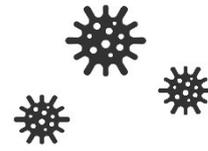


Cat Owner Information Guide





What Is FIP Disease?



Coronaviruses (CoVs) are common and important pathogens that threaten both human and animal health. In humans, diseases caused by coronaviruses include Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and most recently SARS-CoV-2 (COVID-19), which led to a global pandemic.

Coronaviruses affect all groups of living organisms, ranging from fish and reptiles to birds and mammals. Feline Infectious Peritonitis (FIP) is a fatal disease in domestic and wild cats caused by feline coronaviruses (FCoVs). Feline coronaviruses (FCoVs) are known to have two biotypes: the lethal Feline Infectious Peritonitis Virus (FIPV) and the Feline Enteric Coronavirus (FECV), which is localized in the intestinal tract.

FCoV is present in approximately 90% of cat populations, and FIP develops in infected carrier cats due to various factors. It is thought that there are two possible pathways for the development of FIP. The first suggests that highly virulent strains of the feline enteric coronavirus (FECV), meaning strains with a high capacity to cause disease, lead directly to FIP. The second pathway proposes that in cats infected with feline enteric coronavirus (FECV), the virus undergoes spontaneous mutation, and as a result of this mutation, transforms into a lethal virus (FIPV) that gains the ability to replicate continuously within immune cells known as macrophages. Currently, the second pathway is considered more likely, and genetic studies on this mechanism are ongoing.

FIP disease develops in wet or dry forms depending on the immune response of the body against FIPV.

In some cases, both forms may be observed simultaneously depending on the immune status.

- Wet FIP: characterized by clinical signs (symptoms) in the form of fluid accumulation in the abdomen or chest cavity (lungs, pleural space, or pericardial space).
- Dry FIP: characterized by no externally obvious clinical signs, progressing with lethargy, loss of appetite, and depression.
- Neurological FIP: occurs when unrecognized, undiagnosed, or late-diagnosed Dry FIP progresses, leading to the formation of lesions in the nervous system and brain, with the emergence of neurological signs.
- Ocular FIP: occurs when unrecognized, undiagnosed, or late-diagnosed Dry FIP progresses, leading to the formation of lesions in the eye and visual centers, with the emergence of ocular signs.



In the wet form, there is severe inflammation of the blood vessels (vasculitis); the vessels lose protein, and fluid accumulates between the organs in the thoracic and abdominal cavities, as well as between the pericardium and the heart. The cat's abdomen becomes distended. In some cats, shortness of breath is also present due to fluid accumulation in the thoracic cavity. Diagnosis is relatively easy. A fluid sample is collected, the Rivalta test is performed, and the diagnosis is confirmed.

In the dry form, inflammation begins in the internal organs, primarily the intestines, liver, and kidneys. This stage represents the initial phase of the disease and does not produce clear findings in blood tests; it manifests only as mild increases or decreases in laboratory values. Clinical signs observed in the cat include lethargy, weakness, loss of appetite, weight loss, increased body temperature, hiding behavior, and depression. In some cases, pica behavior, such as eating litter or licking walls, may also be observed. If there is no improvement despite a period of antibiotic treatment aimed at these signs, the possibility of FIP should be considered. Experienced veterinarians and cat owners may be able to recognize the disease at this early stage.



In the neurological form, inflammation in the internal organs—primarily the intestines, liver, and kidneys—has progressed. As the virus has reached the brain and the central nervous system, distinct neurological symptoms become evident. In some cases, despite prominent neurological signs, blood test values may remain within normal ranges. At the onset of the neurological form, weakness in the limbs and mild gait abnormalities are observed. As the disease progresses, loss of balance increases, gait becomes severely impaired, and partial paralysis of the hind limbs or forelimbs may occur.



Due to lesions formed in the brain, tremors, episodes, seizures, and eventually generalized paralysis may develop. At the early stage of this phase, conditions such as toxoplasmosis or otitis (ear infection) may be misdiagnosed instead of FIP. Experienced veterinarians can perform appropriate differential diagnosis and initiate FIP treatment without delay.

