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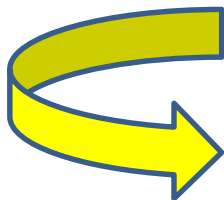
Feline Infectious Peritonitis FIP

Dr. Djemai Samir

Feline infectious peritonitis (FIP) is a serious systemic infectious disease of felids, caused by a Coronavirus, characterized by:

- Either by serous exudates = Wet form (Accumulation of effusion fluid in the abdominal or pleural cavity).
- Or by inflammatory granulomas disseminated in various organs = Dry form (Difficult to recognize / often presents with neurological and ocular symptoms).

It evolves over a period of several weeks to several months



Death

FIP primarily affects young animals between 6 months and 2 years (< 3 years).

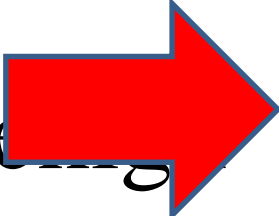
Coronavirus infection in cats manifests as:

- ❑ Self-limiting enteritis (mild diarrhea or even no clinical signs): Very common especially in young cats.
- ❑ Infectious peritonitis = Immune-mediated vasculitis: Mortality disease of low frequency.

History

- ❑ Coronaviruses (CoVs) infect a wide range of animal species: mammals or birds.
- ❑ The first CoV described in 1936 is the one responsible for avian infectious bronchitis.
- ❑ In 1946: CoV responsible for transmissible porcine gastroenteritis.

□ The first human CoV was only described in 1963.

Being  agent involved in upper respiratory tract infections.

Feline coronaviruses (Feline coronavirus:
FCoVs):

➤ Causes a ubiquitous enteric infection in cats.

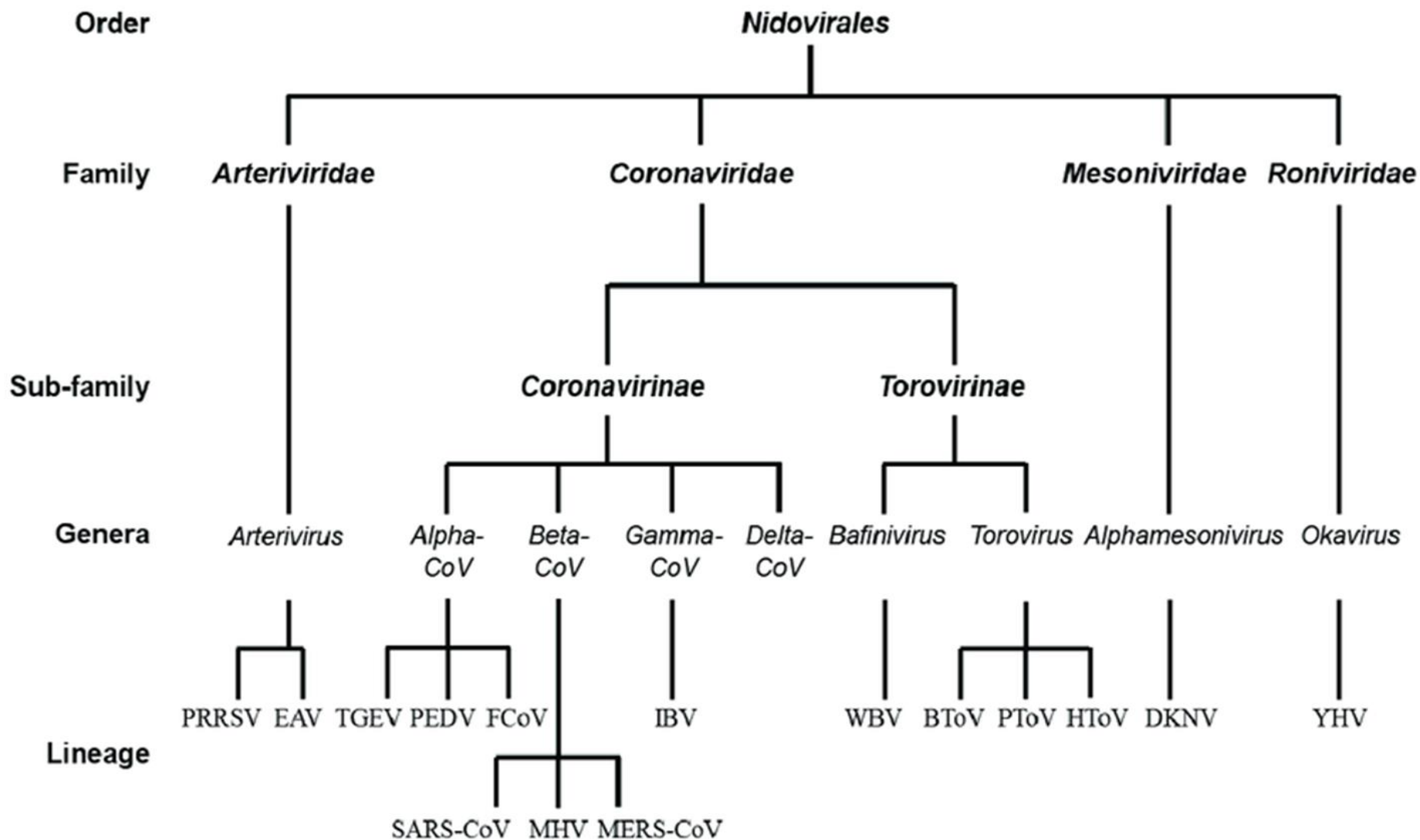
Or

➤ Occasionally cause a highly lethal immune-mediated vasculitis called: Feline Infectious Peritonitis (FIP).

Etiology

Classification

Feline coronavirus is part of the Coronaviridae family.



Antigenic groups of coronaviruses (humans and domestic animals)

Reference:
 Infectious Diseases Of The Dog And Cat/Craig E. Greene

Group	Coronaviruses
GROUP 1 (GENUS ALPHACORONAVIRUS)	
Subgroup a	Human coronavirus Strain 229E Porcine epidemic diarrhea virus Human coronavirus Strain NL-63
Subgroup b (Geselavirus)	Transmissible gastroenteritis virus of swine Porcine respiratory coronavirus Type I: Feline coronavirus Strains: 79-1146, 79-1683 Canine enteric coronavirus Strains: Elm02, 23/03 Type II: Feline coronavirus Strains: Black, KU-2, UCD1 Canine enteric coronavirus subtype IIa Strains: Insavc1, BGF10 Canine enteric coronavirus subtype IIb TGEV-like strains: 341/05, 174/06 Canine pantropic coronavirus biotype Strain CB/05
GROUP 2 (GENUS BETACORONAVIRUS)	
Subgroup a	Murine hepatitis virus Rat coronavirus Human coronavirus Strain HKU-1 Betacoronavirus 1: Bovine coronavirus Human coronavirus Strain OC43 Porcine hemagglutinating encephalomyelitis virus Canine respiratory coronavirus Strains: T101, 430/07 Equine coronavirus
Subgroup b (SARSr-coronavirus)	Human severe acute respiratory distress coronavirus
GROUP 3 (GENUS GAMMACORONAVIRUS)	
	Avian coronavirus: Infectious bronchitis virus Turkey coronavirus

General presentation of Coronaviruses

□ Spherical, large size (= 80-200 nm).

□ **Positive-sense RNA.**

□ Viral RNA is about 29 kilobases (kb)

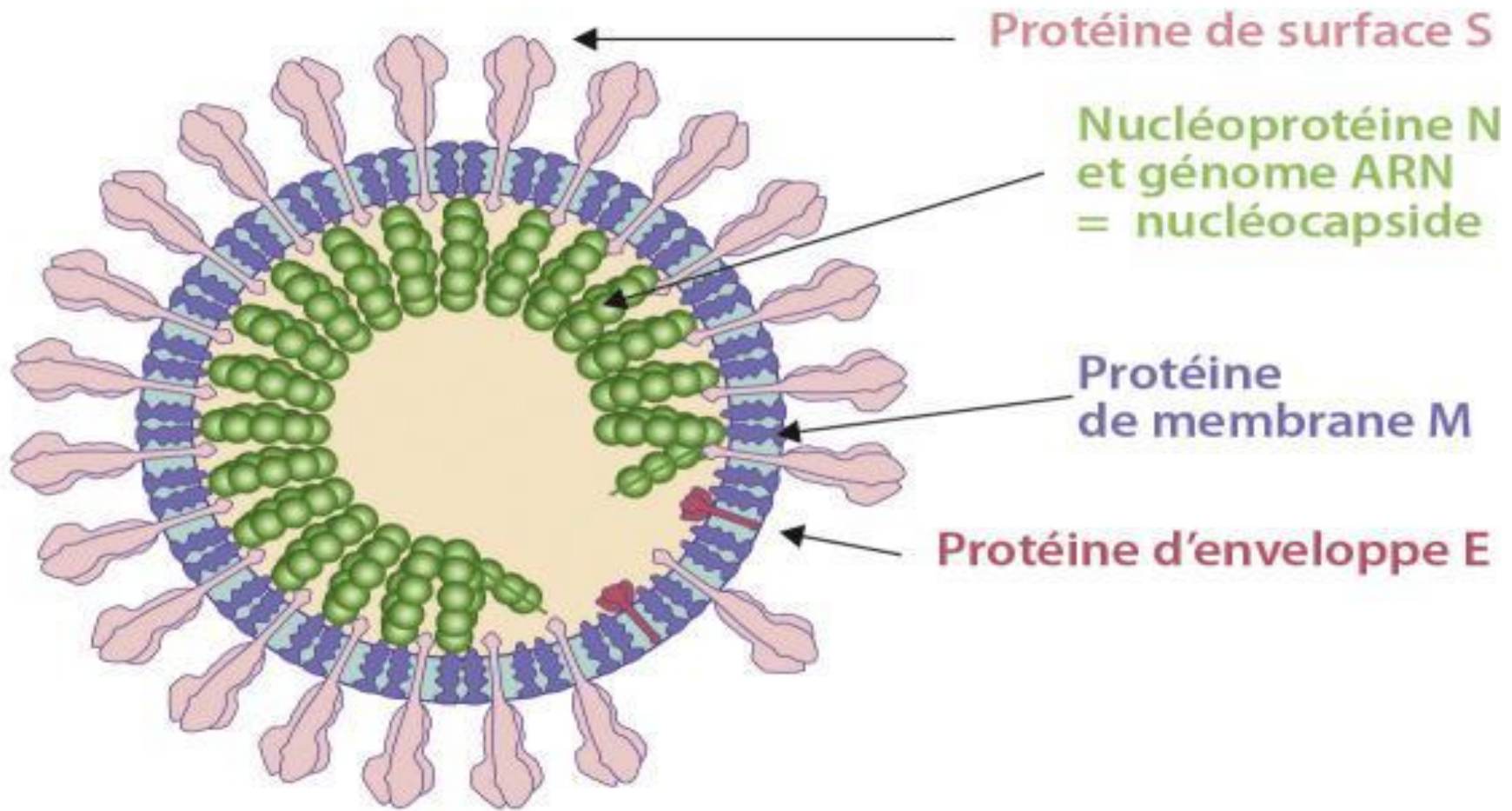
in length.

