with the surrounding pathology. Our laboratory is currently the only one in Australia offering this diagnostic test. All the external laboratories in Australia routinely send sections of the tissue to our laboratory for testing and therefore can be requested on any tissue sample through your usual veterinary pathology service.

Management of FCoV and FIP in breeding catteries

Confirming FIP as the definitive diagnosis using histopathology +/- immunohistochemistry is the essential first step. Once FIP is confirmed, an analysis of the breedline is required. Mapping the pedigree of the affected cat and noting any confirmed cases of FIP along the family tree can be helpful. In several cases it has been possible to identify a common stud or queen that should be desexed and removed from the breeding program.

Determining the Feline Coronavirus load of individuals within the cattery is a useful exercise if the information is used correctly. Using RT-PCR to identify FCoV in the faeces of cats, Diane Addie and colleagues in the UK have determined that there are **four possible outcomes of exposure** to FCoV infection (www.dr-addie.com):

"1. The kitten or cat develops FIP (around 5- 10% of infections).

2. The vast majority of cats shed FCoV for a while, develop antibodies, stop shedding FCoV and their antibody titre returns to zero. 58% of FCoV shedding lasts up to one month and 95% of virus shedding lasts less than 9 months.

3. The cat becomes a lifelong FCoV carrier (13% of infected cats). These cats shed FCoV continually in their faeces and most remain perfectly healthy although some develop chronic diarrhoea.

4. Resistant cats – around 4% of cats appear to be completely resistant to FCoV infection, they don't shed the virus and they mount an almost undetectable antibody response. "

Their work²⁴ also determined that a single faecal RT-PCR result on its own is meaningless because some cats may be intermittent shedders of FCoV. RT-PCR testing has to be part of a series of tests and is best accompanied by immunofluorescent antibody (IFA) testing because RT-PCR can be prone to both false positive results and false negative results. Delays in getting the faeces sample to the laboratory and at the incorrect temperature causes destruction of the viral RNA, leading to a false negative.

Establishing that a cat has eliminated FCoV infection requires five consecutive negative monthly RT-PCR results on faeces OR a reduction in the FCoV antibody titre (by indirect IFA) to less than 1:10. This may take months to years to achieve in some cases. These combined methods can be useful in determining life long shedders of FCoV. Removal of these cats from multicat environments such as catteries is essential for control of FCoV.

In Australia, RT-PCR is **not** currently available however measurement of serum **antibody titres to FCoV using indirect IFA** can provide some helpful information. It is accepted that the magnitude of the FCoV antibody titre broadly reflects the viral load within a given host.^{10, 11} Monitoring of these values over time (**every 6 to 12 months**) can provide information to the breeder and veterinarian as to which cats are chronic shedders and when the results are

examined for the whole cattery they can be an indication of the success or failure of husbandry changes. When measured using indirect IFA with **type 2 FCoV** (Addie et al), cats with low titres (1:25 or below) are not shedding FCoV in their faeces. Cats with high titres (1:400) are almost always shedding high levels of virus. **(NB In Australia, FCoV type 1 testing is performed and these give much higher readings, not comparable with the above).** Some of these cats will stop shedding upon isolation in a single cat household (detected by a decrease in their titre). If the cat is persistently shedding virus the titre will remain high. Some catteries have attained FCoV free catteries using these methods. Screening for FCoV in any cat entering this cattery is essential if the FCoV free status is to be maintained.

Analysis of the husbandry practices of the cattery (cleaning and number of litter trays, use of disinfectants, cleaning and management of food bowls etc) in the cattery can lead to some helpful changes in cattery management, which will assist in reducing the faeco-oral cycling of enteric based FCoV between cats. While it might seem obvious to many, ensuring the food bowls and litter trays are not cleaned in the same area or with the same cleaning instruments is essential. This has been an issue in several catteries and rescue agencies.

Recent studies by Addie and colleagues in UK (unpublished; www.dr-addie.com) have found that there is considerable variation in the virus killing ability of kitty litters. All the UK brands of kitty litter made of Fuller's earth were found to be much more effective at killing FCoV than other types, although these clumping litters have risks associated with oral ingestion in kittens. Further research in this area would be useful. Using dedicated litter trays for each cat or cat group, removing faeces from litter trays as often as possible (1-2 x daily) and using dedicated poop scoops for each cat pen or tray is also recommended.