In the ocular form, the clinical course is similar to that of the neurological form. Inflammation in the internal organs—primarily the intestines, liver, and kidneys—has progressed. As the virus reaches the eye, it causes pronounced ocular signs such as uveitis and glaucoma, including increased vascularization of the eye, reduced transparency, and enlargement of the eyeball. In some cases, despite prominent ocular symptoms, blood test values may remain within normal ranges. The ocular form may develop concurrently with the neurological form. Due to lesions in the visual centers of the brain, symptoms such as unequal pupil size (anisocoria), blindness, and involuntary movements of the pupils may occur. At this stage, intervention with eye drops alone may alleviate symptoms but does not prevent disease progression. Experienced veterinarians initiate FIP treatment without delay, in addition to providing supportive therapies aimed at symptom control.

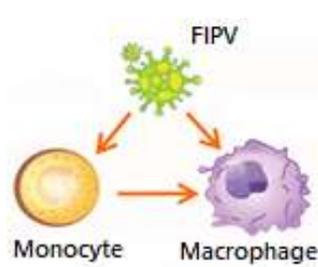
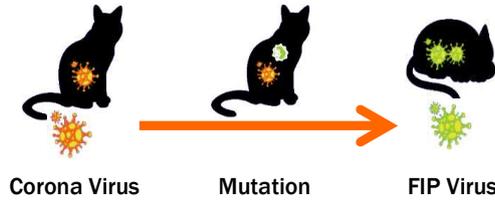




HOW DOES THE VIRUS CAUSE DISEASE?

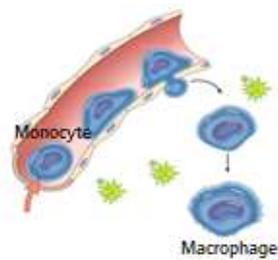
HOW DOES IT BEGIN?

Feline Infectious Peritonitis (FIP), known as infectious peritonitis of cats, is a disease that affects the immune system of cats. Most cats carry coronavirus, and it is not fatal in the majority of cases. For various reasons such as a weakened immune system, stress, vaccination, or surgery, the coronavirus (FCoV) can undergo mutation and transform into the lethal FIP virus.



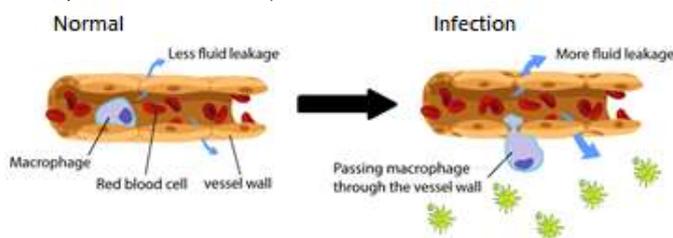
Virus (FIPV) and is initially found in the large intestinal tissues. The cat's immune system mounts a defense against the altered virus. Monocytes, a type of white blood cell circulating in the blood, differentiate into macrophages.

Macrophages are large cells that engulf viruses (and other microorganisms entering the body) and constitute the first line of defense of the immune system. Macrophages patrolling within the blood vessels migrate from the bloodstream into the tissues where the viruses are present in order to engulf the mutated viruses.



In some cats, as a defensive response to the virus, the permeability of the blood vessels increases and the vessels dilate. If this condition persists, the blood vessels become inflamed, resulting in vasculitis.

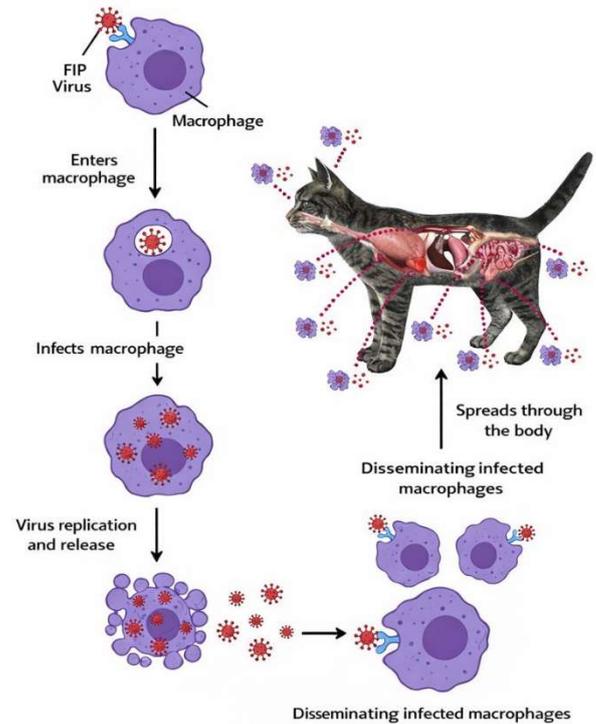
Damage to the blood vessels adversely affects blood circulation. The blood vessels are unable to supply the tissues and internal organs with sufficient oxygen, and tissues and organs deprived of oxygen are consequently damaged. Blood plasma (a protein-rich, yellow-colored fluid) leaks from the vessel walls.