□ The genome of Coronaviridae is the largest

known viral RNA molecule to date.

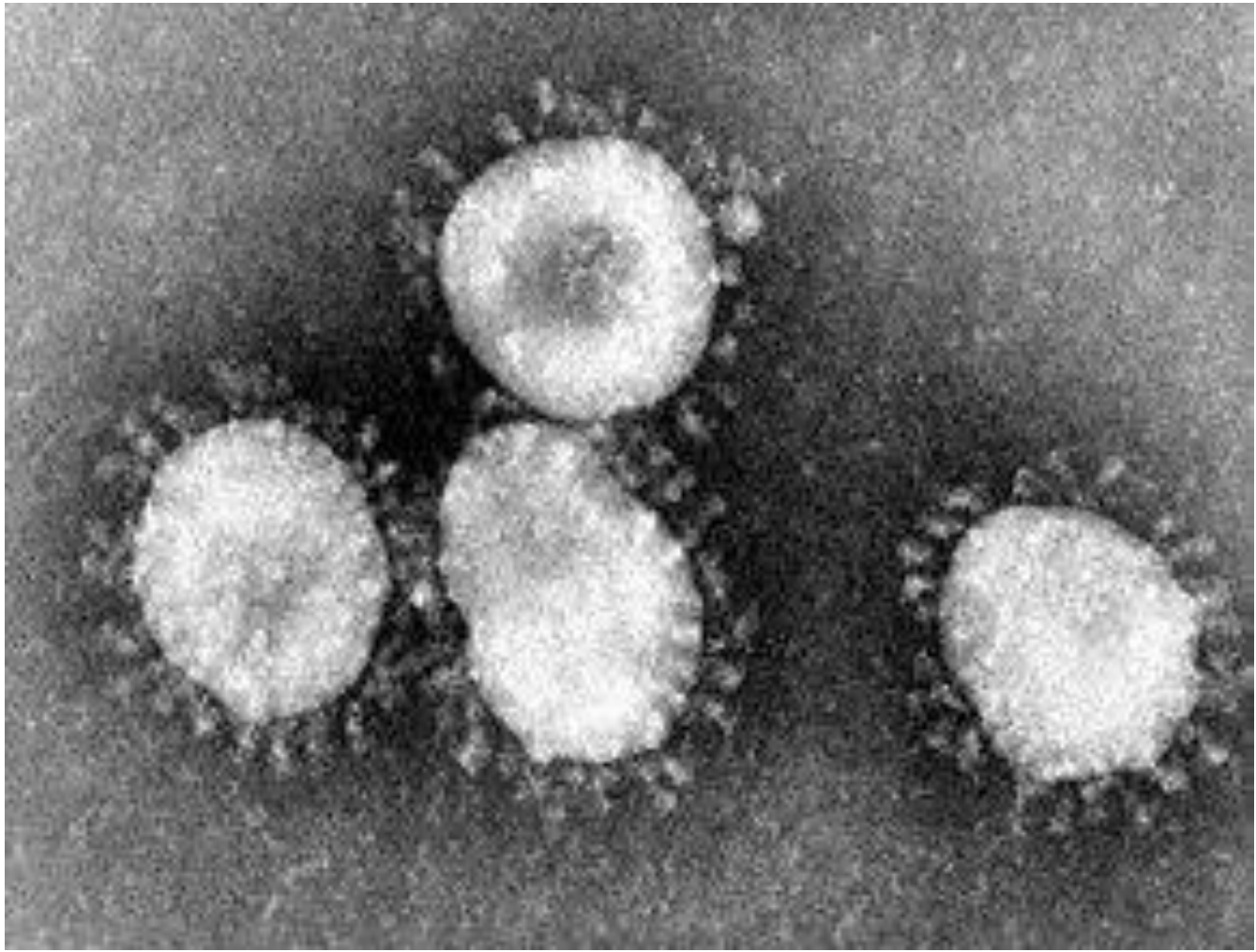
□ Enveloped virus: At least 3 viral proteins called S (Spike), E (Envelope), and M (Matrix) are embedded in the viral envelope.

□ The viral nucleocapsid is formed by the association of the N protein (Nucleocapsid) with the viral genome.



Structure of a coronavirus

- The S protein: Forms spikes; Binds virions to receptors and induces the fusion of the virus envelope with the target cell membrane.
- The M protein: Maturation of the virus.
- E protein: Along with the M protein, regulates the assembly and budding of viral particles.
- The N protein constitutes the nucleocapsid, providing protection for the viral genome.



❖ **Classification into biotypes**

There is a classification of FCoV into 2 biotypes:

➤ **FECV** (feline enteric coronavirus): Mild

diarrhea or asymptomatic infection

➤ **FIPV** (feline infectious peritonitis virus):

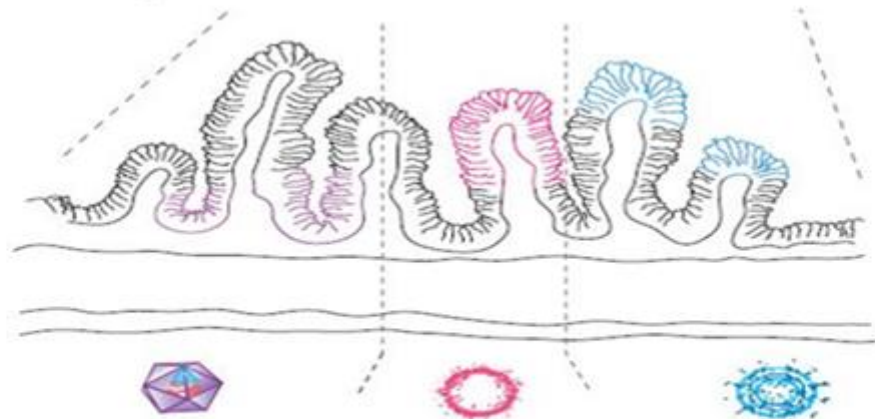
Responsible for FIP

FECV: Exclusively enteric tropism:

- Benign and capable of being transmitted between cats.
- Would reside in the gastrointestinal tract of an infected cat before undergoing a mutation in this same tract giving rise to FIPV.

coronavirus entérique félin

- Infection digestive subclinique
- Tropicisme pour les entérocytes différenciés
- Tropicisme mineur pour les monocytes-macrophages
 - Présence en quantité très faible dans le sang



Parvovirus

Coronavirus

Rotavirus

FIPV:

- Capable of systemic spread and causing FIP, but its peculiarity is that it is very rarely transmitted between animals.
- FIPV strains are rarely shed in feces unlike FECV strains.

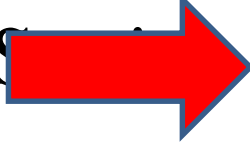
- ❑ It is impossible to distinguish the 2 biotypes both molecularly and antigenically.
- ❑ No diagnostic test can determine whether cats are infected with a strain of biotype FIPV or FECV.

❖ **Classification into serotypes:**

Feline coronaviruses are subdivided based on their serological reactions (with the S protein) into 2 serotypes:

- Serotype 1: The most frequently found in cats in a natural environment (80% of cases).
- Serotype 2 has a lower prevalence.

This classification does not take into account the virulence of the virus:

