

## Feline Infectious Peritonitis (FIP): diagnostics and therapeutics

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### Abstract

Feline Infectious Peritonitis is a lethal viral disease produced by a mutant feline enteric corona virus that presents an array of complicated clinical symptoms. There are two recognized forms of this disease – wet form and dry form. The article presents an overview of the incidence, pathogenesis, clinical signs, diagnosis and treatment of this disease.

**Key words:** Cat, Corona, Fever, Vaccine, Virus

### Introduction

Feline infectious peritonitis (FIP) is a highly fatal viral disease caused by mutant feline enteric corona virus which causes a series of complex clinical signs<sup>1</sup>. FCoV belongs to the family Coronaviridae, a group of enveloped positive-stranded RNA viruses that are frequently found in cats<sup>2</sup>. As it is a corona virus it has been found to be a highly unpredictable virus with several mutations and recombination's shifting the virulence accordingly.

One of the two recognized forms of the disease is brought on by variations in feline immunological responses. In nearly 75% of cases, the 'wet' type of FIP is produced by immune complex deposition in vessel walls and effusions into body cavities, which trigger complement-mediated vasculitis. The 'dry' form of FIP, on the other hand, is brought on by patients who have dominant cell-mediated immune responses that result in pyogranulomatous lesions in different organs<sup>3</sup>.

### Incidence

- It has been observed in cats of all ages but has been found to be highly pathogenic and fatal in younger animals.
- Found commonly in shelters and multi-cat households. Approximately 25% of cats in single-cat households and 75%–90% in multicat households have antibodies to (and are serologically positive for) FCoV<sup>4</sup>.

- It has been suggested that FIP mortality may be higher in densely populated environments but much lower in households with 1–2 cats<sup>4</sup>.
- A polygenic mode of inheritance has been suggested, and heritability is reportedly >50% in some pedigree catteries<sup>5</sup>.
- There appears to be a breed predilection in Bengals, Abyssinians, Himalayans, Birman, Rexes, and Ragdolls.
- Intact males were found to be more prone to obtain the disease as compared to spayed females<sup>5</sup>.
- FIP essentially has two serotypes, however serotype I which has the typical spike protein has been found to be highly prevalent in field conditions as compared to serotype II which has a canine corona virus protein<sup>6</sup>.

### Pathogenesis

- The virus enters enterocytes using a spike (S) protein gene on the viral surface. Usually, FECV causes self-limiting gastroenteritis.
- In certain cases, the S protein gene mutates—the viral 3c gene may also be truncated changing the tropism to shift from enterocytes to macrophages/monocytes; this mutated virus is referred to as FIP virus (FIPV). The mutated virus replicates within immune cells and is no longer transmissible through the fecal–oral route.
- In certain cats and vaccinated cats, a strong cell-mediated immune response can control infection, resulting in viral clearance without clinical disease.
- If a humoral response predominates, antibodies are ineffective at controlling infection and this leads to formation of immune complex, resulting in vasculitis and effusion (ie, wet FIP). In the case of a partial cell-mediated immune response, immune cells are recruited to the site of replication, leading to granuloma formation (ie, dry FIP). The distinction of wet versus dry FIP depends on the ratio of cell-mediated (Th1) and humoral (Th2) responses
- The immune complex is formed by formation of complex and accumulation in the form of granulomatous lesion.
- The virus induces a highly fatal immunopathological disease characterized by severe systemic inflammatory damage of vessels and disseminated pyogranulomatous lesions<sup>7-8</sup>
- Individual response to viral infection, genetic predisposition, and environmental are closely linked with the progress of the disease<sup>9</sup>.

### Clinical signs

- The most common non-specific signs are fever, lethargy, vomiting, icterus, anorexia and significant weight loss. This disease can affect every organ system of the body.
- Signs of abdominal lymphadenopathy, retinopathy, thickened intestinal walls, renomegaly, keratic precipitates have also been observed



- The two distinct manifestations of the disease are Dry (Non-effusive) and Wet (Effusive) Type.
- The dry type especially is incredibly difficult to diagnose.
- The dry type is caused due to granulomatous immune complex formation and may manifest itself according to the location in forms of
  - ✓ Uveitis<sup>10</sup>
  - ✓ Organ dysfunction
  - ✓ Neurological signs
  - ✓ Pyrexia
  - ✓ Lethargy
  - ✓ This has been observed more in geriatric cats
- The wet/effusive type is by immune complex formation causing vasculitis and significant tissue damage.
  - ✓ **Ascites** is the most common sign of the effusive form
  - ✓ Pericardial and Thoracic effusions are also common
  - ✓ **Pleural effusions** lead to significant dyspnea
 Uncommon clinical signs have also been observed such as
  - ✓ Synovitis
  - ✓ Scrotal enlargement
  - ✓ Skin fragility
  - ✓ Cutaneous nodular lesions