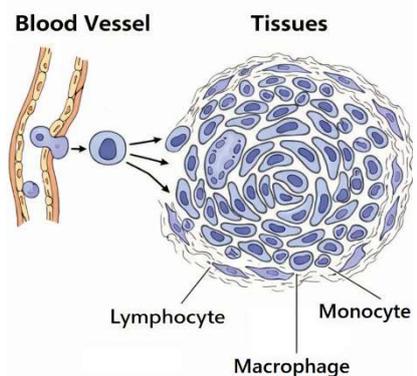
In the wet (effusive) form of FIP, this fluid usually begins to accumulate in the abdomen. In some cats, fluid also accumulates in the thoracic cavity.

HOW DOES IT PROGRESS?

The FIP virus attaches to the surface of macrophages that migrate to the cells of the gastrointestinal wall, enters the macrophage, and infects it. Macrophages infected with FIPV then disseminate the virus throughout the body as they travel to other areas within the abdominal and thoracic cavities, as well as to the internal organs, lungs, heart, nervous system, eyes, and organs such as the brain.



As macrophages travel to other regions of the body, large numbers of other immune cells—including neutrophils, monocytes, and lymphocytes—also begin to migrate from the bloodstream to the areas affected by the virus. As activated macrophages and other immune cells accumulate and congregate at all virus-infected sites, together with connective tissue cells, nodular masses known as granulomas form within the tissues. Due to this activation of immune cells, clusters and accumulations of macrophage-rich inflammatory lesions develop within the tissues. These lesions lead to tissue damage, organ dysfunction, fatal organ disorders, and ultimately Multiple Organ Failure. These pathological changes are responsible for the internal organ damage observed in cats with FIP.



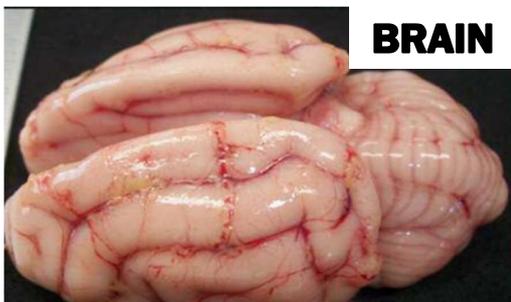
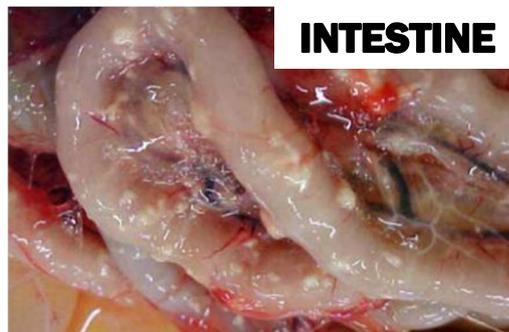
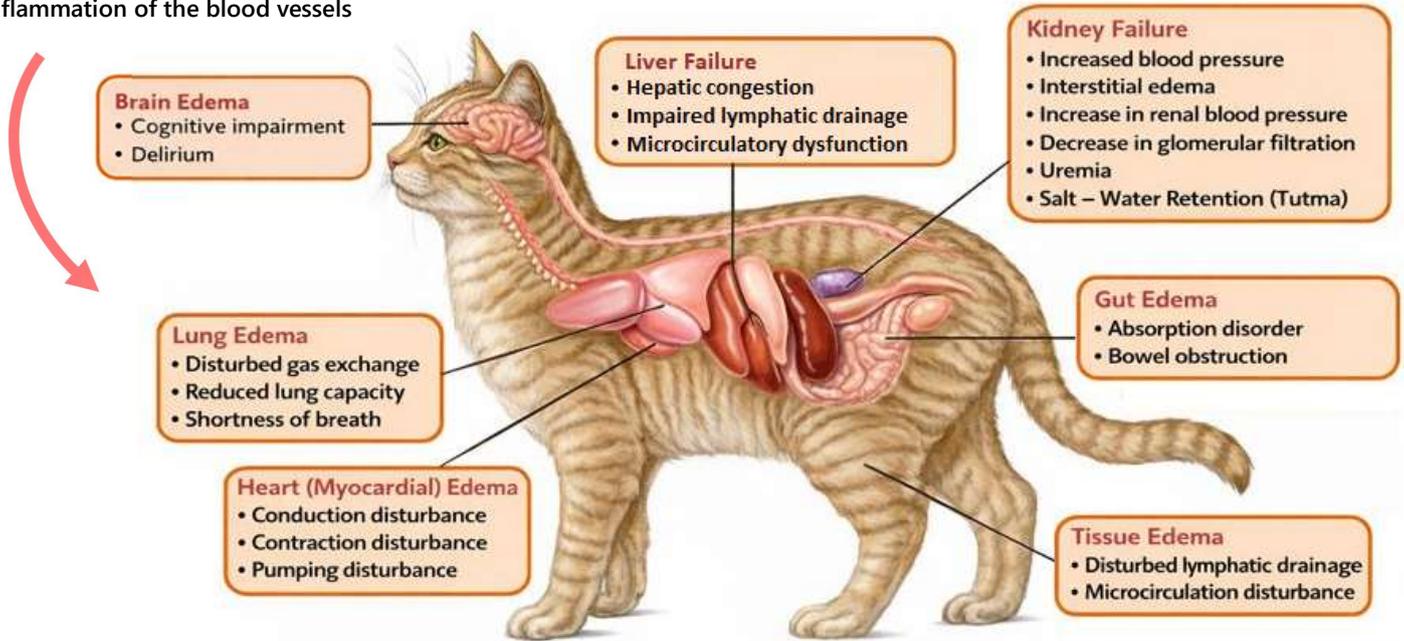
HOW DOES IT WORSEN?