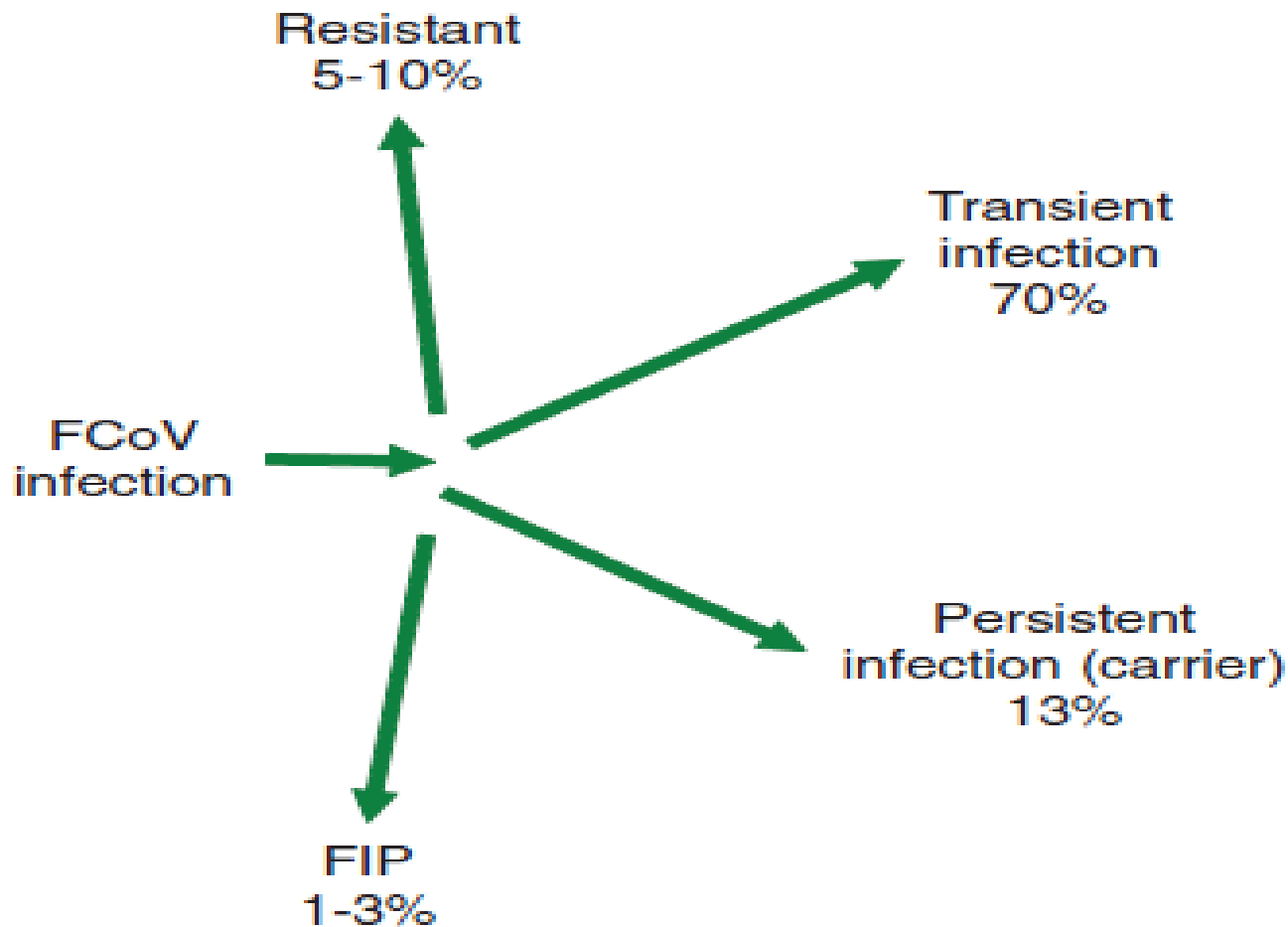
 Some of biotypes FIPV and FECV can be found among feline coronaviruses of serotype 1 and serotype 2.

Les différentes souches de coronavirus félin répertoriées (GONON, 1998 et HOHDATSU *et al.*, 1991)

	FIPV	FeCV
Sérotypes 1	UCD 1 UCD 2 UCD 3	RM
Sérotypes 2	79-1146 DF2 (Nor 15) TN 406 (black)	79-1683

Mutation theory

Despite the ubiquitous nature of FCoV and infected cats (FECV), few cats develop FIP.



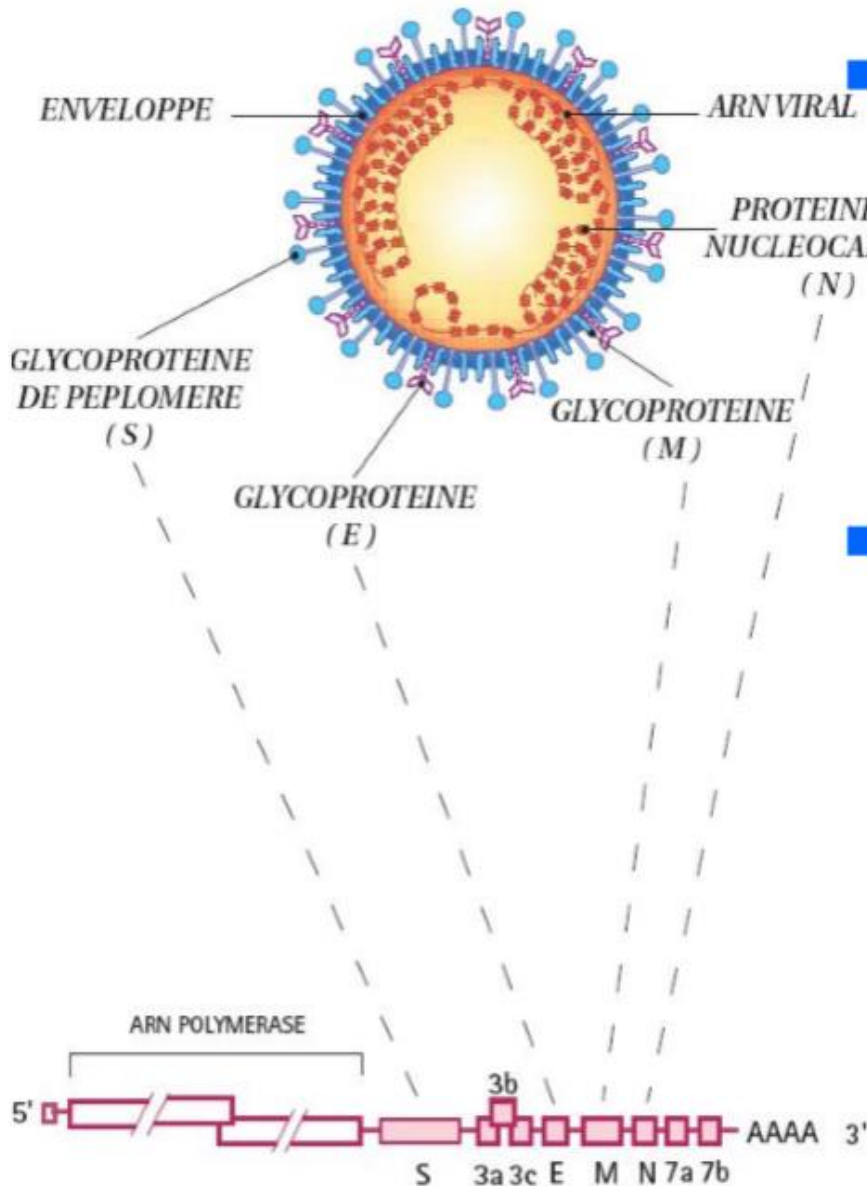
There are 4 possible outcomes of FCoV infection; FIP is only the result in a minority of infections.

The proposed explanations revolve around 2 premises:

- Avirulent and virulent viruses circulate simultaneously.
- Virulent viruses appear as a result of a new mutation in each cat affected by FIP.

CORONAVIRUS FELIN

DEUX BIOTYPES



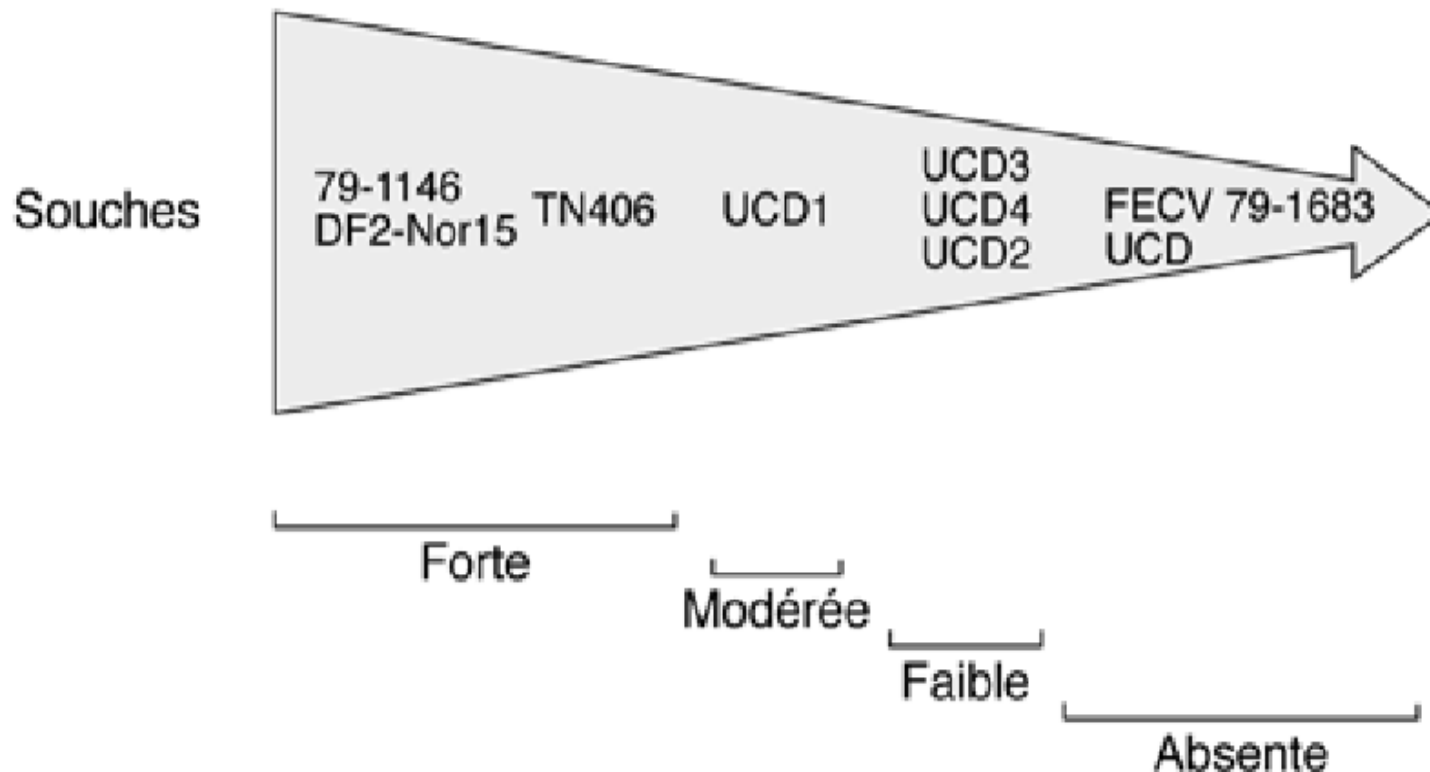
■ Coronavirus félin entérique

- Virus classique
- Tropisme pour les entérocytes différenciés
- Présence très faible dans le sang (monocytes)

■ Coronavirus félin de la PIF

- Mutants « endogènes » : apparaissent chez le chat qui va développer la PIF
- Mutations dans les gènes non structuraux
- Acquisition d'un tropisme pour les monocytes - macrophages

Capacité à induire une péritonite infectieuse féline



Fragility of the virus

❑ Coronaviruses are fragile in the external environment.

