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# Feline Infectious Peritonitis/Feline Enteric Coronavirus (FIP/FECV)

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## Feline Coronavirus and Feline Infectious Peritonitis

### Background

Feline infectious peritonitis (FIP) arises as a mutation of feline coronavirus (FCoV), an enveloped RNA virus. In contrast to the notorious parvoviruses, infection with FCoV is very common in shelter cats and other densely housed feline populations, while mortality due to feline infectious peritonitis (FIP) is generally low. This is fortunate, as many of the tools that help us control panleukopenia and parvovirus are simply not available for management of FCoV and FIP: vaccination is unreliable at best; diagnosis is rarely straightforward; and the murky understanding of transmission and development of disease makes set quarantine policies impossible. One might think this would not matter given the endemic nature of FCoV infection in multicat populations and the fact that FIP is not thought to be transmitted cat-to-cat per se. However, outbreaks involving substantially increased mortality due to FIP do occur in groups of unrelated cats in shelters and catteries.

### Disease course and transmission of FCoV/FIP

Feline coronavirus is shed extensively in the feces of infected cats and is very readily spread by fomite transmission. Viral shedding may begin within just a few days of infection, and antibody titers will develop within 7-14 days. Although most cats eventually resolve their infection, some cats are chronic shedders. Shedding may be intermittent. The only method to detect shedders is PCR analysis of feces. A minimum of three samples obtained a month apart are recommended to consider a cat a negative shedder. Most often no clinical signs of FCoV infection are seen; mild diarrhea or respiratory signs may occur but will generally be indistinguishable from other common conditions in feline populations.

Feline infectious peritonitis generally results from a mutation of FCoV which occurs anew in each individual cat that develops the disease. This mutated virus is cell-associated and thus is not commonly transmitted directly from cat to cat. Disease generally develops within a few weeks to 18 months after infection with FCoV, often subsequent to a stressor such as rehoming or spay/neuter surgery. Disease most commonly occurs in cats < 18 months of age, and in cats > 12 years. There appears to be a genetic component to risk of FIP; thus littermates of kittens that have developed FIP are at substantially increased risk. Unfortunately, there is no way to predict, out of a group of seropositive cats at risk for FIP, which ones are more likely than others to develop the disease.

### Diagnosis of FIP

A positive diagnosis of FIP can be difficult to make, particularly in the absence of characteristic effusion. Diagnosis must generally be made based on a combination of signalment, clinical signs, blood work, titer results and specific tests. The most common signs of FIP in young cats are cyclic, antibiotic non-responsive fever, lethargy,

unexplained weight loss and failure to grow. Common laboratory abnormalities include elevated total protein (mainly globulin), increased numbers of total white blood cells and neutrophils, decreased numbers of lymphocytes and anemia. However, none of these abnormalities are present in all cats with FIP; and there are other conditions which can lead to any of these findings – therefore, FIP can not be definitely diagnosed or ruled out based on these tests alone. Definitive diagnosis is accomplished by visualization of FCoV within macrophages in effusion fluid, on biopsy or necropsy. However, such tests may not always be financially practical in a shelter.

*Coronavirus titers:* Feline coronavirus titers may be used as an adjunct to diagnosis, however these only indicate whether a cat has been exposed to the near-ubiquitous FCoV. There are no titer tests specific for FIP. If the titer is negative at <1:25, it is likely the cat is truly negative and does not have FIP; be aware that not all laboratories test down to such a low dilution, and negative at higher dilutions (e.g. 1:400) is not meaningful. Very high titers (>1:16,000) are strongly suggestive of FIP; however most cats with FIP do not have titers this high. Rising titers are less informative than they would be for other diseases, because cats with benign FCoV and those with FIP both cycle up and down in titer level. This is particularly likely in a shelter cat, who can be presumed to have suffered a recent onslaught of viral exposure. *Diagnosis of FIP, or risk for developing FIP, should never be made based on titers alone.*

