

## FIP treatments: What might work, what doesn't work

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### Prevention of Feline Infectious Peritonitis (FIP)

Prevention is always better than treatment and many attempts have been made to prevent infection. It is generally accepted that Feline Infectious Peritonitis (FIP) virus is a pathogenic mutation of the weakly pathogenic feline enteric corona (FECV) virus that replicates in the intestinal epithelium. The two FCoV (biotypes) are not distinguishable except by their biological behavior. The enteric coronavirus spreads cat to cat by the fecal oral route and is highly contagious. Once established in the intestinal tract the virus may mutate into the pathogenic FIPV and establish itself in macrophages and disseminate throughout the body. The key to prevention of FIP is to avoid infection with the enteric corona virus.

Dr. Diane Addie developed a procedure for isolation of pregnant queens and early weaning before kittens are infected. Virus free kittens must be isolated until adoption into coronavirus free households. Dr. Addie has been successful in some catteries producing corona virus free kittens but the highly contagious nature of the enteric corona virus makes it difficult in shelters and households with many cats to effectively isolate kittens. Some kittens can be infected with coronavirus as early as 3 weeks of age before weaning can be considered.

Primucell is a modified live, heat sensitive corona virus vaccine given intra-nasally that has some protective effect against FIP. It is not effective in kittens that are already infected with enteric corona virus and is not recommended before 16 weeks of age. In households where enteric corona virus is endemic, kittens are infected before 16 weeks of age negating the benefit of vaccination.

Limiting the number of cats in a household greatly reduces the likelihood of developing FIP. In households of 5 or more cats, a cycle of infection, shedding of virus, clearing of the virus and re-infection maintains a household that has one or more cats shedding virus at all times. Careful husbandry helps but rarely can eliminate the virus in multi-cat households. Adoption of antibody tested, uninfected kittens from single cat households helps reduce the likelihood of introducing corona virus into the house.

Stress and immunosuppression appear to be a trigger in the development of FIP. Introducing a new cat into a household of cats is very stressful. Surgical procedures such as neutering is associated with the development of clinical signs of FIP. Exposure of kittens to a variety of other viruses in shelter situations is stressful. The immunosuppression from concurrent infections with feline leukemia virus greatly increases the likely of development of FIP.

### Polyprenyl Immunostimulant

Polyprenyl Immunostimulant was provisionally licensed by the USDA in October 2012 as an adjunct to the treatment of rhinotracheitis (respiratory herpes virus infection) and has been investigated as a treatment for dry form FIP. The current compound was developed by Sass and Sass at their facilities at Oak Ridge, TN. Polyprenyl is an agonist of Toll-like receptors 2 and 4 that promote a Th-1 immune response to enhance cell mediated immunity which is required for elimination of viral infections. A blinded challenge study was done in 6-8 week old kittens challenged with virulent herpes virus. For the herpes virus infections polyprenyl was dosed orally at **0.5 mg/kg twice daily** for 15 days. The polyprenyl immunostimulant reduced the severity and duration of respiratory herpes virus infection. The difference between the treated and placebo group of kittens was significant at the  $p=0.06$  level. A safety study of 390 cats in 10 states was done and no significant toxicity was noted. Mice given a 100X the therapeutic dose had no toxicity. A number of cats with various conditions were treated initially to identify the therapeutic potential of the polyprenyl immunostimulants.

### Pathophysiology of FIP

When monocyte/macrophages become infected with the mutated, pathogenic form of coronavirus, they distribute the virus throughout the body. Some of the virus infected macrophages encircle the vasculature of organs such as liver and kidneys as well as the vessels in the mesentery. The infected macrophages secrete a variety of cytokines to attract inflammatory cells such as neutrophils to the area to produce necrosis and the granulomatous lesions characteristic of FIP. Recent studies have shown increased levels of vascular endothelial growth factor (VEGF) in cats with FIP. VEGF promotes vascular leakage and fluid accumulation. Successful treatment of FIP will require the elimination of the infected macrophages that orchestrate the inflammatory response.

## Summary of Presentation at AAHA Meeting, Phoenix, AZ, March 14-17, 2013

### **Polyprenyl Immunostimulant and dry form FIP**

Treatment of FIP was attempted with Polyprenyl Immunostimulant and subjective improvement in survival times were noted in some cats with the dry form of FIP. These preliminary findings were published in the Journal of Feline Medicine and Surgery in 2009. No benefit was noted with the effusive form of the disease but a limited number of cats were treated. A grant to further study the potential of Polyprenyl Immunostimulant in dry form FIP was awarded by the Winn Feline Foundation.

### **Inclusion Criteria**

Because of the difficulties in making a diagnosis of dry form FIP, inclusion criteria were well defined. The cats had to have clinical signs and histories compatible with dry form FIP and adequate laboratory studies such as CBC and chemistry panels to identify other disease conditions that might mimic FIP. Increased globulin concentrations with decreased albumin concentrations and low A/G ratios were required. High antibody titers to feline corona virus were strongly supportive. Histopathology or cytology of needle aspirates that identified pyogranulomatous reactions without evidence of fungal infection were considered definitive for dry form FIP. Probable FIP has the same criteria except for identification of the granulomatous lesions. The history and diagnostic findings were reviewed by one clinician to include the cat in the study.

### **Treatment group**

The intent of the study was to identify 40 cats with dry form FIP nationally working with local veterinarians in the hope of having 20 that could be studied. First contact for many of the cats included in the study was made by the owners after searching the internet for FIP treatments. A total of 102 were admitted to the study. When cats that died before the polyprenyl was received and cats that died before being treated for a week were eliminated, there were 58 cats available for long term study. About half the cats were non-pedigree cats. Abdominal involvement was noted in 47% of the cats, 24% had ocular form, 21% had the neurologic form and 9% had various other forms of FIP. Over half the cats in the study were less than 2 years of age. All cats were treated with **3.0 mg/kg orally of Polyprenyl Immunostimulant three times a week**. All cats entered into the study were followed for at least a year.

### **Findings**

Twenty-two percent of the cats lived 6 month or longer and 5% were alive at a year. Cats that responded to treatment had improvement in appetite and general well being within 2 to 3 weeks. They became more interactive with the family and resumed their prior play activities. There was not a control placebo group to this study because FIP is considered a consistently fatal disease. Further information can be obtained about Polyprenyl Immunostimulant from [info@sassandsass.com](mailto:info@sassandsass.com)

### **Other treatments for FIP**

Standard of care has always been steroids to decrease the inflammatory reaction that occurs abd to stimulate appetite. Steroids certainly improve the well being of the cats temporarily but do not produce long term survival. Feline origin interferon omega has been used, but a study done by Ritz et al. did not see an improvement in survival times compared to a placebo treatment. Pentoxifyline has been used to treat the vasculitis seen in FIP but has not been shown to be effective.

### **Future treatments**

The emergence of Severe Acute Respiratory Syndrome (SARS) in people has occurred recently. SARS is a life threatening disease caused by a corona virus. This has fostered an increase in research on anti-viral drugs for corona viruses. These new drugs may provide a direct treatment for feline infectious peritonitis virus and be the key to successful treatment. Extensive toxicology testing will be needed before cats are treated.

### **References**

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