

GUIDELINE for Feline Infectious Peritonitis

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The Feline Infectious Peritonitis guidelines were first published by Addie et al. in 2009 in *Journal of Feline Medicine and Surgery* 11 (7) 594-604, and again by Tasker et al. in 2023 in *Viruses* 15 (9) 1847. The present update has been written by Séverine Tasker and ABCD colleagues. It provides an easy-to-read overview of essential facts for quick, non-referenced information. An extensive review, written by the European Advisory Board on Cat Diseases (ABCD), giving a comprehensive and referenced update on feline infectious peritonitis (FIP) and feline coronavirus (FCoV) infection with all sections readable in isolation, can be downloaded [HERE](#).

Key points

- Feline coronavirus (FCoV) is a ubiquitous RNA virus of cats, which is transmitted faeco-orally.
- FCoV is primarily an enteric virus and most infections do not cause clinical signs, or result in only enteritis, but a small proportion of FCoV-infected cats develop FIP.
- The pathology in FIP comprises a perivascular phlebitis that can affect any organ.
- Cats under two years old are most frequently affected by FIP. Most cats present with fever, anorexia, and weight loss; many have effusions, and some have ocular and/or neurological signs.
- Making a diagnosis is complex and [ABCD FIP Diagnostic Approach Tools](#) are available to aid veterinarians. Sampling an effusion, when present, for cytology, biochemistry, and FCoV RNA or FCoV antigen detection is very useful diagnostically. In the absence of an effusion, fine-needle aspirates from affected organs for cytology and FCoV RNA or FCoV antigen detection are helpful.
- Definitive diagnosis usually requires histopathology with FCoV antigen detection.
- Antiviral treatments now enable recovery in many cases from this previously fatal disease; nucleoside analogues (e.g., oral GS-441524) are very effective, although they are not available in all countries. Details on antiviral treatment protocols are given in Table 2 in the review.

Agent properties

Feline coronavirus (FCoV) is the causative agent of the serious disease of feline infectious peritonitis (FIP). FCoV is a large, pleomorphic spherical, enveloped virus particle with a single-stranded RNA genome. It is readily inactivated by most disinfectants.

Being an RNA virus, FCoV has a high level of genetic variation due to frequent errors (mutations) during RNA replication. The hypothesis is that genetic variation and subsequent selection facilitate the switching of cell tropism from a mostly mild enteric (less-virulent) FCoV pathotype to an FIP-associated FCoV pathotype. This switch occurs in an infected cat and FIP-associated FCoV systemically replicates efficiently within monocytes/macrophages and can lead to the serious disease of FIP. However, systemic (non-enteric) FCoV infection can also occur in cats without FIP.

The FCoV genome comprises many genes, including those encoding the spike [S], matrix, nucleocapsid, envelope proteins and non-structural accessory proteins 3a, 3b, 3c, 7a and 7b. Mutations in different genes, including the S gene, have been postulated to be associated with the switch to a more virulent FCoV pathotype. The S protein is a particular focus of attention as it mediates entry into feline host cells and has both receptor-binding and fusion functions. Specific mutations in the S gene have been postulated to be associated with FIP-associated FCoV but the definitive genes and mutations involved in the FCoV virulence genetic shift are still unknown.

Type I and type II FCoV are recognised to differ based on antigenic and genomic properties, with type I FCoV being more prevalent. However, type I FCoVs, unlike type II FCoVs, are difficult to grow in cell cultures and thus many *in vitro* studies are based on the less-common type II FCoV. Type I and II FCoV can both exist as less-virulent FCoV and FIP-associated FCoV.

Epidemiology

FCoV is a contagious virus. Faeces are the main source of FCoV infection and most transmission is faecal-oral in nature.

Kittens are often infected at a young age and shed FCoV in faeces as early as two days post-infection. After infection, shedding continues for days, weeks or months, and a few may be persistently infected. Shedding then stops, or is detected intermittently, and can recur due to re-infection in an endemic environment. Immunity is short-lived, which is why cats, in the face of infection, can undergo multiple cycles of infections.

FCoV infection occurs worldwide (see Table 1 in the review) and is very common, particularly in multi-cat households, but FIP arises in only a small percentage of FCoV-infected cats.

Cats of any breed or age can develop FIP. It is particularly seen in pedigree cats (especially in certain breeds in some studies) and those under two years of age. In some studies, males were more likely to develop FIP than females.

