**Feline Infectious Peritonitis (2012 edition)**

**What's new?**

The pathogenesis and epidemiology of FIP is still a bone of contention. According to one view, two FCoV pathotypes circulate independently in the field. This assumption does not explain the sporadic, non-epidemic occurrence of FIP.

The other hypothesis, that of mutants arising in individual cats upon bursts of replication, (e.g. under immune-suppressive stress) has become more plausible. Here are the arguments:

Functional expression of one of the non-structural proteins (3c) is crucial for FCoV replication in the gut, but dispensable for systemic replication of the FIPV mutant. Whilst intact in all FCoVs, the 3c gene was found mutated in >70 % of FIPV strains - but not in all, implying that mutation in 3c is not the (single) cause of FIP. Most cats with FIP had no detectable intestinal FCoVs and had seemingly cleared the primary infection. In those with detectable intestinal FCoV, the virus always had an intact 3c and seemed to have been acquired by FECV superinfection. Apparently, 3c-inactivated viruses replicate not at all--or only poorly--in the gut, explaining the rare incidence of FIP outbreaks.

**Virus**

Feline infectious peritonitis (FIP) is caused by mutants of coronaviruses arising in individual cats. Feline coronaviruses (FCoV) belong to the family Coronaviridae of the Order Nidovirales (de Vries et al, 1997). These viruses are large, spherical, enveloped, positive-sense single-stranded RNA viruses (Lai and Holmes, 2001). With a genome of 27 to 32 kb, encoding a ~750-kDa replicase polyprotein, four structural proteins (S for spike, M for matrix, N for nucleocapsid, and E for envelope) and up to five accessory non-structural proteins, coronaviruses are the largest RNA viruses known to date (Brown and Brierly, 1995; de Vries et al, 1997). - A biologically important characteristic of these viruses is their capability to undergo recombination (Lai, 1996; Lai and Holmes, 2001).

Together with the canine coronavirus and transmissible gastroenteritis virus of pigs, FCoVs belong to the group I coronaviruses, defined by antigenic and genomic
properties.

Feline coronaviruses have been assigned to two types, which are defined by antigenic and genomic properties. Type I virus is the most prevalent FCoV (Hohdatsu et al, 1992; Addie et al, 2003; Vennema, 1999; Kummrow et al, 2005; Shiba et al, 2007); the less common type II viruses are recombinants between type I FCoVs and canine coronavirus that have repeatedly and independently arisen in the field (Herrewegh et al, 1998). Most studies have been conducted on type II viruses which, unlike type I virus, can be propagated in cell culture (Pedersen et al, 1984).

Importantly, both virus types can induce FIP. Previously, FCoV strains have also been allocated to two “biotypes”: feline enteric coronavirus and feline infectious peritonitis virus (FIPV; Pedersen, 1987). However, since all FCoV may induce systemic infections, as demonstrated by RT-PCR studies, such descriptions should be avoided and will not be used in the present guidelines. Feline coronaviruses can survive for up to seven weeks in a dry environment (Scott, 1988) and can therefore be transmitted indirectly e.g. via litter trays, shoes, hands and clothes. Indirect transmission may also occur at cat shows. However, FCoV is readily inactivated by most household detergents and disinfectants.

**Epidemiology**

Feline coronavirus infection is ubiquitous in domestic cats, and also wild felids may be seropositive. Infection is particularly common under crowded conditions, like in multi-cat households, where the seroprevalence may reach 100% (Horzinek et al, 1979; Addie and Jarrett, 1992; Sparkes et al, 1992; Addie, 2000; Kummrow et al, 2005; Herrewegh et al, 1995; Foley et al, 1997; Kiss et al, 2000). A substantial proportion of FCoV infected cats (some 12%; Addie et al, 1995a, EBM grade III) will go on to develop fatal FIP, again especially in multi-cat environments (Addie & Jarret, 1992; Fehr et al, 1995; Pedersen, 1995b; EBM grade III). Disease prevalence will depend on the cat population, particularly its age distribution, and local housing conditions.