Granulomas, which are an inflammatory response caused by the FIP virus in the body's tissues, represent a defense mechanism developed by the body against the virus. Granulomas can commonly occur in the lymph nodes, lungs, liver, skin, intestines, kidneys, and other organs. Another serious problem observed in FIP disease is vasculitis (inflammation of blood vessels), which occurs when the immune system mistakenly attacks the blood vessels, leading to inflammation of the vessel walls. As a result of this inflammation, the vessel wall may thicken, weaken, narrow, or develop tears, which can restrict blood flow and cause damage to organs and tissues.

Vasculitis

Inflammation of the blood vessels





WHAT ARE THE SYMPTOMS OF FIP?

General Condition

High fever, weight loss, stress, lethargy, apathy, fatigue, tremors, lying in the litter box, eating litter, licking walls, diarrhea, hair loss (neck, back, tail, abdomen), greasy appearance of the coat, pale gums, excessive drinking of water, not drinking water, loss of appetite, depression, hiding behavior, lameness—joint problems, lack of response, confusion, growth and developmental delay (in kittens).

Eyes

Pupil dilation, unequal pupil size, cloudiness of the cornea, red/bloody areas inside the eye, uveitis, conjunctivitis, eye deviation (strabismus), pupil tremors, transient blindness, change in iris color, fluid accumulation within the eye, swelling of the eye, excessive tearing.

Neurological

Neurological seizures, unsteady gait, weakness in the forelimbs, weakness in the hind limbs, urinary–fecal incontinence, inability to urinate or defecate, transient paralysis, transient blindness, head tilt, circling behavior.

Gastrointestinal

Loss of appetite, vomiting, weight loss, diarrhea, black-colored stool, constipation.

Liver – Kidney

Jaundice (yellowing of the ears, eyes, skin, and gums), excessive water intake, frequent urination, yellow-colored urine, brown urine, pale-colored feces, enlargement of the liver and kidneys.

Heart – Lungs – Circulation

Accumulation of fluid in the abdominal cavity (usually yellow in color; in some cases green when mixed with bile or reddish when mixed with blood), fluid accumulation between the pericardium and the heart, fluid accumulation in the thoracic cavity, rapid breathing, labored breathing, diaphragmatic breathing, edema in the limbs, heart failure, anemia, rapid fatigue.

