

## THE PET HEALTH LIBRARY

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### Feline Infectious Peritonitis (FIP)

Imagine a disease that is infectious yet not contagious, has 100% mortality, virtually no diagnostic test to confirm it, and no effective treatment. When feline infectious peritonitis (FIP) becomes a possibility for a pet cat, questions abound yet not nearly enough answers.

#### What is FIP?

Feline infectious peritonitis is a syndrome that results from widespread infiltration of the body's organs with a type of inflammatory tissue called pyogranuloma. The resulting global inflammation leads to the failure of the infiltrated organs, fevers unresponsive to antibiotics, and often an accumulation of thick yellow fluid in the belly or chest. The "wet" form of FIP includes the thick, yellow fluid as noted. The "dry" form is more insidious, leading to death over a much longer period (potentially years, but usually weeks to months.) Symptoms still involve fevers and poor appetite with the dry form, but also commonly involve deep inflammation in the eyes and nervous system. Both forms are felt to have 100% mortality.



*Photo by Karen James*

#### Is FIP Contagious?

Very simply, the answer is no.

#### How Can an Infectious Disease not be Contagious?

Feline infectious peritonitis is a reaction to infection with the feline enteric coronavirus. Most cats who become infected with the feline enteric coronavirus (often simply called feline coronavirus) essentially get the flu and never develop anything that can in any way be described as serious. Some cats, however, react with this devastating syndrome.

#### Transformation of Coronavirus into FIP Virus

The process of immunological defeat of the virus involves a cell called a macrophage. The macrophage consumes infected material, packaging it in structures that it floods with acids and digestive enzymes. Any virus is killed by this process, and its components are then used by the immune system to help mount a specific immunological reaction (i.e. make the proper antibodies, send specific killer cells etc.).

#### What do we Know about the Feline Enteric Coronavirus?

Some basics about this virus are:

- It is common wherever cats are housed in groups and it is readily transmitted between cats.
- Transmission is typically by contact with infected feces. This means that the litter box is the usual place where infection takes place. This infection is unusual in cats that free-roam outdoors (no litter box) or who live in homes where there is only one cat. The virus enters the new host's body through the nose and mouth. Coronavirus readily sticks to clothing and can be transported easily this way. Coronavirus also survives up to 2 weeks in cat litter dust.

- An active infection lasts several weeks to a few months. Virus is shed in the infected cat's stool during this period. If the cat is reinfected, virus sheds again for weeks to months. During this time, the cat may or may not seem at all ill. Some infected cats do not shed virus.
- Households with fewer than 5 cats eventually spontaneously clear of coronavirus. Households with more than 5 cats virtually never clear of coronavirus.
- Most household disinfectants readily kill coronavirus immediately. Room temperature kills coronavirus within 48 hours. Carpeting is protective to the virus and the virus is able to survive in carpeting for at least 7 weeks.
- Once a cat has been infected with the virus and recovered, the cat can be easily re-infected by continued exposure to infected feces. In this way, many catteries where there are always cats sharing litter boxes never rid themselves of this infection.
- The enteric coronavirus attacks intestinal cells and creates gastrointestinal (GI) upset. As long as the infection is confined to the GI tract, there will be no FIP.
- The process of immunological defeat of the virus involves a cell called a macrophage. The macrophage consumes infected material, packaging it in special structures that it floods with acids and digestive enzymes. Any virus is killed by this process and its components are then used by the immune system to help mount a specific immunological reaction (i.e., make the proper antibodies, send specific killer cells etc.) In some cats, a mutation occurs in the coronavirus. This mutation occurs during infection and allows the virus to survive the treatment by the macrophage. Instead of being killed by the macrophage, the virus essentially uses the macrophage to hitch a ride into the body's core. The macrophage response mounts in an attempt to kill the virus but ends up producing heaps of ineffective macrophages and immunologic proteins which make up a special immunologic tissue called a pyogranuloma. FIP is basically the infiltration of normal organs with pyogranulomas.
- The mutation to a form of virus that can cause FIP is more likely to occur in a cat with an immune-compromise. Most cats with FIP are under 1 year of age (their immaturity being their immune-compromise). Crowding is also an important source of immune-compromise.

### **Why isn't the Mutated Virus Contagious?**

We do not know why. We can inject fluids from a cat with FIP into a normal cat and cause FIP, but short of this kind of experimental transmission, the mutated virus doesn't seem to make it into the natural external secretions of an infected cat. This effectively confines the mutated virus inside the sick cat's body, though the sick cat will still shed non-mutated virus. It appears that genetics plays a large role in the mutation of the virus with every FIP cat developing its own unique mutation. A virus that causes FIP in one cat may not do so in another cat.

### **How is it Possible there is no Test for this Classical Disease?**

We used to think that the difference between getting the flu and getting FIP was all about the strain of the virus with which a cat gets infected. Lots of time and effort was spent trying to determine what made the "FIP virus" different from ordinary enteric coronavirus. We no longer think there is a special strain of virus that causes FIP. FIP results, as described above, from a mutation that occurs in the virus after infection has happened. Whether or not this mutation occurs seems to relate more to the cat's immune status than any factor in the virus. The more virus there is replicating, the greater the chance of mutation occurring. Having an immature or suppressed immune system means more virus replicating.