Some breeds, e.g. Bengals, and genetic lines within breeds are more likely to be affected by FIP (Kiss et al, 2000; Pesteanau-Somogyi et al, 2006). Age is an important risk factor: 70% of FIP cats are less than one year old (Rohrer et al, 1993;
Hartmann, 2005) - but FIP has been seen in cats up to 17 years of age. It has been suggested that the prevalence of FIP is lower in neutered cats (Pesteanu-Somogyi et al, 2006).

Since any form of immune suppressive stress experienced by FCoV-infected cats may be followed by FIP (surgery, visit to a cattery, moving, co-infection with retroviruses; Poland et al, 1996; Rohrer et al, 1993), stress management is an important element of control.

In breeding catteries, kittens usually become infected with FCoVs at a young age, often prior to weaning. The queen is often the source of infection, certainly if the litter has been reared in isolation. The age at which kittens become infected varies: it may occur at 5 to 6 weeks of age, after the loss of maternally derived immunity, but in some situations even earlier, at 2 weeks of age (Lutz et al 2002).

Faeces contain FCoV at high concentrations, and the faeco-oral route of transmission is most important, with litter boxes representing the main source of infection in groups. Saliva may play a role in groups in close contact, or in animals sharing feeding bowls (Addie & Jarrett, 2001). Transplacental transmission has been described from a queen that developed the disease during pregnancy (Pastoret & Henroteaux, 1978), but is rare (Addie & Jarrett, 1990).

Susceptible cats obtain FCoV from asymptomatic cats. Although transmission from cats with FIP may occur, it is important to note that this hardly ever leads to disease. Indeed, under natural conditions, FIP is not contagious, but it can be transmitted experimentally.

After natural infection, cats begin shedding FCoV in the faeces within one week (Pedersen et al, 2004) and continue for weeks to months. Some cats become carriers and shed virus for life (Addie & Jarrett, 2001) and at high levels (Horzinek & Lutz, 2000). Whilst a cat remains infected, faecal FCoV excretion is continuous (Addie & Jarrett, 2001).

**Pathogenesis**

Most cats infected by FCoV either develop an asymptomatic infection or show a mild enteritis. Only a fraction of them goes on to develop FIP, a pyogranulomatous polyserositis (Pedersen et al, 1981; Pedersen, 1987).
To explain the pathogenesis, there are two main hypotheses:

Mutants arise which replicate in monocytes and macrophages (Poland et al, 1996; Vennema et al, 1998; Cornelissen et al, 2007 Haijema et al, 2004; Rottier et al, 2005). In support of this hypothesis is the presence of highly virulent strains of FCoV that are capable of consistently inducing FIP, albeit under experimental conditions (Poland and Venema 1996). Any FCoV can cause FIP but a high viral load (with a high probability of mutants occurring in the "quasi species cloud") and the cat’s immune response determine whether FIP will develop (Addie et al, 1995, Dewerchin et al, 2005; Dye & Siddell, 2007; Meli et al, 2004, Rottier et al, 2005; Kipar et al, 2006). Both factors, viral genetics and host immunity, play a role in the development of FIP.

Functional expression of one of the non-structural proteins (3c) is crucial for FCoV replication in the gut, but dispensable for systemic replication of the FIPV mutant. Whilst intact in all FCoVs, the 3c gene was found mutated in >70 % of FIPV strains - but not in all, implying that mutation in 3c is not the (single) cause of FIP. Most cats with FIP had no detectable intestinal FCoVs and had seemingly cleared the primary infection. In those with detectable intestinal FCoV, the virus always had an intact 3c and seemed to have been acquired by FECV superinfection. Apparently, 3c-inactivated viruses replicate not at all--or only poorly--in the gut, explaining the rare incidence of FIP outbreaks (Chang et al., 2010).

According to another view, two FCoV pathotypes circulate independently in the field. This circulating was advocated by Brown et al. (2009); it does not explain the sporadic, non-epidemic occurrence of FIP.

FIP occurs in two manifestations: an effusive, "wet" form which is characterised by polyserositis (e.g. thoracic, pericardial and abdominal effusions), with vasculitis as a consequence of injury to blood vessel walls and extravasating macrophages (Kipar et al, 2005), and a non-effusive, "dry" form typified by granulomatous lesions in organs. These two forms reflect clinical extremes of what is a continuum, with many cats having signs and lesions intermediate between them.