### Laboratory findings

- Mild to moderate anemia (ie, hematocrit, 20%-30%)
- RBC microcytosis, band neutrophilia, and lymphopenia are common
- Significant elevation of globulin levels (ie, >7 mg/dL)
- Albumin is typically normal to low (ie, 2 mg/dL or less)
- Elevated alanine aminotransferase (AST) and alkaline phosphatase (ALKP) levels
- Macrophages, neutrophils, and lymphocytes on cytology; low-to-moderate cellularity (<5000 cells/ $\mu$ L)
- Hyperbilirubinemia (as a result of hemolysis) and hyperglobulinemia are also often observed. The albumin: globulin ratio is classically <0.4
- Lymphopenia and hyperbilirubinemia are more prevalent in wet FIP
- Cerebrospinal fluid cytology
  - ✓ Protein >200 mg/dL
  - ✓ WBC >100 cells/ $\mu$ L (mostly neutrophils, lymphocytes, macrophages)

### Diagnosis

- History and clinical signs
- Laboratory findings
- Biopsy, Cellular cytology
- **Imaging**
  - ✓ **Radiography** – Effusions non-specific lesions are observed. In case of pulmonary involvement, patchy regions of opacity is observed<sup>11</sup>
  - ✓ **Ultrasonography**
  - ✓ **MRI & CT** – non-specific inflammatory lesions in the CNS
- **Reverse transcriptase PCR** – detects presence of corona virus. Can be done on serum, effusion, faeces.



- **Histopathology** – It is the gold standard test to detect FIP. Perivascular granulomatous to pyogranulomatous inflammation and vasculitis is considered to be typical of cats affected with FIP.
- **Immunostaining** (Immunofluorescence/Immunohistochemistry)

## Treatment

The treatment primarily is to alleviate the severity of the symptoms and comprises of supportive care and management

- **Corticosteroids and non-steroidal anti-inflammatory agents** aid in reducing the inflammation and prevention of further formation of immune complex.
- **Chlorambucil or cyclophosphamide:** used in combination with corticosteroids
- **Antiviral therapy** with Galanthus nivalis agglutinin (GNA), a carbohydrate binding agent, or nelfinavir, a protease inhibitor, used alone has been reported being able to partially inhibit feline coronavirus replication in vitro.<sup>12,13</sup>
- **Cyclosporin A**, a cyclophilin inhibitor, which interrupts the interaction between immunophilins and coronavirus nonstructural protein 1 (Nsp1) resulting in blocking the replication of coronavirus of all genera<sup>14</sup> and has been used as an immunosuppressive agent to treat cats affected with FIP including human, feline and avian species.
- Chloroquine, which is a number of amino quinolones, has been used to treat malaria. It has been shown being able to inhibit FIPV replication in vitro via reducing endosomal acidification during viral entry and its anti-inflammatory properties<sup>15</sup>. However, it must be used with caution as it has been observed to increase the aminotransferase activities indicating possible toxic effects of the drug.
- **Pentoxifylline:** may help reduce vasculitis
- **Thromboxane synthetase inhibitor (ozagrel hydrochloride):** inhibits platelet aggregation. However, this is available only in certain regions for research purposes.
- **Aggressive fluid therapy**
- **Removal of effusions** has found to be a source of relief for the cats.
- **Broad spectrum antibiotics** are suggested if there is presence of secondary bacterial infection.
- **The use of immunomodulatory therapy**—including immunostimulants, type 1 interferons (IFNs; eg, human IFN $\alpha$ , feline IFN $\omega$ ) has been proposed<sup>16</sup>. Polyprenyl immunostimulant (PI)<sup>68</sup> is the latest plant extract claimed to prolong the lives of some cats with mild forms of dry FIP but had no effect on cats with severe disease, such as cats with effusive form of FIP.



## Conclusion

Feline infectious peritonitis is an extremely fatal infection caused by the rapidly mutating Feline enteric corona virus. It has been observed to affect cats of all ages and the mortality has been found to be higher in multi-cat households. The gold standard technique remains as histopathology; however, several techniques have developed over time for quick detection of the disease. There is no specific treatment to cure the disease as of now, and treatment primarily focuses on supportive and managemental methods to alleviate the symptoms and increase the quality of the life of the animal. This is done with the help of anti-inflammatory agents, corticosteroids and immunostimulants. Euthanasia must be considered in cases with no improvement. Researches in understanding the genomic and biological differences between FECV and FIPV, more investigations in discovering novel antiviral, anti-inflammatory agents and diagnostic techniques are urgently required to better understand how to deal, diagnose and treat cases of this disease.

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