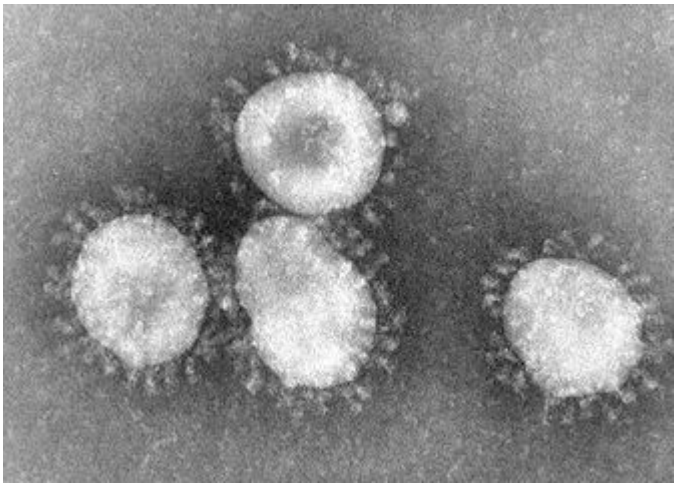
Feline Infectious Peritonitis – What the FIP?!

There are many infectious organisms that cause illness in
our feline friends. One of the most noteworthy diseases in feline infectious peritonitis.
This week's post is dedicated to sharing important information about the debilitating and deadly condition to raise awareness. I hope you find the information helpful. Happy reading!

What is feline infectious peritonitis?

Feline infectious peritonitis – more commonly referred to as FIP – is caused by a virus called feline coronavirus (FCoV or FCV). The most common form of disease is feline enteric coronavirus. It's readily transmitted between cats through contact with infected feces. Watch the video below to learn more about how cats are infected with feline coronavirus.

Inside the body, the FCoV enters a type of white blood cell called monocytes. Once monocytes are invaded by FCoV, there are two potential outcomes – either monocytes kill the virus, or they become infected. The latter happens for reasons not yet completely understood.



Microscopic appearance of feline coronavirus. Image courtesy of Stylisticat.

In 5-10% of cats, either the virus mutates and/or a cat's immune system responds aberrantly to cause progression to clinical FIP. At this point, the virus is now referred to a feline infectious peritonitis virus or FIPV. Factors that increase the chance of coronavirus mutation include:

- Genetics
- Early weaning
- Overcrowding
- Age at the time of coronavirus infection
- Surgery stress
- Sharing litter box with other cats

When the FCoV virus hijacks the immune system to become FIPV, the result is an intense inflammatory response. Infected monocytes secrete chemicals that induce changes to cells lining blood vessels (called endothelial cells). One of these changes is to make endothelial cells stickier. Sticky endothelial cells capture circulating infected monocytes, causing them to roll along the endothelial cell surface and eventually stop. The monocytes continue to secrete chemicals that causes the junctions between endothelial cells to breakdown, allowing monocytes to enter the surrounding tissue. In this location, infected monocytes become macrophages. Macrophages continue to secrete chemicals that attract more inflammatory cells, including monocytes, neutrophils, and lymphocytes. These

cells, too, enter tissues to form structures called pyogranulomas, the hallmark feature of FIP. Check out the video below for more information about the process.

Wet vs. dry form…

Feline infectious peritonitis has both acute and chronic forms. The former is characterized by intense inflammation that causes extensive damage to endothelial cells throughout the body. The damage is associated fluid flooding into body cavities. This form of FIP is called the wet or effusive form. When damage happens in abdominal organs, fluid accumulates in the abdominal cavity. Affected cats develop a pot-bellied appearance. When this process occurs in the chest cavity, fluid accumulates in the space between the lungs and body wall – this is called pleural effusion. Cats with pleural effusion often take short and shallow breaths, and they can develop life-threatening respiratory distress.

A cat with fluid accumulation in the abdominal cavity due to the wet or effusive form of FIP. Note the pot-bellied appearance. Photo courtesy of Steve Dale.

The chronic form of FIP is not associated with fluid accumulation in body cavities and so is called dry or non-effusive FIP. The clinical signs noted in affected cats are quite variable, and may include:

- Weight loss
- Reduced (or loss of) appetite

- Dull hair coat
- Fever
- Icterus / jaundice
- Eye changes – including iris color changes,
  white precipitates in the cornea, inflammation in the anterior chamber (called
  uveitis), changes to blood vessels in the retina
- Lethargy
- Enlarged kidneys
- Neurologic deficits – including ataxia
  (unsteadiness while walking), tremors, abnormal eye movements

How is it diagnosed?