A rare nodular enteric form described in young cats with diarrhoea and vomiting was associated with intestinal pyogranulomatous lesions (Van Kruiningen et al, 1983;
All forms of FIP are lethal. Disease progression may be the consequence of severe immunodepression by T-cell depletion (de Groot-Mijnes et al, 2005). Whether a cat develops the wet or dry form is thought to depend on the strength of the T-cell-mediated immune response, which is probably the only efficient immune response against disease progression (Pedersen, 1987; Cornelissen et al, 2007). The wet forms are presumed to be the consequence of a weak cell-mediated immune response (Pedersen, 1987).

Attempts to identify a tissue distribution of FCoV that is diagnostic for FIP have proved difficult. In the sick cats, virus replicates to high titres in monocytes and can be found in many organs (Kipar et al, 2005). In healthy infected cats, FCoV is mainly found in the intestine. However, using RT-PCR, a low-level monocyte-associated viraemia can be detected (Gunn-Moore et al, 1998b; Herrewegh et al, 1995; Meli et al, 2004). High-level replication has also been demonstrated in organs of asymptomatic cats, at least within the first month after an experimental infection with FCoV type I (Meli et al, 2004). A significant difference in viral replication in haemolymphatic tissues has been demonstrated between cats that died from FIP and healthy long-term infected cats (Kipar et al, 2006).

Monocytes and macrophages remain infected, even in the presence of high levels of antibodies. The mechanism of this immune evasion could be escape from antibody-dependent lysis due to the absence of viral antigens on the surface of infected cells (Dewerchin et al, 2006; Cornelissen et al, 2007). The direct consequence may be a quiescent infection state and a long incubation period. Activation of monocytes and perivascular macrophages may lead to the development of typical widespread pyogranulomatous and vasculitis/perivasculitis lesions in various tissues and organs, including lung, liver, spleen, omentum, and brain of cats with FIP (Kipar et al, 2005; Berg et al, 2005).

**Immunity**

It has been suggested that cats mounting a strong cellular immune do not develop FIP, whereas those with a predominantly humoral response progress to disease (Pedersen 1987). Hypergammaglobulinaemia (Ward et al, 1974; Paltrinieri et al,
1998) is common in cats with FIP. Also, depletion of T cells from the blood (de Groot-Mijnes et al, 2005) as well as from lymphoid tissues has been described (Haagmans et al, 1996; Paltrinieri et al, 2003; Dean et al 2003).

Passive immunity
As in coronavirus infections of other species, maternally derived antibody (MDA) usually provide protection until about 5-6 weeks of age (Addie & Jarrett, 1992). Their levels decline and they become undetectable by 6-8 weeks of age (Pedersen et al 1981).

Active immune response
Cell-mediated immunity: Cats that did not develop disease after experimental coronavirus infection displayed a greater cell-mediated immune response when compared to those that did (Pedersen & Floyd, 1985, de Groot-Mijnes et al, 2005). Cytokine measurements in blood or lymphatic tissues revealed decreased IL-12 responses and low levels of IFN-gamma expression (Kiss et al, 2004; Gelain et al 2006; Kipar et al 2006), indicative of impaired cellular immune responses.

Humoral immunity: The humoral immune responses in FIP is not protective. Although virus clearance has been associated with antibodies directed against the FCoV spike protein (Gonon et al, 1999), their role in protection is questionable. Rather, antibodies directed against the spike protein can be detrimental. In cats with pre-existing antibodies, accelerated disease has been observed in experimental infections, typified by an earlier development of clinical signs, a shortened disease course, leading to earlier death. This phenomenon was observed in cats that had acquired their antibodies through passive or active immunization (Pedersen & Boyle 1980; Weiss & Scott 1981). Furthermore, when cats had been immunised with a recombinant vaccinia virus expressing the coronaviral S protein, they became severely ill 7 days after challenge with the virulent, FIP-causing mutant. In contrast, the unvaccinated control cats survived for more than 28 days (Vennema et al, 1990). This antibody-dependent enhancement (ADE) is likely due to opsonisation of the virus, whereby uptake by macrophages via Fc receptor-mediated attachment is
facilitated (de Groot and Horzinek, 1995; Corapi et al, 1992). The role of ADE in natural infection is not clear since cats develop FIP on first exposure to FCoV (Addie et al, 1995a, 1995b, 2003) - but only after antibody, immune complexes and complement depletion had been observed (Jacobse-Geels et al., 1980).