Pathogenesis

FCoV infection occurs following the ingestion of the virus, which then replicates in the epithelial cells of the small intestinal villi, resulting in faecal shedding. This enteric FCoV infection is often subclinical but can result in enteritis. FCoV is then found in the colon, which is the main site of viral replication alongside the ileum. Thereafter, FCoV infection is thought to spread to the mesenteric lymph nodes before sometimes resulting in viraemia. Whilst low-level FCoV viraemia in monocytes can occur in cats that do not go on to develop FIP, efficient and high-level FCoV replication in activated monocytes and macrophages (which may well be mediated by viral mutations) is believed to be a key event in FIP pathogenesis, alongside the nature of the immune response mounted by the cat in response to FCoV infection.

When FIP develops, there is a reaction between replicating FCoV in monocytes and blood vessel walls, allowing the extravasation of the monocytes, where they differentiate into macrophages. The breakdown of the endothelial tight junctions allows plasma to leak out of the vessels; this can appear clinically as an effusion in the abdominal, thoracic and/or pericardial cavities. In more chronic forms of FIP, fewer blood vessels are affected, but larger perivascular pyogranulomata result on affected organs.

The horizontal transmission of FIP, via an FIP-associated FCoV strain, is believed to be a very unlikely occurrence. However, horizontal transmission may be a feature of the rare outbreaks of FIP occasionally reported, such as in stray cats in Cyprus. Such outbreaks can involve type II or new recombinants of FCoVs.

Immunity

Cats resistant to FIP are known to have strong cell-mediated immunity (CMI), which can be measured by high levels of the cytokine interferon gamma (IFN- γ) in the serum. However, CMI is also likely to be involved in the pathogenesis of FIP, albeit at a tissue level, as

evidenced by high IFN- γ concentration in FIP effusions. Single-nucleotide polymorphisms (SNPs) in the feline IFN- γ gene have been found to be associated with the outcome of FCoV infection, but these associations are not discriminatory enough to be beneficial to deduce susceptibility in individual cats, nor to guide breeding.

The role of humoral immunity in protecting against FIP is ambiguous. Maternally derived antibodies are thought to provide protection until kittens are about five to six weeks old, until they decline by six to eight weeks of age. Antibody development to FCoV takes seven to 28 days post-infection. Following natural infection, antibody titres can decline to zero over a period of several months to years. In cats with pre-existing antibodies, 'antibody-dependent enhancement' (ADE) has been observed experimentally, resulting in a more rapid FIP progression and earlier death. However, in field studies, cats developed FIP on first exposure to FCoV (and thus did not have pre-existing antibodies), and some cats experienced repeated infections by FCoV and did not develop FIP, leading to the conclusion that ADE is likely to be an experimental phenomenon, but it still remains a concern for vaccine development.

Clinical signs

FCoV infection

Cats with FCoV infection are usually subclinical, although occasionally diarrhoea and/or vomiting and poor growth (in kittens) can occur.

FIP

Cats that go on to develop FIP after FCoV infection present with varied clinical signs depending on the distribution of vasculitis (which can lead to effusions) and/or (pyo)granulomatous lesions (which can lead to mass lesions) in the body. Although effusive and non-effusive forms of FIP are often described, there is much overlap between these forms. Clinical signs of FIP can change over time, and therefore repeated physical examinations are important to detect newly apparent clinical signs; for example, an effusion can develop, or ocular changes can become visible on ophthalmoscopic examination. [ABCD FIP Diagnostic Approach Tools](#) are available to help the vet assess clinical signs for FIP.

Non-specific clinical signs include lethargy, anorexia, and weight loss (or failure to gain weight/stunted growth in kittens). A fever that is refractory to treatment is common.

Effusions are common, especially in the abdomen (fig. 1), but pleural effusions and pericardial effusions are also seen, sometimes concurrently. When effusions are present, the disease progression is often quite fast, within a few days or weeks.



Fig. 1. Ascites in a young Sphinx cat presenting with FIP. Image Hannah Dewerchin, Ghent University, Belgium (Addie et al., 2009).

When effusions are not present, FIP is often more difficult to diagnose and it also tends to be more chronic, progressing over a few weeks to months. Additional signs of non-effusive FIP depend on the organs affected but can include the central nervous system, eyes and/or abdominal organs (such as the liver, abdominal lymph nodes [especially mesenteric lymph nodes], kidney [including renomegaly], pancreas, spleen and/or gastrointestinal tract). These signs can also be present in cats with effusions. Abdominal lymphadenomegaly or intestinal masses (sometimes palpable), can occur. Jaundice can occur (fig. 2), more commonly in cats with effusions, but the degree of hyperbilirubinaemia is often not high enough to result in clinical jaundice. Occasionally, cats with FIP show skin signs.



Fig. 2. Icterus can occur in cases with FIP, particularly in cats with effusive FIP. Image Séverine Tasker, Bristol Veterinary School, University of Bristol, UK.