There is no age, sex, or breed predisposition for developing
FIP. However, more than 50% of infected cats are less than two years of age. A common component to an infected cat's medical history is a history of stress within
several weeks of developing clinical signs. To date, there is no simple diagnostic test for FIP. The only way to definitively diagnose FIP is via biopsy or
examination of tissues during a necropsy (the animal equivalent of an autopsy). Given this situation, veterinarians must use clinical signs as mentioned above,
as well as data from a variety of tests, to make a clinical diagnosis of FIP.
These tests include:

Analysis of Effusions – Effusions associated with FIP are clear to cloudy and have a viscous consistency similar to egg-white. The protein level in the fluid is high, and there is a meaningful cellular component, particularly macrophages, neutrophils, and to a lesser extent, lymphocytes. Unfortunately, these characteristics are not definitively diagnostic for FIP.

Abdominal Sonography – This non-invasive test may show changes to the liver, spleen, kidneys, and/or enlarged intra-abdominal lymph nodes. Of course, patients with the effusive or wet form of FIP have abdominal effusion. None of these findings are specific for FIP but raise suspicion when considered along with considerate clinical signs.

Albumin:Globulin Ratios – When the prevalence of FIP is low, a high albumin:globulin ratio (A:G ratio) is useful to rule out FIP. However, a low A:G ratio is not helpful in making a diagnosis of FIP.

Serum Protein Electrophoresis – Many cats with FIP have elevated total protein and/or globulin levels. Serum protein electrophoresis (SPE) provides more information about globulins, and many cats with inflammatory and/or infectious conditions have changes to gamma globulins. Cats with FIP can have both polyclonal (think foothills of a mountain) and monoclonal (think one single mountain peak) elevations, so this test can't be used to definitively diagnose FIP.

Feline Coronavirus Antibody Titers – These tests detect the presence of coronavirus antibodies. Antibodies are unique proteins the body makes when they've been exposed to foreign material, including infectious agents like feline coronaviruses. Available antibody tests are enzyme-linked immunosorbent assay (ELISA), immunofluorescent antibody (IFA), and virus-neutralization tests. A positive result means a cat has been exposed to any feline coronaviruses, but not necessarily to one that causes FIP. In addition, cats vaccinated with some types of modified live virus vaccines can develop antibodies against bovine serum components used in vaccine virus cultures. These antibodies can cross react in some test systems producing a false-positive test result. Cats vaccinated with the Felocell FIP vaccine can develop antibodies that react positively with this test. Test methodologies differ from laboratory to laboratory; this means feline coronavirus antibody titers from different laboratories can't be accurately compared.

One antibody test called the 7B protein ELISA (Antech Laboratories)
detects the 7B protein. The makers of this test claim the 7B protein is only produced
by FIP-producing feline coronaviruses. Unfortunately, further studies showed
not all FIP-producing strains of feline coronavirus produce the 7B protein; furthermore,
some non-FIP coronaviruses do produce 7B, so this test is not specific for
FIP-producing coronaviruses.

Alpha-1-Acid Glycoprotein (AGP) – This protein is hyposialyted in some cats with FIP but not in normal cats or cats with other diseases

Rivalta Test – A few drops of effusion are mixed with a weak acetic acid solution; the appearance of a white flocculent material is a positive test

Polymerase Chain Reaction (PCR) – Real time polymerase chain reaction (RT-PCR) detects viral genetic material in tissue or body fluid. The PCR test detects messenger ribonucleic acid (mRNA) of the M gene of *all* know feline coronavirus strains. Only detection of mRNA outside of the intestinal tract is supportive of FIP because active viral replication occurs in circulating monocytes.

Immunostaining Methods – Immunostaining of infected tissues (called immunohistochemistry or IHC) or effusions by immunofluorescence or immunoperoxidase methods can be helpful. Immunohistochemistry is considered accurate for a definitive diagnosis of FIP, but false-negatives are possible depending on the quality of tissues tested and reagents used in the test.