Clinical signs
The clinical presentation of FIP is variable, and reflects the variability in the distribution of the vasculitis and pyogranulomatous lesions. Classification of FIP in effusive and non-effusive (wet and dry) forms has some value in recognising clinical presentations and contributing to the diagnosis, but there is considerable overlap between the two forms. In cases with predominantly non-effusive features, investigation of possible accumulation of sub-clinical, small amounts of effusion can be helpful to provide samples for diagnostic testing. Fever refractory to antibiotics, lethargy, anorexia and weight loss are common non-specific signs, but occasionally, patients remain active and retain body condition. Ascites is the most conspicuous clinical manifestation of the effusive form (Holzworth, 1963, Wolfe & Griesemer 1966). Thoracic and pericardial effusions may occur in combination with or separate from abdominal effusion. In cases where effusion is restricted to the thorax, the cats usually present with dyspnoea. Serositis can involve the tunica vaginalis of the testes, leading to scrotal enlargement. The non-effusive, "dry" form of FIP is often a diagnostic challenge. Pyrexia, anorexia and lethargy may be the only signs, particularly in the early stages. More characteristic signs will depend on the organs or tissues involved in the vasculitis and pyogranulomatous lesions. Abdominal organs are a common site for lesions. Renal involvement may lead to renomegaly detectable on palpation. Mural lesions in the colon or ileo-caeco-colic junction occasionally occur and may be associated with chronic diarrhoea and vomiting. There may also be palpable enlargement of the mesenteric lymph nodes, which may be misinterpreted as neoplasia (Kipar et al, 1999). - A diffuse pyogranulomatous pneumonia is seen in some cases leading to severe dyspnoea (Trulove et al, 1992). Ocular involvement is common, leading to changes in iris colour, dyscoria or anisocoria secondary to iritis, sudden loss of vision and hyphaema. Keratic
precipitates can be seen and may appear as “mutton fat” deposits on the ventral corneal endothelium (Davidson, 2006). The iris may show swelling, a nodular surface, and aqueous flare may be detected. On ophthalmoscopic examination chorioretinitis, fluffy perivascular cuffing (representing retinal vasculitis), dull perivascular puffy areas (pyogranulomatous chorioretinitis), linear retinal detachment and fluid blistering under the retina may be seen. Neurological signs are reported in ≥10% of cases (Rohrer et al, 1993). They reflect focal, multifocal, or diffuse involvement of the brain, the spinal cord and meninges. The most commonly reported signs are ataxia, hyperaesthesia, nystagmus, seizures, behavioural changes and cranial nerve defects (Kline et al, 1994; Timman et al, 2008). Cutaneous signs occur as multiple nodular lesions caused by pyogranulomatous-necrotising dermal phlebitis (Cannon et al, 2005) and skin fragility (Trotman et al, 2007).

Diagnosis

*Intra vitam* diagnosis of FIP remains a challenge. Sometimes a definitive diagnosis may not be possible, e.g., because of the invasiveness of taking organ biopsies from a sick cat. Difficulties in definitively diagnosing FIP arise from the lack of non-invasive confirmatory tests in cats with no effusion. Effusions should be first looked for, because obtaining them is relatively non-invasive. In cats without effusion, several parameters should be checked, like the background of the cat, history, clinical signs, laboratory changes, antibody titre (Rohrer et al, 1993), and be used to decide about further diagnostic procedures.