Neurological signs seen with FIP include ataxia (with varying degrees of tetra- or paraparesis; figs. 3 and 4), hyperaesthesia, nystagmus, seizures, behavioural and mental state changes, and cranial nerve deficits. Central vestibular clinical signs can include head tilt, vestibular ataxia, nystagmus, obtunded appearance, and postural reaction deficits. Fever was shown to be less common in cats with neurological FIP compared to those without neurological signs.



Fig. 3. Ataxia can occur in cats with neurological FIP. Image Séverine Tasker, Bristol Veterinary School, University of Bristol, UK.



Fig. 4. Ataxia (wide-based stance) and obtundation in a cat with neurological FIP. Image Allan May, University of Glasgow, UK through Diane Addie.

FIP can also cause unilateral or bilateral uveitis. Clinical signs include changes in iris colour, dyscoria or anisocoria secondary to iritis,

sudden loss of vision and hyphaema (figs. 5 and 6). Keratic precipitates can appear as 'mutton fat' deposits on the ventral corneal endothelium (fig. 7), and aqueous flare can occur. On ophthalmoscopic examination, chorioretinitis, fluffy perivascular cuffing (representing retinal vasculitis), dull perivascular puffy areas of pyogranulomatous chorioretinitis, linear retinal detachment, vitreous flare and fluid blistering under the retina can all be seen.



Fig. 5. FIP-associated anterior uveitis can manifest variably such as with the presence of hyphaema. Image Maria Bonino and Erica Carter.



Fig. 6. FIP-associated anterior uveitis can manifest variably such as with the presence of hyphaema. Image Albert Lloret, Universitat Autònoma Barcelona, Spain (Addie et al., 2009).

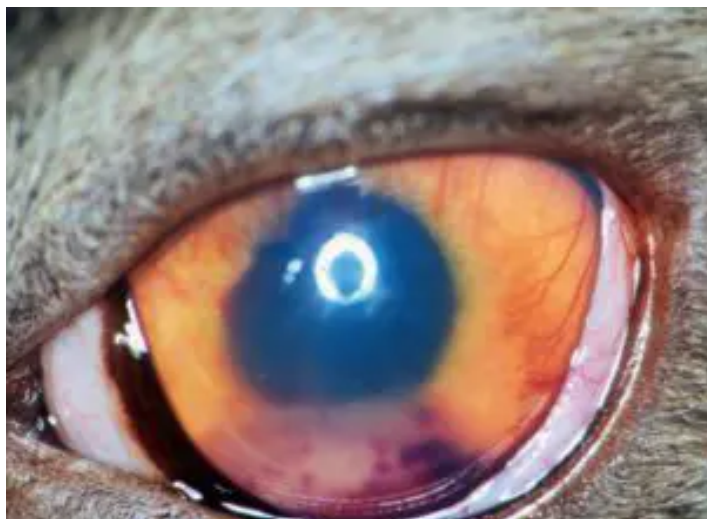


Fig. 7. FIP-associated anterior uveitis can manifest variably such as with the presence of inflammatory keratic precipitates. Image Eric Déan, Vet-Oeil Ophthalmology Clinic, France (Addie et al., 2009).

Other less-common signs associated with FIP have included upper respiratory signs and clinical signs associated with pneumonia and myocarditis.

Diagnosis of FIP

Signalment and history for FIP

FIP is more common in young cats (especially under two years old) and some pedigree breeds, and male cats are at slightly higher risk of disease. Additionally, most cats that develop FIP come from multi-cat households or have a history of having been housed in multi-cat households. A recent history of stress (e.g., adoption, being in a shelter, neutering, upper respiratory tract disease, vaccination) is common.

Approach to the Diagnosis of FIP

If an effusion is present, sampling it is the single most useful diagnostic step because tests on effusions have a higher diagnostic value compared to those on blood samples. Samples of effusion can be easy to obtain; imaging (especially ultrasonography) is used to confirm, identify, localise, and sample smaller volumes. FIP effusions are usually clear, viscous/sticky and straw-yellow in colour.

Diagnosing FIP if there is no effusion present is more challenging due to the large number of possible clinical signs and their non-specific nature (e.g., anorexia, lethargy, weight loss, fever) and because biopsy collection ante-mortem can be very difficult due to, for example, problems accessing affected tissues, contra-indications for general anaesthesia or invasive biopsy collection in a sick cat, and/or costs involved in tissue collection. Cases with neurological or ocular signs can be approached via the sampling of cerebrospinal fluid or aqueous humour, but these techniques are not performed commonly outside of referral clinics. There is no non-invasive, confirmatory test available for cats with FIP that do not have effusions, although in some cases valuable supportive information can be gained through the analysis of fine-needle aspirate (FNA) samples collected from affected organs, if accessible. Tissue FNAs are usually easier to collect than tissue biopsies.