### **Why Can't we just Test for Mutated Virus?**

The mutation isn't the same every time. There are two viral genes and the mutation pretty much always involves at least one of them but the mutation can occur in any number of places within either of these two genes. There are currently too many possible mutations to develop a meaningful test.

### **What Kind of Testing is Available?**

At this time the diagnosis of FIP is clinical. This means that there is no positive or negative test; the doctor must look at the sum of several findings. These are some of the findings that are coupled with the physical examination and history findings to come up with a diagnosis of FIP.

We have already discussed the symptoms (fevers, eye inflammation, poor appetite, fluid accumulation). Most FIP patients are between ages 3 and 16 months. Most patients get the "wet" form and thus have an effusion of fluid in the belly; in fact, 50% of all belly fluid effusions in cats are caused by FIP. Tests can involve blood or a fluid sample from the chest or belly but it is important to realize that test results are just part of the total picture. There is no definitive test for FIP.

#### *Elevations in Total Protein, Alpha-2, and Gamma Globulins*

Total serum protein is a simple value that can be checked in virtually every animal hospital in a matter of minutes. Cats with FIP commonly have high serum protein levels. Now, there are many types of proteins in the blood. The type that elevates in FIP is basically antibody levels of assorted types. If a blood panel is checked on a cat with FIP, serum protein is often divided into albumin and globulin amounts (adding these together provides the "total protein" level.) When protein levels are broken down into these two groups, it will be the globulin level that is elevated. If the globulin level is further broken down, using a test called electrophoresis, it will be found that it is the gamma globulin and alpha-2 globulin levels that are elevated. The gamma globulins include antibodies and the FIP infection classically creates so much immune reaction that all antibody levels are elevated.

#### *The Albumin to Globulin Ratio*

FIP tends not only to elevate globulin levels but it also tends to decrease albumin levels. Albumin is an important carrier protein in the blood and one's body tends to conserve it at all costs. Albumin can be lost through **glomerular disease**, protein-losing enteropathy, or it can be under produced by a failing liver. All these conditions can occur with FIP. If the albumin to globulin level is less than 0.8, there is a 92% statistical chance that the cat has FIP. If the ratio is greater than 0.8, there is a 61% chance the cat does not have FIP.

#### *The FIP Titer*

This test is often included on a feline blood panel and reflects a cat's circulating antibody level against coronavirus. The problem is that exposure to coronavirus is common in cats and is not particularly meaningful in diagnosing FIP. Further, cats with fulminant FIP may not be producing FIP antibodies and have negative titers. The only time such a titer might be useful is if one is screening a healthy cat for coronavirus; in this event a negative titer would indicate that the cat will not be shedding virus and can be introduced into a coronavirus free living situation. Many breeders strive for coronavirus-free catteries and such screening is important. The test is not helpful in diagnosing FIP in a sick cat, however.

#### *Testing the Belly/Chest Fluids*

FIP classically produces a clear but viscous yellow effusion, usually in the belly but possibly in the chest or in both locations. The fluid typically has a total protein level greater than 3.5 mg/dl. Several efforts have been made to find a diagnostic test that could be performed on this fluid. So far we know that typically FIP fluid is high in lactate dehydrogenase, alpha-amylase, and alpha-1 glycoprotein. These proteins provide evidence of the inflammatory nature of the fluid and would be evidence pointing towards FIP (though any other inflammatory fluid would yield similar results).

#### *Rivalta's Test*

This is a test with which few veterinarians are familiar, but it can be helpful in the diagnosis of FIP. A test tube is filled with distilled water and one drop of 98% acetic acid is added. To this mixture one drop of effusion is added. If the drop dissipates, 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.

#### *PCR Testing*

PCR testing is an extremely sensitive method for detecting DNA, in this case coronavirus DNA. The advantage it has over traditional antibody titers is that it distinguishes active virus infection from past

exposure. At least at this time, PCR testing cannot distinguish mutated FIP-causing virus from regular coronavirus.

There is a new test currently only performed at Auburn University that uses PCR technology to detect messenger RNA (produced by patient cells infected with coronavirus DNA) in the patient's blood. The theory is that the benign coronavirus cannot replicate in blood cells (only in intestinal cells) so if there is viral messenger RNA in the bloodstream, it must be from the mutated virus. The supposition that benign coronavirus messenger RNA cannot be found in the bloodstream has been challenged, however. While this may come down to a matter of how much messenger RNA can be detected in which situations, this test is very new and is still controversial.

#### *Immunofluorescent Coronavirus Staining of the Effusion*

In this test the effusive fluid is tested immunologically for presence of coronavirus using antibodies tagged with fluorescent dyes. In a study using a large number of cats, there were no false positives meaning that if this test is positive there is a 100% confirmation that the cat has FIP. Unfortunately, if the test is negative that does not mean the cat does not have FIP (only 57% of negatives did not have FIP).