Haematology

Changed haematological data are often encountered in cats with FIP, but the changes are not pathognomonic. White blood cell counts can be decreased or increased. Lymphopenia is commonly seen; however, lymphopenia in combination with neutrophilia is common in cats as a typical “stress leukogram” and can occur in many other diseases. A normal lymphocyte count makes FIP less likely. A mild to moderate non-regenerative anaemia is also a common, but non-specific, finding, which may occur in almost any chronic disease of the cat.
A common laboratory finding is the increase in total serum protein concentration caused by a rise in the globulin fraction, mainly the γ-globulins (Paltrinieri et al, 2001; 2002). Hyperglobulinaemia was found in about 50% of cats with effusion and 70% of cats without effusion (Sparkes et al, 1994). After experimental infection, an increase of α2-globulins is seen first, while γ-globulins and antibody titres increase just prior to the onset of clinical signs (Pedersen 1995; Gunn-Moore et al, 1998). Serum total protein levels can reach high concentrations, 120 g/l (12 g/dl), and even higher. The albumin to globulin ratio has a significantly higher diagnostic value than either total serum protein or γ-globulin concentrations alone, because a decrease in serum albumin may also occur as a result of decreased synthesis (Shelly et al, 1988; Rohrer et al, 1993; Hartmann et al, 2003). Low albumin levels are usually associated with protein loss caused e.g. by glomerulopathy secondary to immune complex deposition, or by extravasation of protein-rich fluid during vasculitis (Hartmann et al, 2003). An optimum cut-off value (maximum efficiency) of 0.8 was determined for the albumin to globulin ratio (Hartmann et al, 2003; EBM grade I). Serum protein electrophoresis may show hypergammaglobulinaemia - both polyclonal and monoclonal - as well as an increase in acute phase proteins. Other laboratory parameters (liver enzymes, bilirubin, urea, creatinine) can be variably elevated depending on the degree and localisation of organ damage, but are generally not helpful in establishing a diagnosis. Hyperbilirubinemia and icterus are often observed as a reflection of hepatic necrosis (Hartmann et al, 2003). Sometimes, bilirubin is increased without evidence of haemolysis, liver disease, or cholestasis; this is unusual, and otherwise only observed in septic animals. Bilirubin metabolism and excretion into the biliary system is compromised due to high levels of TNF-α that inhibit transmembrane transport. Thus, high bilirubin in the absence of haemolysis and elevation of liver enzyme activity should raise the suspicion of FIP. The diagnostic value of acute phase reaction parameters has been realised, including α1-acid glycoprotein (AGP), that is elevated in cats with FIP (Duthie et al, 1997; Paltrinieri, 2008). High serum AGP levels (>3 mg/ml) can support the diagnosis of FIP (Paltrinieri et al, 2007a), but again levels also rise in other inflammatory conditions. Also, AGP may be high in asymptomatic cats infected with FCoV, especially in households where the infection is endemic (Paltrinieri et al,
Tests on effusion fluid

If there is effusion, the most important diagnostic step is to sample the fluid, because tests on effusion have a higher diagnostic value than those performed on blood. However, only about half of the cats with effusions suffer from FIP (Hirschberger et al, 1995). Although transparent, yellow ("amber-coloured") effusions of a sticky consistency are often called typical, this alone is not diagnostic. Sometimes the fluid has quite a different appearance, and purely chylos effusion have been reported (Savary et al, 2001). Usually the protein content is high (>35g/dl) and consistent with an exudate, whereas the cellular content is low (< 5000 nucleated cells/ml) and approaches that of a modified transudate or pure transudate. Cytology shows a variable picture but often consists predominantly of macrophages and neutrophils. Electrophoresis of effusion fluids is a diagnostic tool with a high positive predictive value if the albumin/globulin ratio is <0.4, and a high negative predictive value if the ratio is > 0.8 (Shelly et al, 1988). Differential diagnoses include inflammatory liver disease, lymphoma, heart failure, and bacterial peritonitis or pleuritis.

The “Rivalta test” is a simple, inexpensive method that does not require special laboratory equipment and can be performed in practice. It was invented by the Italian researcher Rivalta around 1900 for differentiating between transudates and exudates in human patients. It is also useful in cats, to differentiate between effusions due to FIP and those caused by other diseases (Hartmann et al, 2003; EBM grade I). Not only the high protein content, but high concentrations of fibrinogen and inflammatory mediators lead to a positive reaction.