The integration of multiple test results is most useful to help direct the clinician to a diagnosis of FIP being very likely, in the absence of confirmatory testing.

Laboratory Changes in FIP

Routine haematology and serum biochemistry

Routine haematological changes are not specific for FIP, but common abnormalities include lymphopenia, neutrophilia, sometimes with a left shift, and a mild-to-moderate normocytic, normochromic anaemia.

Serum biochemistry changes are more helpful and include hyperglobulinaemia, accompanied by hypoalbuminaemia or low-to-normal serum albumin and a low albumin to globulin (A:G) ratio of less than 0.4 (an A:G ratio of greater than 0.8 makes FIP very unlikely). Increased bilirubin levels in the absence of haemolysis or elevations of liver enzyme activity raise the suspicion of FIP.

Acute phase proteins (APPs) are produced in the liver in many inflammatory and non-inflammatory diseases; the major APP in cats is

α 1-acid glycoprotein (AGP), and moderately elevated serum AGP concentrations of greater than 1.5 mg/mL often occur with FIP, although cut offs depend on the laboratory and assay used. Another important APP in cats is serum amyloid A, more readily available in some countries, which is also markedly increased in cats with FIP.

Cytology and biochemistry of effusions

FIP effusions are highly proteinaceous, with a total protein concentration greater than 35 g/L, consistent with an exudate. Cell counts are variable, from relatively low, i.e. less than 5×10^9 /L cells (less than 5000 cells/ μ L), which would be more consistent with a modified transudate, to higher cell counts of 20×10^9 /L cells or above. Elevated AGP concentrations are often found in the effusions of cats with FIP, as well as the serum. Effusion AGP measurements may well be more discriminatory between FIP and other diseases than serum AGP measurements.

Cytology is pyogranulomatous, with macrophages, non-degenerate neutrophils and few lymphocytes, although sometimes neutrophilic inflammation predominates. Thick eosinophilic (pink-red) proteinaceous backgrounds on cytology slides are often described. If cytology reveals a septic neutrophilia (typically with degenerate neutrophils containing bacteria), neoplastic cells or a marked lymphocyte population, other diseases are more likely.

The Rivalta's test is a crude point-of-care assay to identify proteinaceous inflammatory exudates, which occur with FIP, but also septic peritonitis and lymphoma. If positive, effusion cytology can be helpful to discriminate between these causes. A negative Rivalta's test, however, is more helpful to rule out FIP. To perform the Rivalta's test, 8 mL of distilled water at room temperature and one drop of 98% acetic acid (or white vinegar) are mixed in a test tube, and then one drop of effusion is carefully placed or layered onto the surface of the solution. A positive result is indicated by the drop staying attached to the surface of the solution, retaining its shape with a connection to the surface, or floating slowly to the bottom of the tube as a drop or like a jellyfish. A negative test is indicated by the drop disappearing and the solution remaining clear. However, the interpretation of results can be subjective, and it can be hard to decide whether a result is positive or negative.

Cytology of fine-needle aspirates (FNAs), cerebrospinal fluid (CSF), aqueous humour or broncho-alveolar lavage (BAL) samples, and biochemistry if applicable

Typical FNA features of FIP are highly cellular samples containing the normal cell population of the sampled tissues with the additional presence of neutrophils (these can predominate), macrophages, plasma cells, and lymphocytes, consistent with pyogranulomatous inflammation. An examination of the CSF can show a pleocytosis, predominantly neutrophilic, mononuclear, mixed or pyogranulomatous in nature, with elevated protein concentrations. The cytology of aqueous humour or BALs can show pyogranulomatous or mixed inflammation with non-degenerate neutrophils, with or without macrophages, and maybe occasional lymphocytes.

Please note that samples collected for cytology and biochemistry may also be suitable to submit for direct detection of FCoV (see Direct Detection of FCoV section below), either by immunostaining for FCoV antigen or by reverse-transcriptase PCR for FCoV RNA, providing important additional diagnostic information.

Diagnostic imaging in FIP

No specific ultrasonographic or radiographic findings exist for FIP.

Ultrasonography (especially of the abdomen) and radiography can show the presence of effusions. Pneumonia due to FIP is sometimes reported and can be associated with radiographic changes.

Ultrasonography can reveal abdominal lymphadenomegaly or lymphadenopathy and/or lymph node hypoechogenicity and/or abnormalities of the liver, intestines, spleen and/or kidneys (which can include a medullary rim sign or hypoechoic subcapsular rim), depending on which organs are affected. Imaging can also be of use to the direct sampling of abnormal tissues, e.g., fine-needle aspirate for cytology examination to reveal non-septic pyogranulomatous inflammation, or ultrasound-guided needle core (e.g., tru-cut) biopsies can be collected and submitted for histopathology.