Blood Tests, Biochemistry Analysis, Measurements

Increased total protein levels, decreased albumin/globulin ratio, increased globulin levels, decreased lymphocyte count, increased neutrophil count/percentage, elevated bilirubin, non-regenerative anemia, detection of high FCoV antibody titers (rapid antibody test kits in cats with FIP usually yield coronavirus-positive results—however, a negative result does not rule out FIP), detection of fluid in the abdomen and thorax on radiographs, golden-colored effusion and a positive Rivalta test, ELISA test S4, S5, S6 levels, detection of granulomatous structures in tissues and organs on ultrasound, microscopic examination of body fluid samples (lung, thoracic cavity, abdominal cavity, cerebrospinal fluid) revealing dense populations of macrophages and neutrophils.



WHAT ARE THE SYMPTOMS OF FIP?

FLUID IN THE ABDOMEN



ANOREXIA



DEHIDRATION

CORNEAL INFLAMMATION



BLOOD IN THE EYE



ALOPECIA



ANISOCORIA



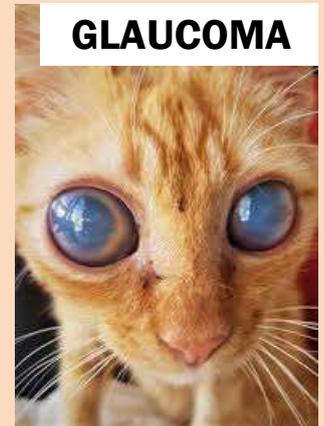
JAUNDICE



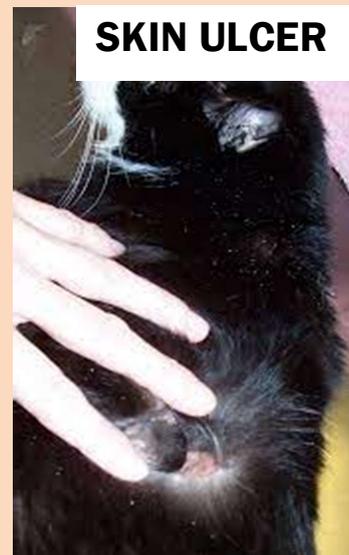
ALOPECIA



BLOOD IN THE EYE



GLAUCOMA



SKIN ULCER



PARALYSIS IN THE LEGS



JAUNDICE



ANEMIA



WHAT IS THE LIKELIHOOD THAT MY CAT HAS FIP?

Medical history: Incomplete development, recurrent infections, and a recent stressful event (surgery, rehoming, travel, accident, vaccination, other diseases, urinary tract obstruction, pregnancy–parturition) may increase the likelihood of developing FIP, particularly following weight loss and decreased appetite.

 Kittens and young cats have a higher likelihood of developing FIP.

 Kittens have a higher likelihood of developing the wet (effusive) form of FIP.

 Cats experiencing growth retardation or failure to thrive have a higher risk of developing FIP.

 Male cats have a higher likelihood of developing FIP.



 Aging is a contributing factor in the development of FIP. In cats over 5 years of age, FIP may develop due to age-related changes.

 In purebred cats, FIP is observed at a higher rate compared to mixed-breed cats, due to genetic factors.



 Cats originating from crowded or stressful multi-cat environments have a higher likelihood of developing FIP.

 Cats adopted from the street may develop FIP due to stress associated with environmental change. The introduction of a new cat into the household may also create stress for resident cats.



 Kittens raised in the home may have an increased likelihood of developing FIP after adoption due to stress related to relocation.

 In abandoned cats that have been rehomed, there is a possibility of stress-related development of FIP.



 The likelihood of FIP onset is higher after estrus, mating, pregnancy, and parturition.



 The likelihood of FIP development is higher following urinary tract obstruction or a severe infection.

 The likelihood of FIP development is higher after undergoing surgery (neutering/spaying, tooth extraction, or other procedures).



 In cats that escape from home or experience an accident, FIP may develop due to stress and immune suppression.



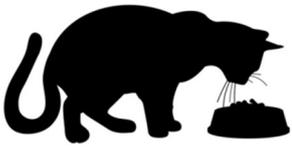
 There is a possibility of FIP development due to immune suppression during seasonal transitions.

 In cats that travel, stay outside the home (such as at a summer house), or are temporarily boarded in a kennel, the appearance of weight loss, depression, and deterioration in coat quality after returning home may indicate the possibility of FIP.



 There is a possibility of FIP development following vaccination and grooming (shaving) procedures.