❑ Inactivated by most common detergents and disinfectants: alcohol, quaternary ammoniums, iodophores, bleach.

- ❑ Thermolabile, inactivated in one hour at 56°C.
- ❑ Persists for 7 weeks in dry environments and 2 weeks in moist environments if protected by proteins (fecal matter).
- ❑ Resistant to low temperatures (4°C).
- ❑ Resistant to acidic pH: Allows passage through the gastric barrier.

Epidemiology

Sensitive species

All Felidae can be infected:

➤ Domestic cat.

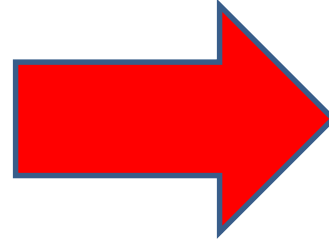
➤ Wild felids (puma, lion, tiger, leopard, lynx, jaguar, and sand cat, etc.) especially the cheetah.

Age

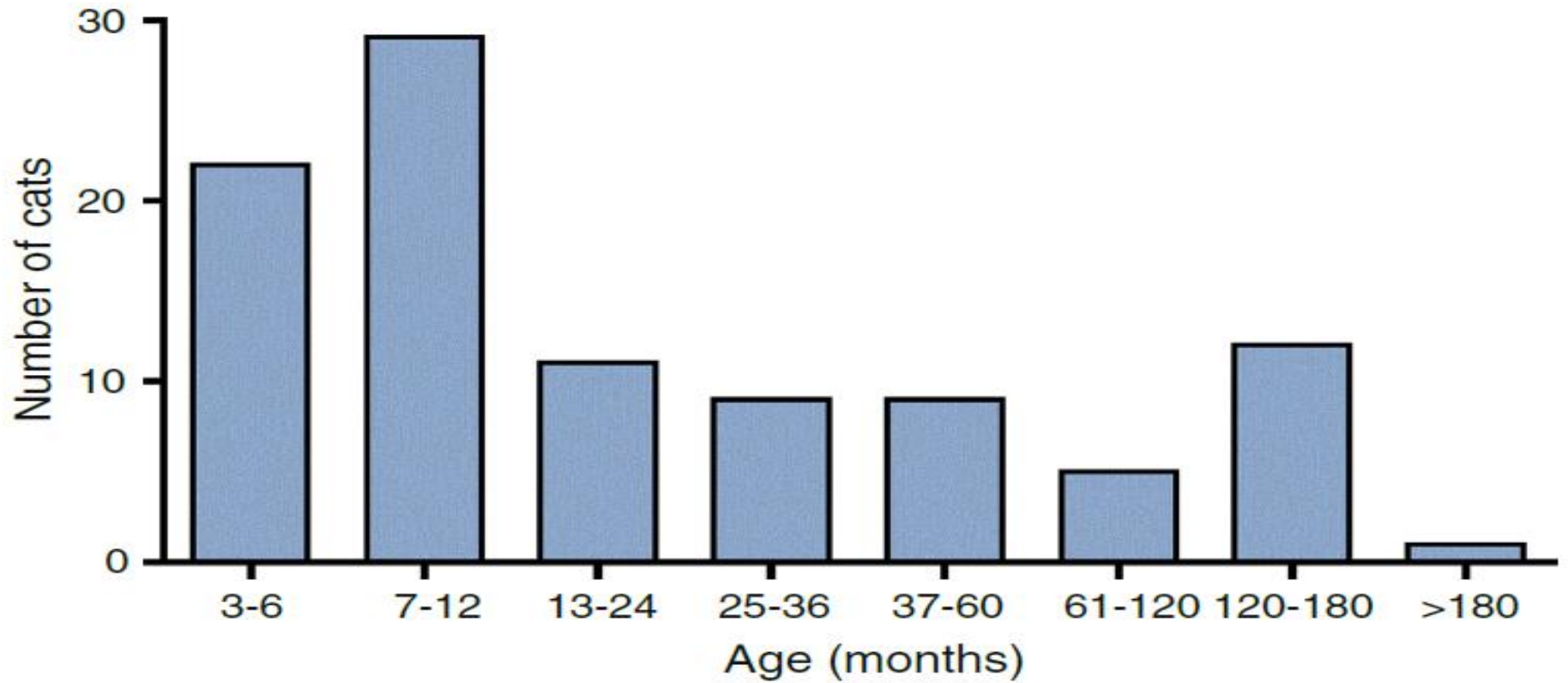
The vast majority of domestic cats that develop FIP:

- Are aged from a few months to 3 years.
- At least 50% of affected cats are 12 months old or younger.

PIF can occur at any age:



There is a secondary peak incidence in geriatric cats (> 10 years), probably due to suboptimal immune function.



Age distribution of 99 cats affected by PIF (confirmed by autopsy).

Sex

- There is no consensus regarding the existence of a sex-related predisposition.
- Intact males have been predisposed in some studies.

Breed

Although the disease affects all breeds, purebred cats are more sensitive:

- Probably due to a greater viral pressure in breeding.
- Maybe due to a genetic sensitivity present in certain lines.

The breeds:

Burmese, Ragdoll, Bengal, Rex,

Abyssinian, British shorthairs,

Himalayan seem to be more affected.

SACRED BIRMAN CAT



Bengal Cat



Burmese



Season

According to some studies: a peak in disease may occur in autumn and winter.

Distribution and frequency

➤ FCoV  global distribution.

➤ Endemic (non-mutated) virus,
particularly in communities.

Cats kept together in a small space =
Catteries, shelters, pet stores.

➤ **There is no multi-cat household without**

FCoV = endemic households:

□ **United States and Europe = At least**

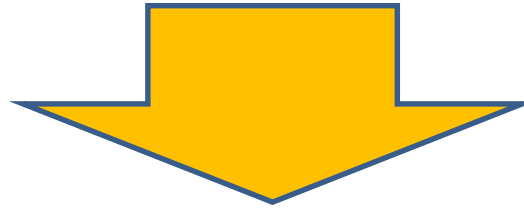
50% of cats have antibodies against

coronaviruses.

- ❑ Switzerland = 80% (breeding cats) and 50% (cats living alone) tested positive for antibodies.
- ❑ Great Britain = 82 % (show cats), 53 % (cats in breeding) and 15 % (of cats in single cat households) had antibodies.

NB:

Although the prevalence of FCoV
infection is high



**Only about 5 % of cats living in
communities develop FIP**

Lifestyle

❑ Major issues in communities (shelters, purebred catteries).

❑ 50-100 % of cats living in environments with more than 6 cats are infected with FCoV.

□ As soon as FCoV is present in a breeding facility or shelter, all cats will quickly become contaminated since the virus is highly contagious.

□ The seroprevalence is lower in cats living alone (such as house cats) and in stray and wild cats.

Transmission

Oro-Nasal

Contamination

Pathological products



- ❖ Mainly fecal matter = Direct contamination.
- ❖ Objects contaminated with fecal matter = Indirect contamination (clothes, toys, grooming tools, etc.).

Virus excretion

The excretion of non-mutated FCoV begins in the week following the infection.

Non-mutated FCoV is excreted by:

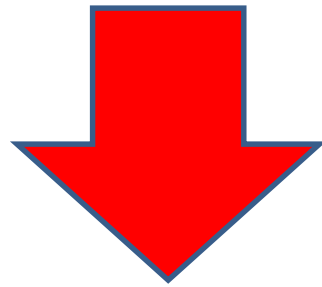
➤ Primarily in feces.

➤ To a lesser extent, in oro-nasal secretions.

Non-mutated FCoV is excreted by:

- Cats affected by enteric coronavirus infection.
- Cats affected by FIP.

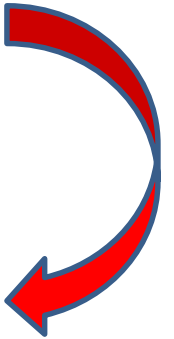
**Many cats are healthy carriers,
naturally infected.**



Excrete FCoV for at least 10 months.

❑ A healthy carrier may develop FIP a few weeks to a few months after infection (non-mutated FCoV):

Following a stress: Surgery, moving, visit to a cattery or co-infection with FeLV or FIV.



NB:

Mutated FCoV causing PIF has not been found in the secretions or excretions of cats affected by PIF.

Incidence

□ PIF is generally a sporadic disease that does not transmit from one cat to another.

❑ In households with 1 or 2 cats ~

1 case in 5000.

❑ In catteries = 5% to 10%.

Pathogenesis

□ The epidemiology and pathogenesis of PIF have fascinated virologists and veterinarians around the world for decades.

□ Most widely accepted theory: Internal (endogenous) mutation hypothesis.

❑ Mutated FCoV replicates in enterocytes.

Asymptomatic infection or diarrhea.