When a cat is showing neurological signs, the imaging of the brain by magnetic resonance imaging (MRI), if available, with contrast, can be useful to demonstrate neurological abnormalities (such as obstructive hydrocephalus, syringomyelia, foramen magnum herniation and marked contrast enhancement of the meninges, third ventricle, mesencephalic aqueduct, and brainstem). A description of computerised tomography findings in cats with neurological FIP has not been published, but MRI is likely to be more sensitive in the detection of subtle intraparenchymal lesions. Advanced imaging of the central nervous system is indicated before performing cerebrospinal fluid sampling to assess the potential risk of herniation.

Direct Detection of FCoV

FCoV antigen detection by immunostaining

Immunostaining exploits the binding of antibodies to host-cell-associated FCoV antigens, which are subsequently visualised by enzymatic or immunofluorescent reactions producing a colour change in a process called immunohistochemistry (IHC) on biopsies or immunocytochemistry (ICC) or immunofluorescence (IF) on cytology samples (such as effusion and fine-needle aspirate [FNA] sample smears).

The histopathological and cytological changes associated with FIP are typically pyogranulomatous.

Definitive diagnosis of FIP relies on consistent histopathological changes in affected tissues in addition to FCoV antigen immunostaining by IHC.

Consistent cytological (typically pyogranulomatous) changes in affected tissues in addition to FCoV antigen immunostaining by ICC or IF is also highly supportive of a diagnosis. Although positive FCoV antigen immunostaining can usually be used to confirm the diagnosis, a negative result does not exclude FIP as FCoV antigens can be variably distributed within lesions and might not be detected in all samples prepared from FIP-affected tissues or samples (e.g., if an effusion is cell-poor and/or the FCoV antigen is masked by FCoV antibodies in the effusion). It is important for clinicians to be aware of variations in immunostaining techniques and to be familiar with the specificity of the methodology employed by their local laboratory, as well as confirmation of the inclusion of negative controls in testing, when interpreting positive results.

Differential diagnoses for pyogranulomatous inflammation include other infections (mycobacteria, toxoplasmosis, actinomyces, nocardia, rhodococcus, bartonella, pseudomonas and fungi) as well as idiopathic sterile pyogranulomatous disease.

The sample sites most likely to be useful are those that are affected by the FIP disease, and inference of this can be gained from the clinical signs as well as results of diagnostic testing (e.g., ascites, neurological signs, imaging results, pyogranulomatous inflammation on FNA cytology). Biopsy samples of affected tissues (e.g., liver, kidney, spleen, mesenteric lymph nodes, lungs) can be collected, for example, by laparotomy, laparoscopy or ultrasound-guided tru-cut for histopathology and immunostaining, whereas effusions, FNAs (e.g., of mesenteric lymph nodes), cerebrospinal fluid (CSF), aqueous humour and BAL samples can be collected for cytology and immunostaining. It is wise to consult the diagnostic laboratory before submitting samples for ICC or IF as their preferences for how samples should be prepared before sending vary.

FCoV RNA detection by reverse-transcriptase polymerase chain reaction (RT-PCR)

FCoV RT-PCR assays can be used to detect FCoV RNA in blood, effusion, tissue (including samples obtained by FNAs), CSF, or aqueous humour samples. The RT-PCR assays used should be quantitative and report the FCoV load (amount) present in the analysed sample. The load is helpful because the systemic FCoV infection that can occur in healthy cats and cats without FIP have lower FCoV viral loads than in cats with FIP. Thus, a positive FCoV RT-PCR result on a sample is not totally specific for FIP, but positive results with a high FCoV load on samples from cats with signs consistent with FIP are very supportive of a diagnosis of FIP, and often this is adequate evidence upon which to start a cat with antiviral FIP treatment. However, a negative result cannot rule out a diagnosis of FIP since the levels of FCoV in samples can be too low or have too variable a distribution (and thus not present in the sample analysed) to be detectable by PCR. It is wise to consult the diagnostic laboratory before submitting samples for RT-PCR, as their preferences for how samples should be prepared before sending vary (e.g., centrifugation of effusions, preservation advice).

Recent studies using RT-PCR on blood samples have shown more promising results than previously, with high levels of FCoV RNA detectable, suggesting that blood samples could be revisited as a diagnostic sample to support a diagnosis of FIP.

RT-PCR analysis of effusion samples in cats with FIP is often positive (72–100% of samples) for FCoV RNA, and cats without FIP are usually RT-PCR-negative, and the presence of FCoV RNA, particularly in high levels, in an effusion that also has cytological and biochemical features suggestive of FIP, is highly supportive of a diagnosis of FIP.