Stress is the primary trigger for cats. Cats are animals that are more prone to stress. For this reason, during such periods, it is necessary—if possible—to increase the cat's immune strength before FIP symptoms appear and to take protective and preventive measures, even if only for a short time. **During periods when there is a risk of FIP development, the coronavirus load in the body should be reduced by administering short-term prophylactic antiviral treatment.** During these periods, the cat should be closely observed, and for necessary evaluations, the opinion of **a veterinarian experienced in FIP** should be sought.



HOW SHOULD I FEED MY CAT WITH FIP? (Encouraging cats with poor appetite)



When cats become ill, they often stop eating. The less they eat, the worse they feel, and the likelihood of eating decreases even further. This creates a vicious cycle that must be stopped immediately for a cat to recover. Eating is essential for providing the energy the cat needs. In cats that do not eat, anemia and liver failure may develop, or pre-existing organ failure caused by FIP may worsen.



Cats can survive slightly longer without food, but water is critically important. Any cat that is unable to drink water deteriorates rapidly. Cats that refuse to drink may require slow and careful administration of water orally using a syringe. In cats that do not drink and become dehydrated, kidney failure develops, blood circulation deteriorates, and cardiac arrest may occur.



In cases where the cat refuses to drink water and becomes severely dehydrated, intravenous fluid therapy at a veterinary clinic may be necessary. To prevent the development of pulmonary edema, fluids must be administered at a slow rate, and during this time, the cat may need to remain hospitalized for several days.



In FIP disease, highly digestible diets containing high-quality protein, as recommended by your veterinarian, should be preferred. However, sick cats may stop eating their usual dry food. Finding a food that your cat likes is not easy.



While treatment continues, it is essential to ensure that the cat continues to eat in order to remain strong. To encourage a cat with poor appetite to eat, you can place small amounts of food in front of them; adding more as they finish helps keep the food fresh-smelling. **Rather than placing a large amount of food in the bowl at once, it is best to offer small portions frequently.** To make the food more appealing, treats or fish oil may be added on top. **You may also give commercial wet food; however, although wet foods are palatable, they lack sufficient nutritional value.**



If your cat refuses dry food or has poor appetite, you should grind a high-quality dry food into a powder, dilute it with water, and feed small amounts frequently using a syringe. Some sick cats may be encouraged to eat more through hand-feeding. You may offer your cat palatable, high-energy, highly digestible protein-based foods prepared in a liquid or semi-liquid consistency, such as purées or soups, given in small, frequent meals. In cats with a risk of kidney failure, providing high-protein foods is not recommended.



You can prepare bone broth with marrow. Unseasoned bone broth is palatable, nutritious, and rich in protein and collagen. You can pour the broth into ice cube trays, store it in the freezer, and thaw and offer one or two cubes daily. Small, lickable portions of bone broth may also be appealing.



You may feed your cat plain cooked meat without added spices. Poultry, beef, or lamb can be tried. The meat can be cut into small pieces and lightly sautéed in a pan or baked in the oven. If your cat likes them, organ meats such as liver and heart may also be cooked and offered.



You may also try plain cooked fish. Some white fish, such as sardines or whiting, can be boiled or lightly pan-fried with a small amount of oil. Occasionally, canned fish may also be tempting for a sick cat. **Fish should not be given raw.**



Boiled eggs may also be offered as a good source of protein and nutrients. Eggs provide the essential amino acids required by cats. Nutritional value increases when eggs are cooked, and **raw eggs should not be given.**



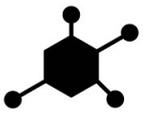
Kefir and yogurt provide probiotic support and help regulate digestion. If your cat does not like the taste of kefir, it should not be forced. However, in cases of severe diarrhea, probiotic supplementation prescribed by your veterinarian may be necessary.