❑ Mutated FCoV replicates in

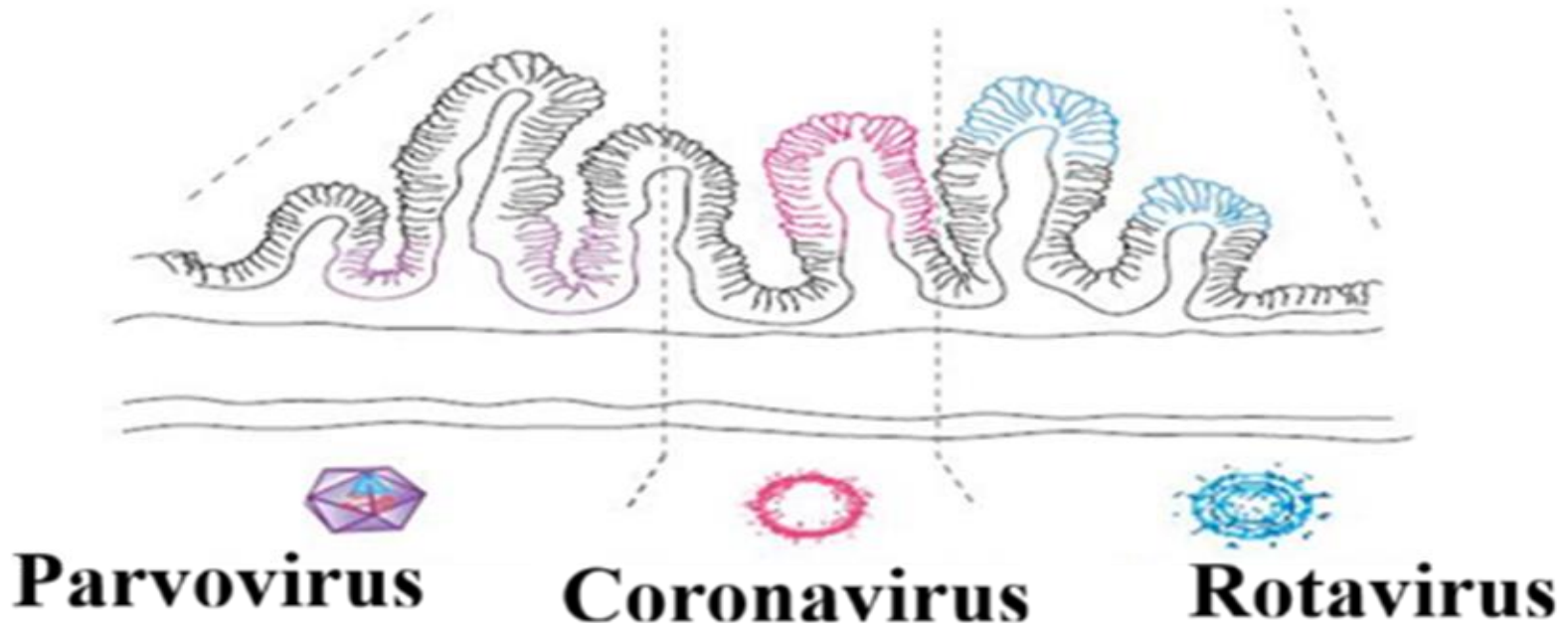
macrophages-monocytes PIF.

Pathogenesis of feline enteric coronavirus infection (FECV = non-mutated FCoV)

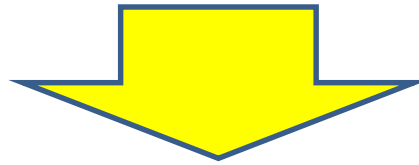
❑ Cats are infected by: Oro-nasal exposure
(Ingestion / rarely by inhalation).

❑ The virus replicates in the epithelial cells of the oropharynx, the small intestine, or the upper respiratory tract depending on the route of entry.

□ The main site of viral replication is the intestinal epithelium = Tips of the villi.

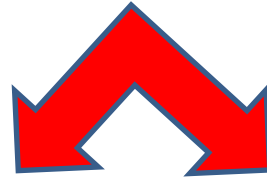


**Replication of FCoV (non-mutated) in
the cytoplasm can lead to**



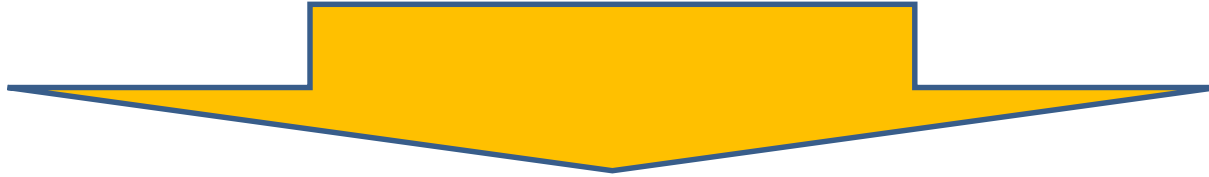
Destruction of intestinal epithelial cells

**Infection
asymptomatic**



**Enteritis
mild**

Mild enteritis



Diarrhea (acute or chronic) persistent or intermittent (involvement of the small intestine), vomiting and/or a lack of appetite, can cause benign short-duration low-grade viremia.

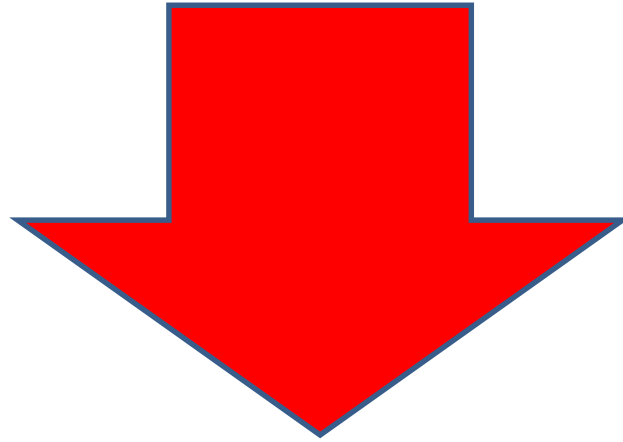
**The infection can persist for a long time
without causing clinical signs.**

Intermittent or occasional viral shedding

=

Source of infection

Virus is excreted in feces



Onset: 1 week post-infection

**Duration: can be shed for at least
10 months**

NB:

➤ **FCoV avirulent remains in the digestive tract; does not cross the intestinal mucosa and does not spread beyond the intestinal epithelium and regional lymph nodes.**

Pathogenesis of feline infectious peritonitis

- ❑ PIF is a sporadic disease.
- ❑ Caused by a variant of the enteric virus =
After mutation.
- ❑ **Mutation develops in a specific cat.**

❖ Appearance of the mutation

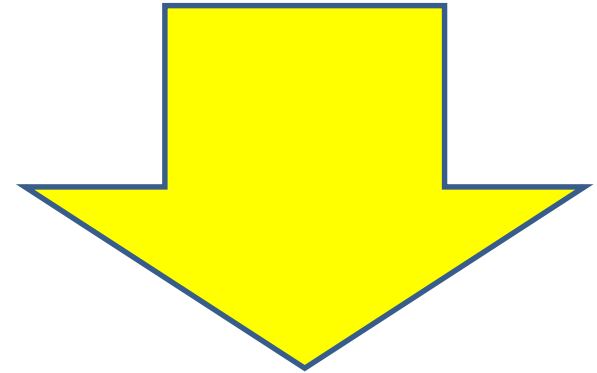
In some infected cats, the virus with low pathogenicity mutates into a virulent strain that can replicate in macrophages (tropism)

Causes:

Systemic pyogranulomatous vasculitis



So: PIF develops following a spontaneous mutation in certain regions of the FCoV genome



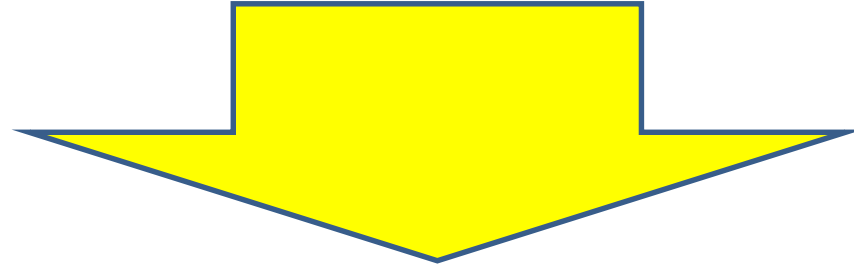
Genes: 3c and 7b (secondarily the genes of structural proteins S and M).

□ The mutation leads to changes in the surface structures of the virus

Allowing the phagocytosed virus to replicate within macrophages.



Key event in the pathogenesis of PIF



The mutated virus, unlike its harmless parent, suddenly becomes capable of replicating within macrophages

NB:

The mutation can occur shortly after the initial infection, or years later, which may explain why some cats develop PIF several years after contracting the virus.

NB:

- ✓ Virulent strains are not capable of replicating effectively in the intestine = This is why the transmission of PIF from cat to cat does not occur.
- ✓ The disease can be effectively transmitted by inoculating naïve cats with a drainage from a cat affected by FIP.

NB:

The FCoV responsible for FIP spreads to many organs, most likely through monocytes via the hematogenous route.

❖ Disease development

FIP = Immune complex disease

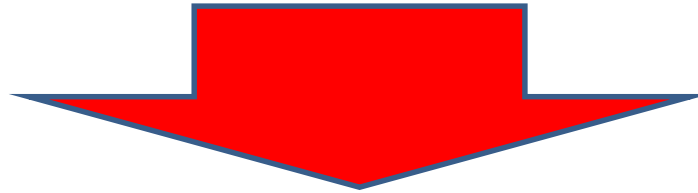


**Virus or viral antigen +
Antiviral antibodies + Complement**

❑ It is not the virus itself that causes major damage, but the cat's own immune reaction.

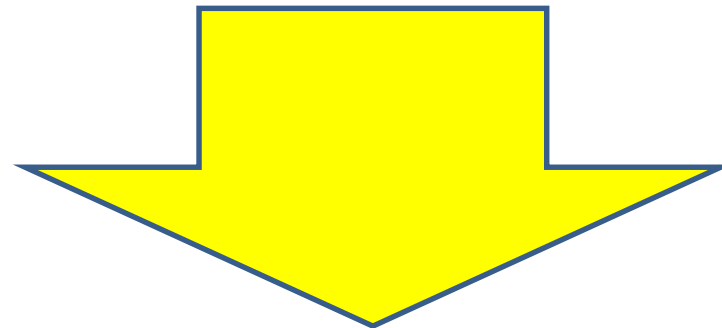
□ About 14 days after the mutation:

**Mutated virus is carried by macrophages
throughout the body**




Cecum, colon, intestinal lymph nodes, spleen,
liver, central nervous system (CNS).