*Characteristic effusion:* Wet FIP can often be diagnosed with reasonable confidence based on presence of yellow to clear modified transudate effusion (protein levels > 3.5 g/dl, low cellularity of < 5000 cells per microliter). Protein content can be readily assessed in-house using a refractometer. The Rivalta Test can be done in-house to further assess suspicious fluid: A test tube is filled with distilled water and one drop of 98% (glacial) acetic acid is added (this can be obtained from chemical supply companies). One drop of effusion is added to this mixture, watch carefully while doing so: if the drop dissipates (disappears), the test is negative. If the drop retains its shape, the test is positive. A negative Rivalta's test is 97% accurate in ruling out FIP. A positive test is 86% accurate in ruling in FIP. Further evaluation of the fluid at a laboratory can include cellular count and characterization and albumin to globulin ratio. However, other rule outs for a modified transudate in the abdomen are virtually all serious conditions; therefore in a shelter that must make euthanasia decisions about some cats, it may be reasonable to euthanize cats based on a strong suspicion of an untreatable condition rather than investing resources on further testing.

#### **Vaccination for Feline Coronavirus/FIP**

There are inherent challenges to creating a truly reliable vaccine for FCoV. Even natural infection does not convey lasting immunity, and a vaccine is unlikely to do better than this. There is currently only one vaccine available for feline coronavirus, a modified live intranasal product labeled for use in cats > 16 weeks of age, to be given as a series of two vaccines 3-4 weeks apart. Results of studies regarding the efficacy of this vaccine have been variable, some showing no efficacy and others showing limited efficacy under certain circumstances. One study showed a significantly decreased risk of FIP for cats that were seronegative at the time of vaccination. Although there may be some benefit to giving the vaccine to cats that have never before been exposed to a multi-cat environment (and are therefore relatively likely to be seronegative), most shelter cats will have long since been exposed by the time the recommended booster vaccine can be administered. Unlike the parvoviruses, vaccination will be an adjunct at best and will not be sufficient in itself to control outbreaks of FIP.

#### **What is an outbreak of FIP?**

The frequency of FIP in "coronavirus endemic" catteries, multiple cat homes, rescue or hoarder homes is reportedly about 5-10% most of the time<sup>1,2</sup>. "Outbreaks" of FIP in > 10% of cats occurred in 4/7 catteries followed over five years. However, these are all environments where cats are chronically housed in a high-risk multiple cat environment. In a research cattery following introduction of coronavirus the rate of FIP was only 0.8% of 1000 exposed cats<sup>3</sup>, and in a study of cats adopted from an open-intake shelter where cats were only in the environment relatively briefly, the rate of FIP was similarly low at less than 0.6%<sup>4</sup>. Therefore, rates higher than ~1% in a shelter are cause for concern.

Given that FIP itself is not generally transmitted cat-to-cat and coronavirus is so commonly present in multiple cat populations without causing apparent harm, what account for FIP outbreaks? Although the dynamics of outbreaks are poorly understood, several factors likely contribute:

- **Virulence of FCoVstrain:** While FIP itself is not usually directly transmitted, there are strains of coronavirus that are relatively likely to mutate to FIP. For the purposes of this discussion, I will call these "virulent coronaviruses".
- **Exposure to high doses and/or high replication in the intestine:** Cats receiving high doses, and/or undergoing high levels of replication are more likely to develop FIP. Higher rates of replication and consequent higher doses shed into the environment are likely to occur with stress, concurrent illness, and in kittens. One study found that coronavirus mutated readily in FIV infected cats and was shed in a more virulent form at high rates<sup>5</sup>. Dose effect will also obviously be increased by crowding and poor sanitation.
- **Exposure to chronic shedder(s):** Some cats are more likely than others to become chronic shedders of coronavirus. In one study, 11% of cats from multiple cat households shed coronavirus continuously over a period of up to 5 years<sup>6</sup>. Many chronic shedders will never develop FIP themselves, nor any other