Understandably, making a clinical diagnosis of FIP is challenging. Pet owners may find it helpful to partner with a board-certified veterinary internal medicine specialist to help them develop a logical and cost-effective diagnostic plan.

How is it treated?

Feline infectious peritonitis is ultimately a fatal disease
at this time. There is no known cure or effective long-term treatment to date. Traditionally,
therapy has been considered palliative with a goal of suppressing the immune-complex
component of the disease. One of the most common treatments is a combination of
prednisolone and cyclophosphamide. Other potential therapies are:

Anti-Viral Drugs – Several drugs, including cyclosporine, itraconazole, various antibiotics, and several herbal extracts, inhibit FIP virus in cell-culture. Unfortunately, the amount of drug required to achieve the needed level of virus inhibition is toxic and damaging to cells and thus to infected cats. The antiviral drug called adenine arabinoside (Vidarabine®) also appears to be effective against FIPV.

Non-Specific Immunostimulants – These types of immunostimulants include

substances such as Staphylococcal A protein, ImmunoRegulin (Propriobacterium acnes), Acemannan (mucopolysaccharide extract of aloe vera leaves) and Imulan (lymphocyte T-cell immunomodulator). There is no evidence that these biologics have any beneficial effect on actual cases of FIP.

A newer product – polyprenyl immunostimulant – improves the number of helper T lymphocytes, thus enhancing a patient's immune response against the coronavirus. This medication is labeled for feline herpes virus infection but has also shown success in treating the non-effusive form of FIP.

Specific Immunostimulants – Recombinant DNA human alpha and beta interferons, as well as feline interferon omega (Virbagen Omega®), have significant antiviral effects against FIPV. The latter is not approved by the US Food and Drug Administration (FDA), but small quantities (less than three months use) may be imported based on the Regulatory Procedures Manual, section 9-2. Although an initial study with feline interferon omega showed efficacy, a large double-blinded and placebo-controlled drug trial did not confirm efficacy.

Researchers at the Kansas State University College of Veterinary Medicine and the University of California – Davis School of Veterinary Medicine and investigated two novel drugs – GC376 and GS-441524. Based on initial clinical findings, a company called Anivive purchased the rights for GC376, and they're pursuing FDA approval in the United States. The second drug – GS-441524 – also showed promise in the treatment of FIP. The treatment period for naturally occurring FIP is a minimum of 12 weeks. If you're interested in learning about preliminary clinical results for treatment with GS-441524, click here.

To date, neither GC376 nor GS-44154 is legally available in the United States. As such, there's a growing black market for these drugs given their initial impressive clinical results. Both are being illegally produced in China, and there is an active Facebook community called FIP Warriors wherein members discuss all things GS-441524, including helping owners of FIP cats obtain this drug. One should note veterinarians don't know the purity or biological activity of black-market compounds.

How can I prevent FIP?

Minimizing exposure to infectious agents decreases the likelihood of cats developing FIP in multi-cat environments. Litter boxes should be cleaned regularly, and they should be located away from food and water dishes. Newly acquired cats (and any cats suspected of being infected) should be separated from other cats. Overcrowding should be minimized, and cats should be fed a well-balanced diet.

There is one approved vaccine available against FIP – Felocell FIP made Zoetis (previously known as Primucell FIP). It's a temperature-sensitive, modified-live virus designed to grow only at the cooler temperatures of the upper respiratory tract. The vaccine virus will not replicate at core body temperatures, so it's effective only if exposure is via the mucous membranes of the nose and mouth. The vaccine is administered in the nose, and protection is apparently mediated by secretory immunoglobulin A (IgA) produced at the level of the upper respiratory tract and oral mucous membranes combined with an enhanced cell-mediated immune response. The efficacy in preventing FIP has not been established, and the vaccine is not recommended by the World Small Animal Veterinary Association Vaccine Guidelines Group. Cat owners should consult their veterinarian to help them decide if their cat should be vaccinated.

The take-away message about feline infectious peritonitis?

Feline infectious peritonitis or FIP is a deadly infectious disease caused by specific strains of feline coronavirus. When white blood cells called monocytes become infected with an FIP-producing strain, the result is an intense inflammatory reaction. To date, there is no known effective long-term treatment, but some novel drugs have shown exciting promise.

To find a board-certified veterinary internal medicine specialist, please visit the American College of Veterinary Internal Medicine.

Wishing you wet-nosed kisses,

CriticalCareDVM