Box 1. Rivalta test

A transparent tube (volume 10 ml) is filled with approximately 7-8 ml distilled water, to which 1 drop of acetic acid (98%) is added and mixed thoroughly. On the surface of this solution, 1 drop of the effusion fluid is carefully layered. If the drop dissolves and disappears and the solution remains clear, the Rivalta’s test is read as negative. If the drop retains its shape, stays attached to the surface or slowly floats down (drop- or jellyfish-like), the Rivalta’s test is read as positive.
The Rivalta test had a positive predictive value of 86% and a negative predictive value of 96% for FIP, in a study in which cats with effusion were investigated (prevalence of FIP 51%; Hartmann et al, 2003). Positive Rivalta’s test results can be obtained also in cats with bacterial peritonitis or lymphoma, but those effusions are usually easy to differentiate through macroscopic examination, cytology, and/or bacterial culture.

Cerebrospinal Fluid
Analysis of cerebrospinal fluid (CSF) from cats with neurological signs due to FIP lesions may reveal elevated protein (50 - 350 mg/dl; normal value <25 mg/dl) and pleocytosis (100 - 10,000 nucleated cells/ml) with mainly neutrophils, lymphocytes, and macrophages (Li et al, 1994; Rand et al, 1994; Foley et al, 2003). This, however, is a non-specific finding - many cats with neurological signs caused by FIP have normal CSF values.

Antibodies
Antibody titres measured in serum can contribute to FIP diagnosis, if interpreted with care. Because of the ubiquity of FCoV, a high percentage of healthy cats are antibody-positive, and most of them will never develop FIP. Thus, antibody titres must be interpreted with extreme caution, and a high titre in a healthy cat has neither diagnostic nor prognostic value; it has been contended that more cats have died of false interpretation of FCoV antibody test results than of FIP disease (Pedersen, 1995a). There is no “FIP antibody test”, all that can be measured is antibodies against FCoV. Also, methodology (and thus titre results) differs between laboratories. It is important to realise that the presence of antibodies does not prove FIP and their absence does not exclude FIP. Low or medium titres do not rule out FIP: approximately 10% of the cats with clinically manifest FIP are seronegative (Hartmann et al, 2003). In cats with fulminant FIP, titres may decrease terminally (Pedersen, 1995a), because of in-vivo immune adsorption: antibody binds to the large amounts of viral antigen in the cat’s organism and renders it unavailable for the test. Very high titres can be of a certain diagnostic value in the sense of an increased likelihood of FIP (Hartmann et al, 2003).
Measuring antibodies in fluids other than blood has been investigated (Boettcher et al, 2007; Foley et al, 1998), but is not recommended.

FCoV Reverse-transcriptase polymerase chain reaction (RT-PCR)
A FCoV RT-PCR in blood is sometimes used as a diagnostic tool, but no varian of the technique can distinguish between FIP-inducing mutants and the resident, non-mutated population of FCoV (Fehr et al, 1996). Positive FCoV RT-PCR results are obtained not only from cats with FIP, but also in healthy carriers that did not develop FIP for a period of up to 70 months (Gunn-Moore et al, 1998b; Meli et al, 2004; Gamble et al, 1997; Herrewegh et al, 1997; EBM grade I). Negative FCoV RT-PCR are also commonly encountered in cats with FIP (Hartmann et al, 2003).
A more plausible approach is to measure messenger RNA by RT-PCR in blood, with the rationale that their levels correlate with the level of replication of FCoV and thus with the probability of mutation. However, the validity of this assumption remains to be shown, since 5 to 50 % of healthy cats were PCR-positive (Simons et al, 2005; Can-Sahnak et al, 2007); the test is not available in Europe.