Whilst tissue biopsy samples obtained from affected tissues in cats with FIP usually show high levels of FCoV RNA in them, as determined by RT-PCR, such samples, if collected, should ideally be submitted for histopathology and IHC, as this allows for a definitive diagnosis of FIP.

FNAs are a good sample type for FCoV RT-PCR, with the advantage of relatively easy collection. The sample site should be guided by where pathology is likely based on clinical signs and other diagnostic investigations, but promising results on FNAs collected from mesenteric lymph nodes from cats with FIP that did not have effusions have been obtained.

CSF and aqueous humour FCoV RT-PCR in cats with neurological signs or ocular signs, respectively, can also be helpful.

RT-PCR on faecal samples is only useful to identify cats shedding FCoV for the management of FCoV in multi-cat households. Faecal RT-PCR is not useful for the diagnosis of FIP as many healthy cats without FIP shed FCoV.

Characterising FCoV spike (S)-gene mutations following positive RT-PCR for FCoV RNA

Following the detection of FCoV RNA in a sample by RT-PCR, varied molecular techniques (e.g., pyrosequencing and Sanger sequencing often used in research, or methods that detect and quantify specific FCoV mutation sequences, such as the commercially available allelic discrimination assay) can be used to derive S-gene sequence data for the FCoV present. Such techniques are only successful at determining the FCoV sequence present when high loads of FCoV RNA are present, so successful S-gene-mutation analysis at least suggests that the sample contained high levels of FCoV RNA, which is highly supportive of a diagnosis of FIP. However, research has shown great variability in results when detecting S-gene mutations using the different methods, making it difficult to rely on S-gene-mutation analysis as being confirmative for FIP, especially when the commercially available allelic discrimination assay is used.

Indirect Detection of FCoV

Serum FCoV antibody tests, performed on blood, are usually enzyme-linked immunosorbent assays (ELISA), indirect immunofluorescence antibody tests or rapid immunomigration tests.

A positive FCoV antibody test indicates that the cat has been infected with FCoV and has developed antibodies. Although cats with FIP tend to have higher FCoV antibody titres than cats without FIP, there is much overlap, so there is little value in an individual cat undergoing serum FCoV antibody testing. In addition, negative serum-FCoV antibody results cannot rule out FIP, as cats with confirmed FIP can be FCoV antibody-negative.

There is no 'FIP antibody test'; all that can be measured is antibody against FCoV.

Epidemiological Considerations in the Management of Cats Following a Diagnosis of FIP

It is likely safe to take a cat that has been diagnosed with FIP back into a household with cats that have already been in contact with it, as these cats are likely to be already FCoV-infected following exposure to the same FCoV isolate that originally infected the FIP cat. In the cat that has developed FIP, the infecting FCoV has likely undergone mutations to result in FIP-associated FCoV infection, and the understanding is that the horizontal transmission of FIP, via an FIP-associated FCoV strain, is a very unlikely occurrence.

In households where a cat with FIP has been euthanised, with no remaining cats in the household, it is recommended that the owner waits for two months before obtaining new cats, as it has been suggested that FCoV might preserve its infectivity for days to a few weeks.

Cats with FIP in a veterinary practice should be handled and housed like other cats, with routine infection-control measures, as any cat is a potential source of FCoV infection. There is no need to keep cats with FIP in infectious disease isolation wards.

General Prognosis for FIP

Before effective antiviral treatments became available, cats with FIP usually died or were euthanised within a few weeks. Occasionally, cats with FIP did survive for several months or years after diagnosis, with variable treatments, although the influence of treatment on survival was not proven.

Disease progression seems to be quicker in younger cats and cats with effusions than in older cats and cats without effusions.

Treatment of FIP

The availability of effective curative antiviral treatments for FIP, particularly the nucleoside analogue GS-441524, has totally changed the landscape of this previously fatal disease. These antiviral treatments act quickly, with fever and other clinical signs often improving markedly within a few days, allowing for the diagnostic trial treatment of cats in which FIP is very likely. However, antiviral treatment is often expensive, not licensed (in cats and/or humans) and not available legally in many countries, which complicates its use in some parts of the world. Some countries have access to veterinary compounded GS-441524 products whereas others have access to antivirals developed for humans such as remdesivir or molnupiravir. In others, owners source antivirals themselves online, but the quality, purity, and concentration of active ingredients in these preparations is usually unknown, and can be variable, although they are clearly often effective, based on published studies.