**□2 possible explanations for the events
that occurred after viral dissemination
from the intestines:**



■ 1st mechanism

Virus-infected macrophages exit the bloodstream
allowing the virus to penetrate tissues

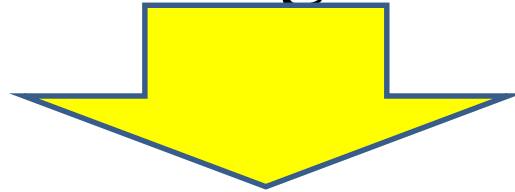
Virus attracts antibodies + complement activation =
more macrophages and  atrophils are attracted =

Lesions

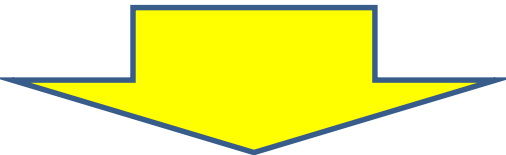
As a result: typical omatous changes
develop

- **2nd mechanism**

FIP occurs as a result of circulating immune complexes exiting the circulation



In the walls of blood vessels Activation of complement

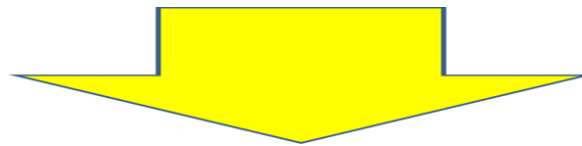


Leading to the development of granulomatous changes.

The deposition of immune complexes is very likely to occur



At the sites of arterial hypertension and turbulence = At the level of blood vessel bifurcations




PIF lesions are common in the sites of arterial hypertension and turbulence

Peritoneum, kidneys, uvea

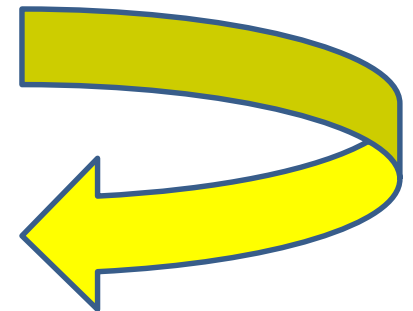
Development of PIF

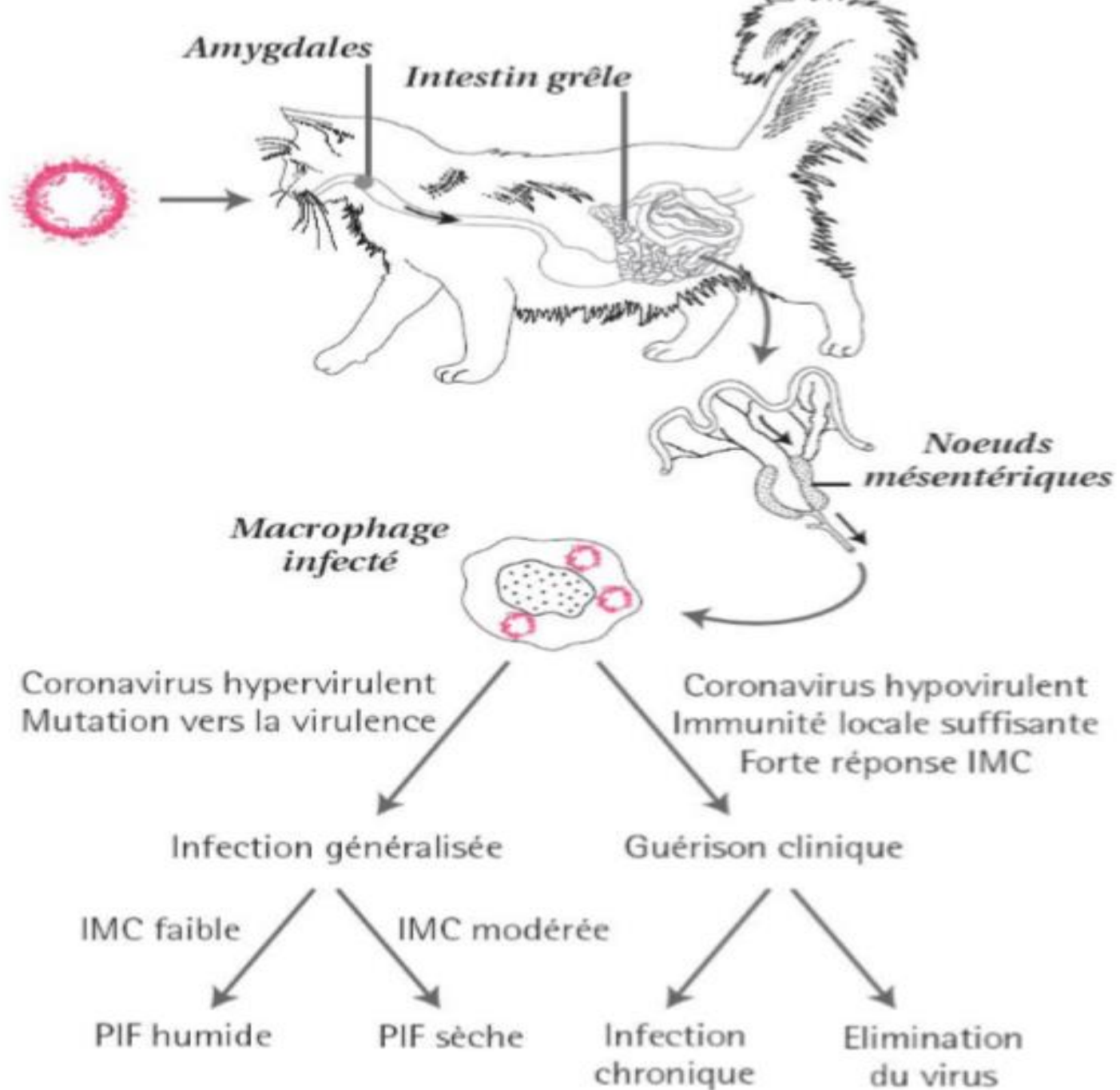
□ If: Strong cellular response = No clinical signs
and viral replication will be halted.

□ If: Replication of virulent strains in
macrophages 2  forms of disease, depending on
the host's immune response:

Dry form of PIF.

Wet form of PIF.





❖ Dry PIF (non-effusive)

- ❑ Partial immune response: Average humoral and a weak cellular response.
- ❑ Characterized by: Pyogranulomatous to granulomatous inflammation in various organs (kidneys, liver, lungs, brain, eyes), especially the mesenteric lymph nodes.

❖ Wet FIP (effusive)

- ❑ Humoral response occurs without cellular response.
- ❑ Characterized by an accumulation of protein-rich exudate in the thorax and/or abdomen, which generally contains a low number of cells.

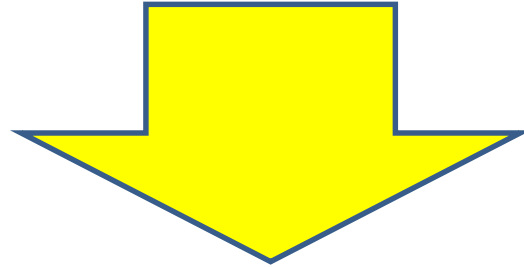
NB:

- ❑ Many cats may exhibit both forms of FIP.
- ❑ Dry FIP can progress to wet FIP.

Risk factors for FIP

- Physical characteristics and genetic factors (young age, racial predisposition).
- Stress: Overpopulation, surgery, transport, weaning, vaccination, etc.
- Viral load and virulence of the strain.

➤ Reinfection rate in communities:



Significant proportion of cats in a cattery
that chronically excrete the coronavirus.

➤ Immune status of the cat:

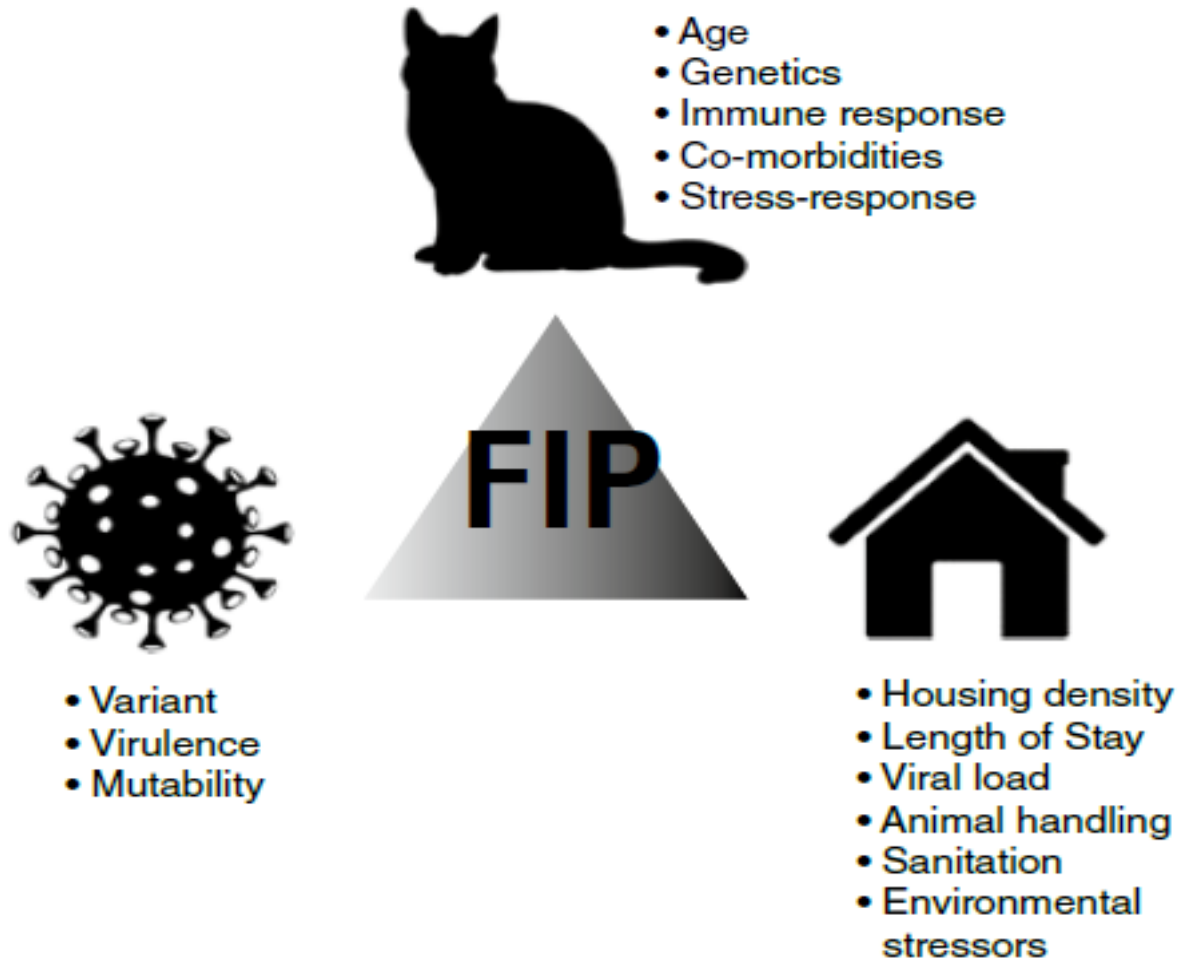
✓ Treatment with glucocorticoids.