Immunostaining of FCoV antigen in macrophages
Methods to detect the FCoV include the search for the antigen in macrophages using immunofluorescence (in effusion macrophages) or immunohistochemistry (in tissue macrophages of biopsy specimens). While FCoV may be present systemically in healthy cats, only in FIP cases will there be sufficiently large amounts of viral antigen in macrophages to obtain a positive signal. Indeed, immunofluorescence of intracellular FCoV antigen in macrophages of effusions was 100 % predictive of FIP; the low negative predictive value (57%) found in a controlled study may be due to the low numbers of macrophages in effusion smears - even though the cats had confirmed FIP (Hartmann et al, 2003).
Immunohistochemistry to detect FCoV antigen in tissue also proved to be 100% predictive of FIP if positive (Tammer et al, 1995; Kipar et al 1998b). However, invasive methods like laparotomy or laparoscopy are usually necessary to obtain the tissue samples. When true-cut biopsy (TCB) and fine-needle aspiration (FNA) of liver and kidney tissue obtained at necropsy were compared, their diagnostic sensitivity
was similar, but a higher sensitivity of liver versus kidney tissue was observed (Giordano et al, 2005). The value of ultrasound-guided FNA to diagnose FIP in vivo is an avenue to be investigated.

In summary, there are two diagnostic strategies to obtain a definitive diagnosis of FIP: if there is effusion, immunofluorescence staining of FCoV antigen in macrophages proves FIP. If there is no effusion, tissue samples from affected organs have to be obtained. A diagnostic algorithm is shown in Figure 1.

Figure 1. Diagnostic approach to FIP

**Disease management**

Any cat in a hospital is a potential source of FCoV infection, and routine hygiene measures should be taken. A cat with FIP will likely shed FCoV - but rarely the disease producing mutants - and precautions to avoid virus spread are important. In a multi-cat household, all animals will probably have been infected earlier, so there is no benefit in isolating the FIP cat.

In situations where a cat with FIP had been euthanised, and there is no cat left in that household, it is recommended to wait for two months before obtaining a new cat. If other cats in that household remain, they most like carry FCoV.

**Treatment**

Treatment (or euthanasia) should only be considered after every effort had been made to obtain a definitive diagnosis. Once FIP is established, the prognosis is fatal. The median survival after diagnosis is about 9 days. Factors that predict a short survival time are low lymphocyte counts, high bilirubin, presence of large volumes of effusion. Cats that do not improve within 3 days are unlikely to show any benefit from treatment and euthanasia should be considered.

Occasionally, cats have survived for several months after clinical diagnosis, but it is unclear whether this was due to the treatment. There have even been reports of "recovered" cats, but in these a laboratory diagnosis had not been obtained. As FIP is caused by inflammatory and inappropriate immune-responses to FCoV, supportive treatment is aimed at suppressing them, usually with corticosteroids.
There are, however, no controlled studies that prove any beneficial effect. Occasionally, cases treated with corticosteroids have shown improvement for up to several months, but these are anecdotal, not rigorously controlled observations (EBM grade III).

Numerous treatments have been tried, and data from one controlled field study have been published. In this placebo-controlled study of 37 cats, treatment with feline interferon omega showed no benefit when compared to the placebo (Ritz et al, 2007; EBM grade I). Other drugs (table 1) have been used, but there are no controlled studies to support their efficacy.

Table 1. Drugs that have been suggested for use in FIP

Vaccination

Many attempts have been made to develop vaccines against FIP. Unfortunately most of these studies have failed, with ADE observed in several trials. At present, there is only one vaccine commercially available (Primucell®, Pfizer), in the USA and some European countries. Primucell® contains a temperature sensitive mutant of the type 2 FCoV strain DF2. The vaccine is administered intranasally and aims at inducing local mucosal immune responses through the induction of IgA and cell-mediated immunity. However, it does induce seroconversion, although rarely, and titres are generally low. Also the efficacy of this vaccine is in question - it contains a type-2 strain, whereas type-1 coronaviruses are the prevalent ones in the field in most countries. The results of experimental protection studies have not been consistent, with success rates between 0 and 75 % (Hoskins et al, 1995; McArdle et al, 1995; Scott et al, 1995; Gerber et al 1990). The results of field studies have been equally contradictory. No difference in the development of FIP between the vaccinated and placebo group was found when the vaccine was used in Persian breeding colonies (Fehr et al 1995). In a double-blind trial including 609 cats, no differences between the vaccinated and placebo group were found during the first 150 days after vaccination. However, after 150 days, fewer FIP cases occurred in the vaccinated group compared to the placebo group (1 against 7). In another trial, a preventable
fraction of 75% was found when the vaccine was tested in a large cat shelter in the USA (Postorino Reeves, 1995). In this study all kittens were seronegative prior to vaccination. Primucell® consequently is ineffective in cats that have already experienced a FCoV field infection, which is hardly surprising and not the vaccine's fault. Since Primucell® is licensed for use from 16 weeks of age and is not effective in younger cats (Lutz et al 2002), most kittens (especially those living in breeding colonies and multiple cat households) have already been infected and are seropositive. This is an important limitation for its use. The ADE that was a feature in some experimental vaccine trials has not been observed in field studies, suggesting that the vaccine can be considered safe.