Success rates of 81% to 100% have been reported in cats treated with different preparations of compounds believed, or known, to contain GS-441524. In initial studies, GS-441524 was administered by subcutaneous (SC) injection, which was often painful, but oral GS-441524 preparations (usually tablets but a liquid/suspension preparation is also available in some countries) are available, which are very effective, and are cheaper and better tolerated than SC injections. Injectable preparations are now usually reserved for cats that cannot tolerate oral medication due to severe disease or intestinal signs. A dosage of 15 mg/kg q 24 h PO of GS-441524 is effective in

most cats (neurological cases may need higher dosages). Most studies have used 84-day treatment courses, but evidence has now been published that shorter courses of 42-days' duration are effective for cats with effusions; such shorter courses will enable improved access to treatment for cost and/or compliance reasons. Non-clinically significant transient adverse effects of GS-441524 can include elevations in ALT (hepatoprotectants are sometimes given but are unlikely to be needed), lymphocytosis, and eosinophilia. Weight gain has been cited as a simple long-term measure of treatment efficacy too as it is easy to measure using paediatric weighing scales, every one to two weeks, allowing for an increased dose to be calculated to maintain the appropriate dosage despite weight gain during recovery. The hyperbilirubinaemia usually resolves most quickly, followed by the effusion (if present), then an improvement in haematocrit, increasing A:G ratio and the hyperglobulinaemia, which might take up two to three months to normalise. Overall, a good appetite and/or activity level, a higher temperature, a lower bilirubin concentration (in cases with effusion) and fast normalisation of α 1-acid glycoprotein (AGP) appear to be prognostically useful to predict survival with GS-441524 treatment. Two consecutively normal AGP measurements at least a week apart may well confirm recovery from FIP and may be helpful to guide when treatment can be stopped. Studies have shown that AGP concentrations decrease continuously after two days of oral GS-441524 treatment, usually normalising by day 28 of treatment. Concentrations of serum amyloid A (SAA) also decrease with effective GS-441524 treatment, even more rapidly than the AGP concentrations (probably due to the shorter half-life of SAA) mostly reaching normal values by seven days of treatment. FCoV antibody concentrations are not useful to track response to treatment. Residual abdominal lymphadenomegaly has been reported following effective GS-441524 treatment but does not signify FIP relapse. Residual neurological signs are sometimes reported following GS-441524 treatment, and often these signs are static and not associated with FIP relapse but occasionally may be associated with FIP relapse.

Remdesivir is a nucleoside analogue and the prodrug of GS-441524. It is usually expensive. A human-licensed preparation is available, as well as a veterinary compounded product in some countries. Remdesivir has usually been injected, either intravenously or SC, but SC administration is usually painful, possibly dependant on the remdesivir preparation. Most veterinarians thus favour oral GS-441524 treatment for FIP to avoid painful infections, unless remdesivir is the only antiviral available and/or the cat is unable to tolerate oral medication (e.g., due to being very sick) making injectable treatment necessary. Papers are emerging on the use of oral remdesivir, which may be another option for treatment.

Molnupiravir is another oral nucleoside analogue. It is usually cheaper than remdesivir and has shown promising results as a first-line agent and a rescue agent for cases that relapse, although it may not be as effective as GS-441524 in cases with non-effusive signs of FIP. Rules vary in different countries as to whether molnupiravir may be used in cats.

Protocols have emerged on how nucleoside analogues are used to treat FIP; these usually include recommendations for higher dosages in cats with ocular or neurological signs. Antiviral dosages and information on administration are given in Table 2 of the full FIP guideline. In the future, therapeutic drug monitoring (TDM) methods are also emerging for the measurement of GS-441524, which may enable tailoring of GS-441524, or remdesivir, dosage and frequency of administration to the cat being treated although further studies are required.

Vaccination and neutering have both been performed during, or following, successful treatment of FIP with nucleoside analogues, in cats in which these procedures have been deemed necessary. No relapse of FIP has been recorded although employment of feline-friendly methods is recommended to minimise stress.

GC376 is an injectable protease inhibitor that has been used successfully for the treatment of FIP. Dentition adverse effects were reported. No legal preparations are currently available although it is hoped that a cat-licensed product will be available in the future making this treatment accessible.

Some veterinarians have used **mefloquine**, recombinant feline interferon-omega (**rfIFN- ω**) and/or **polyprenyl immunostimulant** (PI) for the treatment of FIP, although none of these are as effective as the antiviral nucleoside analogues.