- symptoms of infection. If one of these chronic shedders happens to be infected with a relatively virulent strain, this could lead to an increase in FIP cases in exposed cats.
- **Age at exposure:** Cats exposed at an early age are more likely to experience infections leading to high levels of replication, shedding, and relatively high risk of FIP.
  - **Length of exposure:** Although in one study cats were most likely to develop FIP subsequent to a first infection with FCoV7, chronicity of exposure may also play a role. In laboratory studies, a second exposure in previously infected cats led to greater likelihood of FIP (antibody dependent enhancement). Although antibody dependent enhancement has not been documented in the field, the risk of housing cats long term in a rescue home or shelter in which many cats enter carrying various strains of FCoV is unknown. There may be factors common to environments housing many cats long term that predispose to increased risk of FIP. In one study, cats that had been in a shelter for > 60 days were over 5 times as likely to be coronavirus positive as cats sheltered less than 5 days<sup>8</sup>. As noted above, higher prevalence of FIP has been documented in environments in which multiple cats are housed long term compared to more traditional shelters that house most cats for no more than a few weeks.
  - **Genetic risk:** Littermates of kittens that develop FIP are at higher risk than unrelated but equivalently-exposed kittens. This is in part because of shared genetic risk, and in part due to exposure to an identical, possibly relatively virulent strain of FIP at a relatively vulnerable time period (very early in life). Mothers of such litters may not be at an appreciably increased risk – although they may share some genetic risk factors, they may not have been exposed at such a vulnerable time. However, they may be shedding a strain of FeCV that mutated in at least one kitten to FIP.

### What are the practical implications for outbreak management?

The difficulties in diagnosing infection and predicting which cats will get ill; the lack of a reliable vaccine; the ease with which FCoV can be spread; and the poorly understood basis of FIP outbreaks combine to create unique challenges for control. Shelters and catteries must decide what to do in the face of an outbreak; whether to quarantine all exposed cats, depopulate, or continue business as usual. The same questions apply on an individual or household basis when a group of cats have suffered a known exposure to FIP. It is commonly agreed that cats remaining in a household from which a cat developed FIP, or those cats casually exposed to a cat with FIP (for instance, at a veterinary clinic) are not at appreciably increased risk of developing infection themselves. However, the risk of maintaining these cats in a shelter in which they are exposed to an ongoing parade of vulnerable new intakes is unknown. While the risk of introducing cats from such an environment into a home containing naïve cats is likely low, this also poses some problems as described below.

*Can all exposed cats be effectively and safely quarantined?* There is no way to predict which cats from a shelter having FIP problems are going to get FIP, although littermates of affected kittens are known to be higher risk. There is no realistic way to quarantine cats possibly exposed to a virulent coronavirus: if they are going to get FIP, it could happen any time in the subsequent couple of years. Even if they are not going to get FIP, they may continue cheerfully shedding coronavirus while under “quarantine” and beyond, which may place other cats (especially kittens) entering the facility in which the cats are quarantined at risk. Spread via fomites is so easily accomplished, it is unlikely that true quarantine can be achieved in a shelter facility, even if housed in a separate room from other cats (virus can be easily spread via clothing and shoes).

*Risk to adopter's pets:* Most likely, if cats from an outbreak-environment are adopted out to homes with resident cats, the other cats in the household will not get FIP as a result of this exposure. This is true even if the newly adopted cat happens to be shedding a relatively virulent strain of feline coronavirus or itself eventually succumbs to FIP: the resident pets are likely under less stress than newly admitted shelter cats, and therefore at lower risk from exposure, and development of FIP is even less likely if all cats in the adopter's household are over 2 years of age, and therefore in a lower risk period for development of FIP. In general, the risk of FIP is lower in households with less than five cats, as shedding of coronavirus is less likely to be chronically maintained. However, occasionally a cat in an adopter's home will happen to get FIP following adoption of a cat from a shelter having FIP problems. This may be due to transmission of coronavirus from the newly adopted cat and mutation of that virus to FIP in the resident cat; although uncommon this is possible. Or, it may be that the resident cat already harbored a coronavirus infection from a prior exposure, and the stress of adding a new pet to the household, by an unfortunate coincidence, triggered the manifestations of FIP. Regardless of the reason, this obviously puts the shelter in a difficult and painful position of wondering if a fatal disease was transmitted to an adopter's pet.