Primary vaccination course
In line with other guideline bodies, ABCD does not consider the FIP vaccine as a core vaccine. Vaccination can be considered in kittens that are unlikely to have been exposed to FCoV, e.g. from an early weaning programme, particularly if they enter an FCoV endemic environment.

If immunisation is considered, a primary vaccination course consisting of 2 doses of the vaccine 3 weeks apart from an age of 16 weeks onwards should be given. Vaccination before 16 weeks was not shown to afford protection against infection (Lutz et al 2002). Therefore there are two particular problems in breeding catteries; firstly most kittens are already seropositive at the age of vaccination and secondly FCoV infection occurs at a much younger age than 16 weeks (Lutz et al., 2002, Addie & Jarrett 1992).

Booster vaccination
In cats of which the lifestyle has justified primary vaccination, annual boosters may be considered. Although studies on the duration of immunity are lacking, it is thought to be short lived and regular boosters may be required. But this is rather a conjecture than a conclusion - the boosting effect of a FCoV-contaminated environment has not been studied.

Control in specific situations
FIP is a problem of cats kept in groups, particularly in breeding catteries and rescue shelters. Since the most important route of transmission is faeco-oral, hygiene is the mainstay of FIP control in any multi-cat environment. FCoV infection is maintained by continual cycles of infection and re-infection (Foley et al, 1997, Addie et al, 2003), the source of infection being the litter tray. FIP is rarely a problem amongst cats leading a natural, indoor-outdoor lifestyle. The goal in every cat household has to be to reduce the FCoV infection pressure and risk of transmission. This can be done by keeping not more than 3 (well-adapted) cats per room, observing strict hygiene, and providing outdoor access to allow them to bury their faeces. If the latter is not possible, enough litter boxes should be provided (one more than the number of cats), cleaned frequently, and positioned in different rooms from food and water bowls.

Breeding catteries
Breeding catteries are high-risk environments for FIP. In most European countries FCoV is endemic today. In some catteries, attempts have been made to control the virus spread by segregation. A policy of separating cats shedding high amounts of FCoV from low-level shedders and negative cats has been suggested. The value of this approach is controversial. High shedders can be detected using RT-PCR screening of faeces, but repeated sampling from the same cat is necessary, which presents practical difficulties. Virus shedding occurs over several months and is sometimes life-long, especially in multi-cat households. Kittens typically develop FIP in the post-weaning period (Cave et al, 2002). Breeders are often unaware of an endemic FCoV infection, since FIP deaths usually occur once the kittens are in the new household. Most kittens are protected by maternally derived antibodies until they are between 5 and 6 weeks of age. It is possible to prevent FCoV infection of young kittens by isolating pregnant queens 2 weeks before birth and removing kittens from their mother to a clean environment when they are 5-6 weeks old and maintaining them there until they go to a new home (Addie & Jarrett, 1990, 1992 and 1995). For this technique to work, the breeder is required to follow surgical or even microbiological hygiene precautions, which he is not trained to do. Also, controversy exists about the efficacy of this method - in another attempt, it
has not worked.
Although documented in rare cases, transplacental transmission of FCoV is not a problem (Addie & Toth, 1993).

Rescue and boarding catteries
Strict hygiene precautions should be enforced at all times to attempt to minimise viral spread and to keep virus load at a minimum. Ideally, cats should be kept separately. Architectural design of new catteries should take infectious disease control and stress reduction as a priority.
Vaccination of a cat that is unlikely to have been exposed to FCoV, and is entering a boarding or rescue cattery may be considered.

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