✓ Concurrent viral infection (For

example: Feline Immunodeficiency

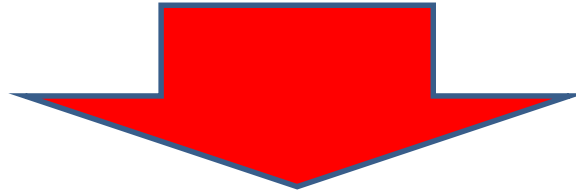
Virus 'FIV', FeLV infection).

Epidemiological triangle



The question that ALWAYS arises:

Why does one cat develop FIP while others do not exhibit it?

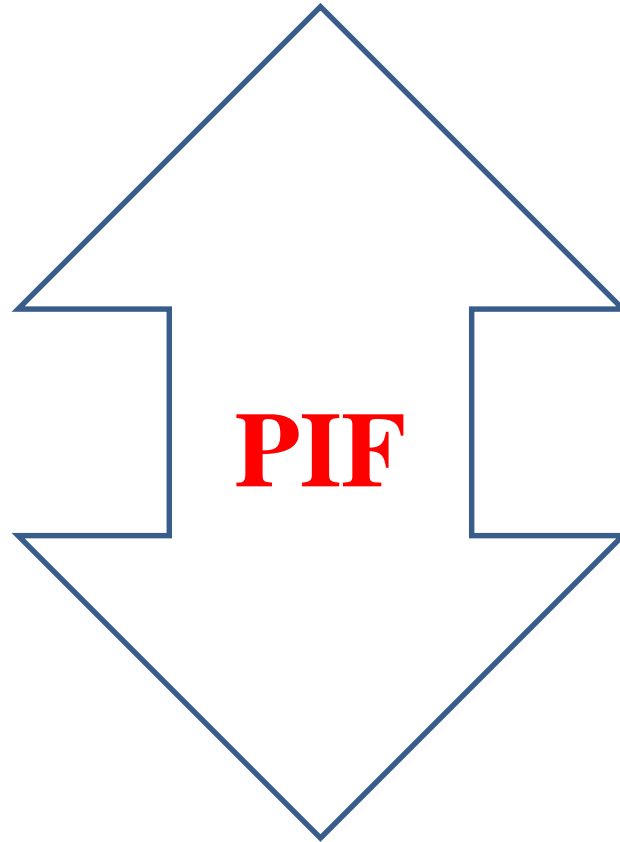


This subject is the focus of intensive research

Symptoms

Primarily affects young animals:

6 months - 2 years

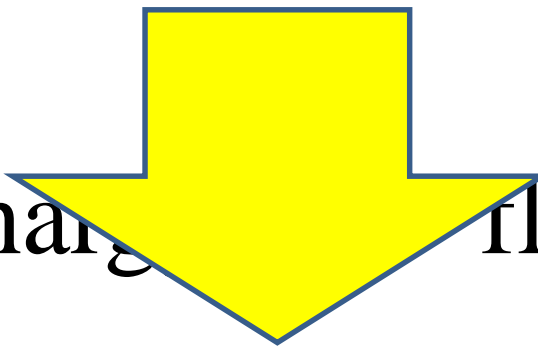


Mortality rate = 95 %

- ❑ The incubation period of PIF is highly variable.
- ❑ Difficult to objectify as the date of infection in animals is often unknown.
- ❑ Kittens are generally infected between 4 and 8 weeks, when maternal antibodies begin to decrease, but infections have been reported in kittens as young as 2 weeks.
- ❑ The disease can occur a few weeks after infection or years later, but most often 6 to 18 months after the initial infection.
- ❑ Even after the appearance of FIP, clinical signs may not be apparent for months.

□ Begins with nonspecific symptoms:

Anorexia, lethargy, fluctuating
hyperthermia (39.6-40 °C) not
responding to any therapy.



□ Chronic phase can take 2 forms:

➤ Exudative form (wet FIP): abdominal and/or thoracic effusions.

➤ Non-exudative form (dry form):

Clinical expression varies according

to the affected organs.

Wet form

Fluid collection of effusion:

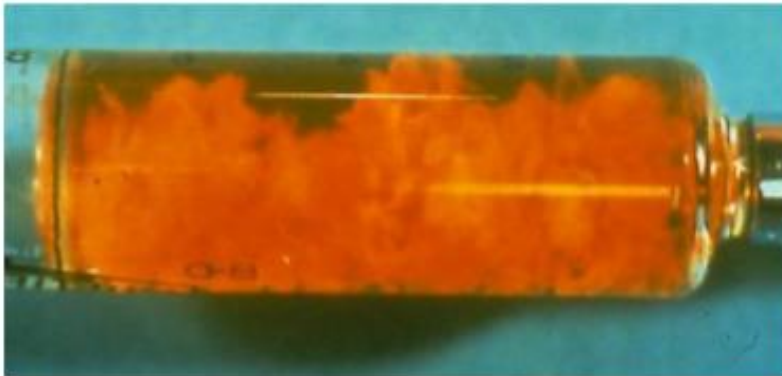
- Most often in the abdominal cavity = Ascites
Abdominal cavity distension.
- Sometimes, either together or not, in the pleural and pericardial cavities.

➤ The amount of fluid collected in the abdomen can be:

Of moderate volume, from 10 to 20 ml, or very high, up to over 1 l.

➤ The distended abdomen, with a fluid wave sign
+.

➤ Respiratory symptoms of dyspnea (often) resulting from diaphragmatic compression due to abdominal effusion or pulmonary compression due to pleural effusion.



**Forme humide de la PIF :
le chat en forme de poire**





➤ The presence of the effusion can be confirmed by a radiographic (or ultrasound) examination of the abdomen and/or chest, but especially by a paracentesis (abdomen).

➤ At the puncture=
Paracentesis

The effusion fluid is frequently: Citrine yellow, viscous and very rich in proteins.



➤ **Other symptoms:**

- ✓ The cat may be lively or subdued; Appetite preserved or anorexia.
- ✓ Temperature Mild hyperthermia (39 °C to 39.5 °C); Weight loss.
- ✓ Dyspnea, tachypnea.
- ✓ Scrotal hypertrophy.
- ✓ Dull heart sounds (weak); Pale mucous membranes or jaundice (yellowish mucosa).
- ✓ Abdominal and thoracic adhesions.

✓ Pericardial effusions can cause congestive heart failure.

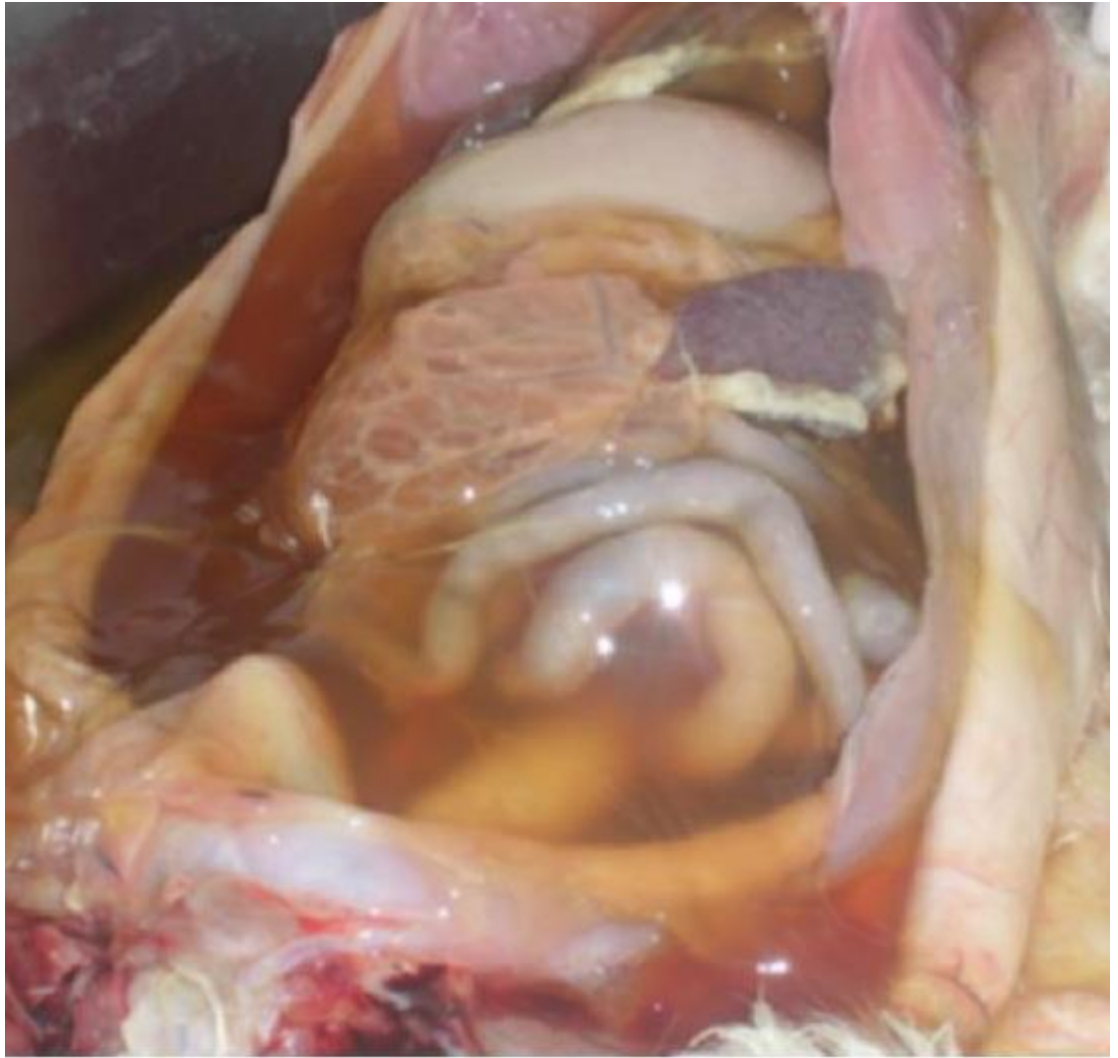
✓ Abdominal masses can be palpated, reflecting an adhesion between the omentum and the viscera, and/or hypertrophy of the mesenteric lymph nodes.