#### *Tissue Biopsy*

Most FIP cats are too sick for surgery, though sometimes flushing away the belly effusion surgically provides a temporary "rally" of improvement. A tissue sample is the best method for confirming FIP as there are few conditions that create pyogranulomas throughout the body, but if regular biopsy is equivocal, tissues can be stained for the presence of coronavirus and only in FIP will there be enough coronavirus within macrophages for positive staining. A positive tissue stain is 100% accurate in confirming FIP.

### **Is there Really no Effective Treatment?**

There really is no effective treatment for FIP and it has virtually 100% mortality (death). The goal of confirming FIP (as best as can be done) is to rule out other diseases that might be treatable. Currently the best we can offer with treatment is the possibility of temporary palliation of signs. It is important to realize that since this is a progressive disease one should become familiar with criteria for euthanasia and emotionally prepare for this decision.

### **Isn't there at Least Experimental Treatment?**

There is virtually always experimental treatment. Here are some treatments that are being explored or which have been explored:

#### *Immune suppression*

FIP is a disease created by the cat's own immune system. Immunosuppressive drugs such as [cyclophosphamide](#) have been used to slow the progression of FIP.

#### *Removing the effusion*

Suctioning of the effusion will ease the difficult breathing of a cat with fluid in its chest, but even removing the effusion from the belly helps remove a large source of inflammation. Some cats experience a temporary improvement with the fluid removed.

#### *Antiviral Drugs*

Ribavarin was tested and not found to be helpful. Some types of interferon have been studied but no benefit has been definitive.

### **When a Cat Dies of FIP, What is the Infection Risk to the Remaining Cat?**

You can bet that the roommate has already been infected with the coronavirus. If there are only one or two surviving cats, the chances are that in time the virus will completely clear and they will stop getting reinfected. Surviving cats are felt not to have any higher risk over the general population for

developing FIP from their coronavirus, though a littermate of the FIP cat might have a slightly higher incidence due to predisposing genetic factors.

### **When is it Safe to get Another Cat after one Dies of FIP?**

Since this is not a contagious disease, you do not need to wait before getting another cat. If you want to see that there is no remaining coronavirus around the house leftover from the deceased cat, a 3-month period has been advocated; however, since coronavirus is common (in one study 90% of shelter kittens were infected and shedding virus), it is not easy to ensure that the new cat will not be carrying virus already. The short answer is, as long as there are fewer than five cats in the home, FIP is not likely to continue to be of concern.

### **Isn't there a Vaccination?**

Developing a vaccination has historically been fraught with difficulty simply because it is the immune response against the virus that causes the disease. How does one make a vaccine without creating the same immune response against the virus? Pfizer has developed the only FIP vaccine on the market by using a temperature-sensitive mutant coronavirus. This virus is inoculated into the cat's nose. The virus is incapable of spreading beyond the nose and throat because it cannot survive at body temperature. In the nose and throat, however, it generates a localized immune response that prevents a coronavirus from effectively entering the body. The effectiveness of this vaccine has been questionable and remains controversial. The vaccine is given to cats over 4 months of age and is thus not helpful in the chief situation where a vaccine could do the most good: the breeding cattery. Most veterinary teaching hospitals do not stock this vaccine because most cats are not at risk for FIP infection and those that are at risk are at risk at an age too young for the vaccine. The ideal candidate for vaccination would be an uninfected cat going to a cattery where litter box sharing is likely. This would seem to be an unusual situation but it might come up in these circumstances:

- A feral cat is moved into an indoor or shelter colony. (It is not unusual for FIV+ cats from feral colonies to be removed from the colony and put in a sanctuary for FIV+ cats).
- A cat from a single cat home is released to a rescue group goes to a foster home where there are already a number of other cats.
- A cat moves from a single cat home to live in a multi-cat home.

Vaccination was able to reduce the infection rate in exposed cats but not all cats will be protected.

### **Is Infection Limited to Cats?**

Yes. Dogs and humans cannot get sick from feline coronavirus. The feline coronavirus is not involved in SARS (severe acute respiratory syndrome) although SARS is caused by a coronavirus.

*The information in this summary was largely drawn from the following article:*

K. Hartmann. Feline Infectious Peritonitis. Veterinary Clinics of North America Jan 2005; 39-79.

### **For General Information**

*A Good Starting Point*

<http://www.newmanveterinary.com/fip.html>

*For a Really Good FAQ:*

<http://web.vet.cornell.edu/public/fhc/fip.html>

**The FULL TECHNICAL DETAILS**  
**(Dr. Alice Wolf's famous article)**  
*Feline Infectious Peritonitis*

FIP is a serious disease with near 100% mortality, no good test, no good treatment, and no good vaccine. If your cat is an FIP suspect, we know how painful the lack of knowing can be. We hope this information can provide facts and understanding during this difficult time.

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