FREQUENTLY ASKED QUESTIONS

- 1** Is FIP fatal? FIP is definitely fatal if left untreated.
- 2** Is FIP contagious? There is a risk of transmission among cats that defecate in the same area. During burying of feces, the virus from the feces of a cat with FIP can contaminate the paws. While grooming, the virus may pass from the paws to the mouth, and from there to food bowls, entering the digestive system.
- 3** How can I start treatment? Treatment should be initiated based on a diagnosis made by a veterinarian or test results showing signs consistent with FIP.
- 4** How long does recovery take? The minimum duration is 90 days. In neurological and ocular forms, the duration may be longer. Treatment shorter than this period is not successful, and the risk of relapse increases.
- 5** My cat seems better—can I stop treatment? No. The disappearance of symptoms does not mean that the virus has been completely eliminated from the body. Treatment must not be discontinued before the full course is completed.
- 6** Can I treat my cat while it stays outdoors? No. Since the medication must be administered on time and treatment must be carried out regularly, the cat should be kept in a suitable controlled environment throughout the treatment period.
- 7** Will the medications be too much for my cat? No. If medications are not given regularly, the disease progresses and the cat's condition worsens. Insufficient dosing is actually dangerous.
- 8** Do the medications damage my cat's internal organs? No. It is the virus causing FIP itself that damages the internal organs.
- 9** If antibiotics are needed, should I stop FIP treatment? No. Antibiotics may be used during treatment. While using non-prohibited antibiotics, FIP treatment should not be discontinued or interrupted due to concerns that medications are too much.
- 10** Which antibiotics are prohibited? In neurological cases, fluoroquinolone-class antibiotics and metronidazole should be used with caution.
- 11** When does treatment end? After completion of the 90-day treatment period, the duration is either extended or terminated based on follow-up tests and the veterinarian's assessment. If treatment is stopped earlier, the likelihood of the disease resuming from where it left off increases. This is called a relapse.
- 12** I have other cats at home—will it spread to them? The FIP virus is present in feces. For the first 30 days after starting treatment, the affected cat should be kept separate from other cats and should not share litter boxes or food and water bowls.
- 13** Can my cats with FIP stay together? Cats that have FIP can be kept together.
- 14** Can I give my cat any type of food? The cat must be fed according to its test results, age, and clinical condition. Cats with kidney failure should be fed a low-protein diet. In cases of severe diarrhea, a special gastrointestinal diet should be used.

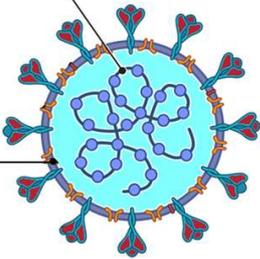
- 15** My cat is not drinking water—what should I do? Preventing dehydration is vital. Without waiting for the cat to drink on its own, you should encourage drinking, prepare broth, and if the cat still does not drink, carefully administer fluids orally.
- 16** My cat is not eating—what should I do? An anorexic cat must be fed and should not be left without energy. Without waiting for the cat to eat on its own, you should encourage feeding, prepare its favorite foods, and if it still does not eat, hand-feeding (force-feeding) should be performed.
- 17** My cat is eating litter—what should I do? Eating bentonite litter can cause poisoning and intestinal obstruction. Instead of bentonite litter, pine pellets, newspaper, or similar alternatives should be used. In this situation, vitamin and mineral supplementation is necessary.
- 18** My cat is not urinating—why? In cats with neurological FIP, not urinating for more than one day can cause acute kidney failure. It is essential to check whether the urinary bladder is full, and if it cannot be emptied manually, the cat must be taken to a veterinarian immediately.
- 19** My cat's legs and hips are constantly wet and it is leaking urine—why? Due to FIP, the nerve cells controlling the urinary bladder are damaged. When the bladder fills, the nerves fail to send signals to the brain, excessive urine accumulation puts pressure on the bladder muscles, and urine leakage occurs. In this case, protective measures for the kidneys must be taken.
- 20** My cat is not defecating—why? Constipation lasting longer than two days must be addressed. As feces remain in the intestines, they lose moisture and harden. In such cases, oils (such as St. John's wort oil, olive oil, etc.) may be given, or the veterinarian may prescribe intestinal lubricants.
- 21** My cat's diarrhea does not resolve—what can I do? Diarrhea is common in cats with FIP. Fatty foods and wet food may trigger diarrhea. Severe diarrhea lasting longer than three days is a serious condition. Due to diarrhea, the body rapidly loses fluids. Probiotic supplementation may be given. Persistent diarrhea requires veterinary evaluation.
- 22** My cat cannot control defecation and defecates everywhere—when will it improve? FIP causes damage to the nerves controlling the anal muscles. Nerve regeneration takes time. Some cats improve after 2–3 months, while in others the condition may persist. In some cases, fecal incontinence may continue. Treatment may be extended in such situations.
- 23** When will my cat's urinary incontinence improve? FIP causes damage to the nerves controlling the bladder muscles. Nerve repair takes time. Some cats improve by the end of treatment, while in others the condition may persist. In such cases, treatment may be extended.
- 24** What should I do after treatment ends? After treatment, nutrition and supplementation are required for tissue repair and regeneration. However, immune boosters should not yet be administered. During the first 6–8 months after treatment, monitoring should be performed against the risk of residual viruses causing reinfection, and prophylactic supportive measures should be used.