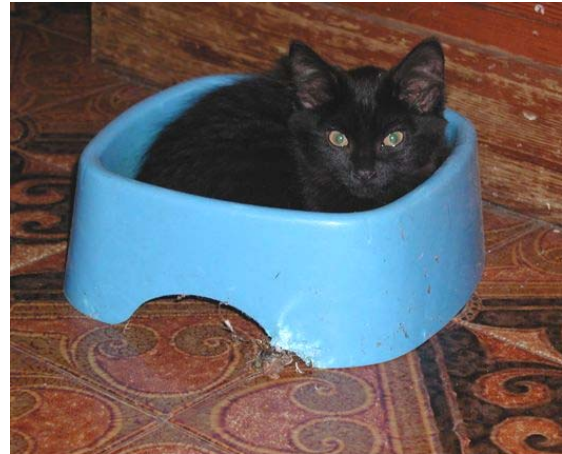


Figure 6: Ensuring that food bowls and litter trays are not cleaned in the same area is essential

Addie and Jarret have successfully implemented early weaning protocols for the prevention of FCoV infection in kittens born in FCoV endemic catteries. This involves isolating the queens 2 to 3 weeks before parturition, strict quarantine of the queen and her kittens in a separate room from the rest of the cattery, and weaning at 4 to 6 weeks of age. This protocol is based on the finding that kittens are protected from FCoV infection by their maternal antibodies until 5-6 weeks of age, when the maternal antibody wanes. The maintenance of an isolated quarantine area requires strict vigilance. Some find it difficult to achieve and argue that the early weaning has a social cost on the kittens. Although a kitten may be successfully raised free of FCoV it may become infected later in life and therefore the purpose of isolation and early weaning is to delay the age at which FCoV infection occurs.

Management of a cat in contact with an FIP affected housemate

There is no current evidence to suggest that a cat with FIP sheds the mutant virus in his/her faeces. It is likely that the cats in the household have been exposed to the same enteric based FCoV depending on their toileting habits in the household (ie cats that defecate outside are thought to be at lower risk of receiving the enteric form of FCoV from their housemates). Clients however will commonly present a housemate of an FIP affected cat for examination to determine its prognosis. It is likely that this in-contact cat may have an antibody titre to FCoV but this is in **no way**

predictive of its fate. If a high FCoV titre is found the cat should be tested in 6 to 12 months. Most cats in single or two cat households will usually clear FCoV over a few months to years. A persistently high antibody titre does **not** necessarily indicate a poor prognosis. Conversely, a consistently low or negative titre is indicative that the cat is highly unlikely to develop FIP.

Treatment options

No therapies have been proven to effectively treat FIP. Many immunosuppressive (prednisolone, cyclophosphamide, chlorambucil, thalidomide) or immunomodulating drugs (pentoxifylline) have been tried with several providing temporary and often short-term improvement.

One immunomodulating drug, feline recombinant interferon omega (Virbagen Omega®) has produced some encouraging results²⁵ when used with prednisolone. The researchers used 1MU/kg s/c eod in combination with glucocorticoid (prednisolone at 1mg/kg bid or dexamethasone), to treat 12 cases of FIP. Of the 12 cases, 4 cats were still alive and well after 2 years, 4 cats survived 2 to 5 months while 4 cats survived less than a month. Eleven of the 12 cats had effusive disease. The age of the 4 cats who were in remission at 2 years, ranged from 6 to 16 years and therefore were older. While criticism of the criteria for FIP diagnosis has been suggested by some, it remains the only drug protocol with the potential to limit the immune mediated tissue damage and limit viral replication. The exact mechanism by which this drug effects changes in the cat's immune response is not understood at this time.

Use of this drug combination so far in our hands has not met with overwhelming success. We have had marked improvement in clinical signs in two cats (of 15) with confirmed FIP. Both have been less than 3 years of age with pleural effusion. One cat (a 9 month old Burmese female desexed with effusive FIP (pleural fluid)) had a noticeable response to treatment with considerable reduction in

pleural fluid and clinical control of the disease for 9 months before she had to be euthanased due to deterioration of the quality of life. The second cat (2.5 year old male neutered Scottish Fold) with noticeably improvement in clinical signs and is currently going well (6 months since diagnosis).

Katrin Hartmann and colleagues in Germany have recently completed a placebo controlled double blind clinical trial. In this study to soon be published (late 2007 or early 2008), 37 cats with FIP were treated randomly with feline interferon- ω (10^6 IU/kg s.c. every 48 hours 7 days, subsequently once every week) or placebo. In all cats, FIP was confirmed by histology or immunostaining of FCoV antigen in effusion/tissue macrophages. All cats received glucocorticoids, either as dexamethasone (in case of effusion) or prednisolone. They found that there was no statistically significant difference in the survival time of cats treated with interferon- ω versus placebo. Cats survived for a period of 3 to 200 days (mean 18 days). There was only one long-term survivor (> 3 months) that appeared to be in the interferon- ω group. This cat had been presented with effusion that totally disappeared; it did not show signs until euthanized 200 days after treatment initiation due to recurrence of FIP. Although there was no difference in the mean survival time, few cats may benefit from treatment including interferon- ω .

Considerably more research is required to understand the complex immune response to FCoV and the development of FIP. With this will come opportunities to develop effective treatments or, even more importantly, methods of preventing FIP.

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