Keeping these difficulties in mind, there are three general strategies for responding to an outbreak of FIP in a cat population:

- **Clean up and carry on as usual:** Continue normal operations of intake and adoptions while addressing stress/crowding/sanitation/concurrent GI infections as effectively as possible. Obviously, there is never any harm in revisiting these issues in a shelter. While I often hear from shelters experiencing FIP outbreaks that don't believe they are doing any worse than usual in these areas, it is reasonable to think that if there is a

particularly virulent strain of coronavirus in the environment, there would be increased benefit to reducing the dose and reducing cat stress at the time of exposure. In most cases, it seems FIP outbreaks peter out on their own within a few months to a year even if no special measures are taken. It may be that the virulent strain of coronavirus loses the mutation that conferred its increased propensity to cause disease, as seems to happen with some hypervirulent caliciviruses. Or it may be that the chronic shedders happen to get adopted out, or it may be that the predominant strain of coronavirus circulating in the population gets replaced by a less virulent one. In the meantime, however, the “wait and see” approach has several risks to consider:

- Poor reputation for the shelter which may compromise future adoptions and community support if many adopted cats end up with FIP
- Heartbroken adopters (and foster care providers, if they are involved) if adopted cats develop FIP
- The small risk that an adopter’s resident cat will develop FIP as described above.
- **Depopulate and deep clean.** This is obviously the most definitive approach, though not necessarily the one I most often recommend. However, if euthanasia is going to be used to control an FIP outbreak, it is important to realize that limited depopulation – such as only kittens or only sickly cats – is unlikely to be effective. *Healthy appearing adult cats can chronically shed virus and pose a risk to newly introduced youngsters.* In shelters that have to euthanize some cats because intake numbers are higher than adoption numbers, depopulation is unlikely to impact overall euthanasia numbers for the year. However, the emotional and political impact of depopulation can nonetheless be substantial. Some of the risks of depopulation include:
  - Poor reputation for the shelter which may compromise future adoptions and community support if shelter is seen as heartless for depopulating apparently healthy cats.
  - Heartbroken staff and volunteers if cats to which everyone has become attached are euthanized.
  - Massive frustration if, by a horrible coincidence, FIP problems recur shortly after depopulation.
- **Make a break between populations:** This is a compromise between the above two approaches. I usually recommend trying to make a clean break between a “dirty population” that has been possibly exposed to a virulent coronavirus during an FIP outbreak and a “clean” incoming population. This would involve effectively segregating/removing all current residents and thoroughly cleaning the environment before admitting a new group of cats. However, this is hard to accomplish in many shelters– what are you going to do with all the current residents? Will you adopt them out to new homes from some other facility, in which case you run into the adoption dilemmas described above? Or will you euthanize them, in which case you run into the depopulation dilemmas? Will you hold them in sanctuary forever, or at least for a couple of years until you are reasonably sure they aren’t going to come down with FIP? A compromise is to at least separate kittens as well as possible from the resident longer term population. Although it is nearly impossible to prevent all transmission of coronavirus via fomites, you can reasonably hope to improve matters by at least decreasing the dose new incoming kittens are exposed to by creating very clear separations between populations, having staff handle with separate clothing (or separate staff), and routing visitors through such that they visit the new/clean cats first then the resident/exposed cats. This has the obvious disadvantage, though, of meaning the exposed cats are even less likely to get adopted – these risks will have to be balanced as best possible.

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