Oral mefloquine is an affordable human-licensed anti-malarial treatment that has been used anecdotally for FIP and has been tested on healthy cats but no published FIP treatment studies exist. It might be useful as adjunct treatment to maximise effectiveness of antivirals if relapse is suspected, or in cases where other more effective antivirals cannot be used due to cost or availability. It is given with food to avoid vomiting as a side effect.

rfIFN- ω is licensed for use in cats in some countries and, for FIP, it has been used most recently following antiviral therapy with GS-441524 to prevent relapse. However, controlled studies are needed to confirm efficacy of, and need for, rfIFN- ω , as many studies have shown excellent survival following nucleoside analogue (including GS-441524) treatment without follow-up rfIFN- ω .

PI might be helpful in the treatment of FIP without effusions although response to treatment is slow, over several months. It has been found that concurrent systemic glucocorticoid treatment should be avoided with PI, as this worsens prognosis.

Although more studies are needed, systemic glucocorticoids should probably be avoided in the treatment of FIP, although topical

steroids for uveitis are permitted.

Veterinary supportive care (e.g., intravenous fluids, appetite stimulants, anti-emetics, analgesia, vitamin B12, non-steroidal anti-inflammatories) is very important in the recovery of cats that are very sick due to FIP. However, veterinary support is often not sought by owners who have obtained antiviral drugs illegally for their cats as veterinarians are unable to advise, obtain or prescribe illegal drugs, leading to a disconnect between owners and veterinarians. It is possible for vets to give supportive care to cats in this situation for welfare reasons, as long as documentation is created to confirm there has been no veterinary involvement in the illegal drug procurement or administration.

Further details on antiviral, immunomodulatory and supportive treatments for FIP (including dosages) are given in Tables 2 and 5 in the full FIP guidelines, which should be used in conjunction with this summary.

Vaccination

An intranasal vaccine for FIP is available in some countries for cats aged 16 weeks or over. However, it should only be given to cats that have not yet encountered FCoV infection, which is difficult as FCoV infection is widespread in cat populations. Additionally, its **efficacy has been questioned**. Its use is **not recommended by ABCD**.

Control of FCoV infection and FIP

As FCoV is transmitted predominantly via the faecal-oral route, hygiene is the mainstay of FCoV (and therefore FIP) control. FCoV infection is maintained in households by continual cycles of infection and re-infection and is less of a problem amongst cats with access outdoors that bury their faeces outside. A reduction of FCoV infection pressure can also be helped by not keeping more than three well-adapted (consistent) cats per room and providing outdoor access. If outside access is not possible, the number of litter trays should be one more than the number of cats present. Litter trays should be positioned in different rooms, away from food and water, have faeces removed twice a day and completely cleaned once weekly. Non-tracking clumping bentonite-based Fuller's earth cat litter can be helpful to reduce FCoV spread.

The identification and separation of FCoV shedders can be helpful for reducing transmission rates of FCoV in a household. No universally accepted protocol for identification of shedders exists, and testing results represent the situation at only that timepoint, with changes in results occurring over time. Although positive correlation exists between FCoV serum antibody titres and the likelihood and the frequency of faecal FCoV shedding, as well as the FCoV faecal viral load, this relationship is not straightforward. Serum antibody-negative cats can be positive for FCoV RNA in faeces and serum antibody-positive cats can be negative for FCoV RNA in faeces.

The use of nucleoside analogues, such as GS-441524, to eliminate FCoV shedding in cats without FIP is very controversial. Some suggest there is a potential risk of development of drug-resistant escape mutant FCoVs, and are concerned that clearing a household of FCoV is difficult to achieve and maintain, due to the high prevalence of FCoV infection in cat populations. Those wishing to eradicate FCoV from their household should be reminded of the importance of both hygiene and keeping cats in small groups, as well as other measures to reduce FCoV load (e.g., non-tracking litter, avoiding stress) and the use of quarantine and testing prior to introducing cats or kittens into households.

The commercially available genetic PCR tests that purport to detect cats that are resistant to FIP are currently not recommended as a basis for breeding decisions as they are not accurate in identifying resistant cats.

Stress experienced by FCoV-infected cats (e.g., due to surgery, boarding, adoption) or immunosuppression caused by infections, e.g., FIV or FeLV, can predispose cats to developing FIP, so the minimisation of stress and immunosuppression are important to prevent the development of FIP in FCoV-infected cats. The FIP vaccine is not useful in FCoV-infected cats.

Conclusions

FIP typically occurs in young cats, and effusions, fever, anorexia, and weight loss are common presenting signs. The sampling of effusions or abnormal tissues by fine-needle aspirates for cytology and FCoV analysis (either RT-qPCR for FCoV RNA load and/or immunostaining for FCoV antigen) can aid diagnosis. Antiviral compounds, especially oral GS-441524, are effective curative treatments. Trial treatment of cases might be warranted if a diagnosis is very likely, as response to effective antivirals is usually rapid. Without effective antiviral treatment, FIP has a very poor prognosis.

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