HOW DOES EIDD-2801 WORK?

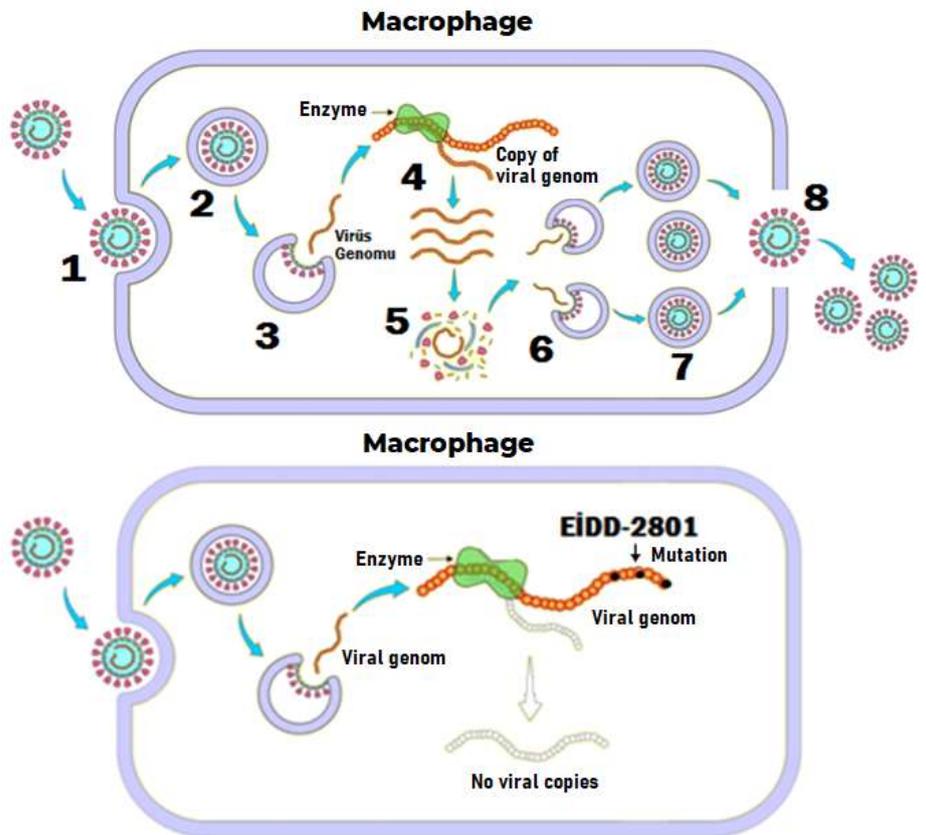
Viral genome

Envelope



The reason viruses cause disease is their ability to replicate rapidly. However, they cannot do this on their own; they use the cells of the host organism they enter. FIP viruses, in order to produce copies of themselves, use macrophages, which are immune cells of cats. When the virus enters a macrophage, it requires a biological molecule called an enzyme in order to replicate itself. Viruses are structures composed solely of a genetic code sequence (genome) and a surrounding envelope. In coronaviruses, including the FIP virus, the envelope also contains spike-like projections. Through these structures, the FIP virus attaches to the cell it will enter—namely the macrophages, which are the cat's defense cells—and gains entry into them.

- 1 The FIP virus attaches to the surface of macrophages.
- 2 It enters the macrophage.
- 3 It opens its envelope and releases its genome into the cell.
- 4 Using the enzymes of the macrophage, it replicates its genome.
- 5-6 Envelopes are produced for the replicated genomes.
- 7-8 The newly formed viruses exit the macrophage.



EIDD-2801 replaces the building blocks of the genetic code of the FIP virus, causing errors to occur. When the viral genome is subsequently copied to produce new viruses, it becomes a degraded sequence containing numerous errors, known as mutations, and can no longer be replicated. As a result, the activity of the virus that is unable to produce copies comes to a halt.



Difference Between GS-441524 and EIDD-2801

GS-441524 binds to the enzyme and stops replication, without directly interfering with the virus itself, whereas EIDD-2801 does not interfere with enzyme activity but instead targets the virus itself.

EIDD-2801 disrupts the viral genome, causing the amplification of faulty copies from an erroneous genome, ultimately leading to the virus completely losing its lineage.