➤ The duration of disease progression can be brief, lasting a few days, especially in young cats, or conversely much longer, evolving over several weeks.

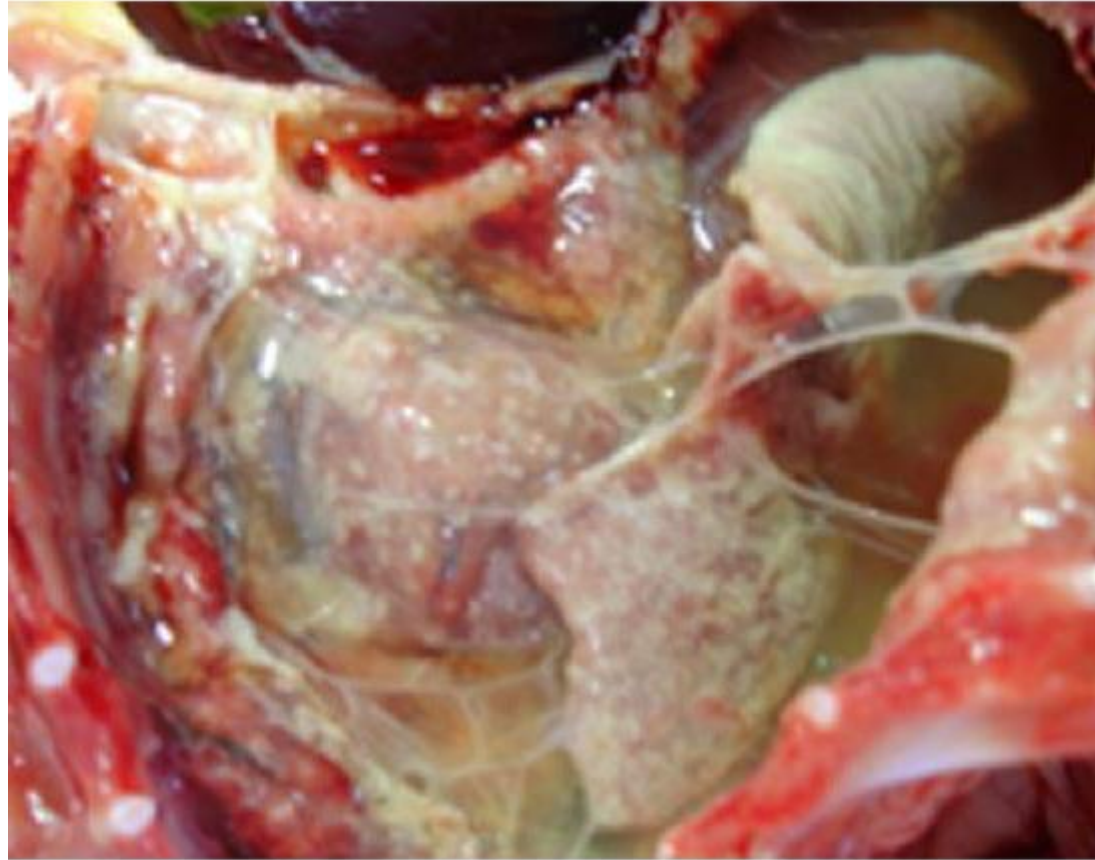
➤ **In all cases, the outcome is fatal.**

Abdominal cavity of a cat affected by wet FIP =

A considerable amount of ascitic fluid can be observed in the abdominal cavity.



Pleural cavity of a cat with wet FIP. Fibrinous inflammation of the pleura and adhesions with the lung (with strands of fibrin).



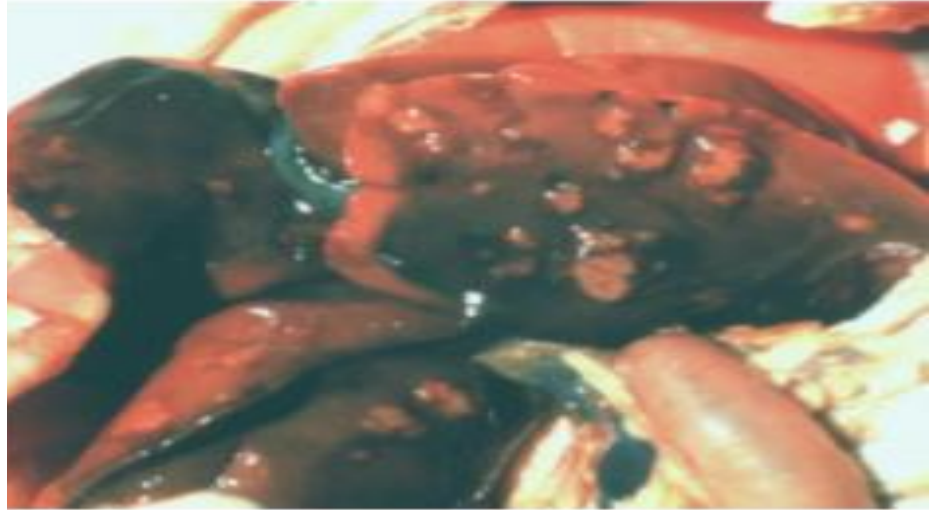
Dry form

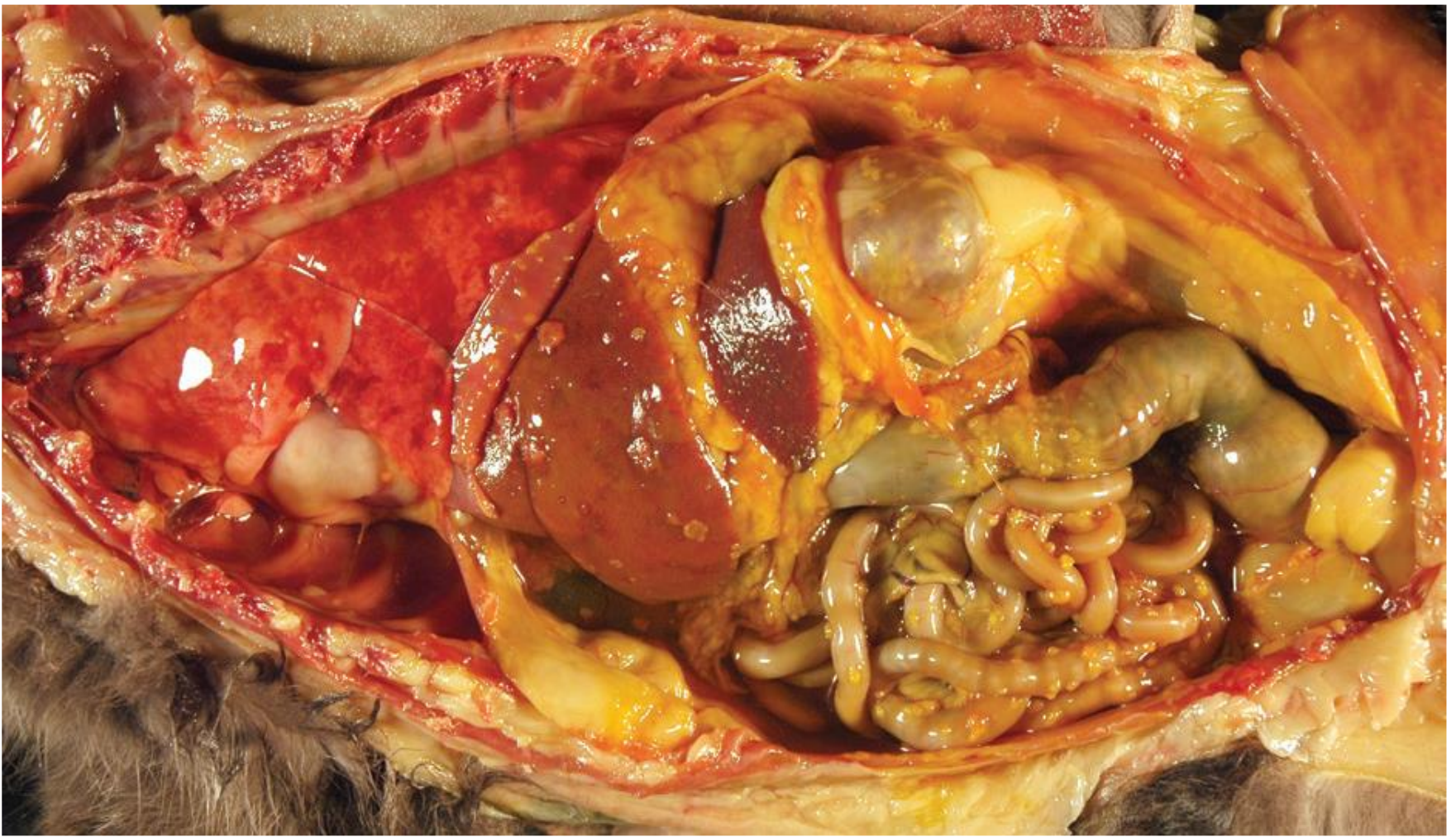
- The observed symptoms are due to granulomatous lesions of varying locations, hence the diversity of clinical presentations.
- The effusions are minimal, or even absent.

➤ Duration: 1 to 12 weeks; Fluctuating fever; Lethargy; Anorexia.

➤ Granulomatous masses on the abdominal organs (sometimes palpable).

✓ Digestive disorders: vomiting, diarrhea.





Intestinal granuloma lesions in a cat with dry FIP = Manifests as diarrhea.

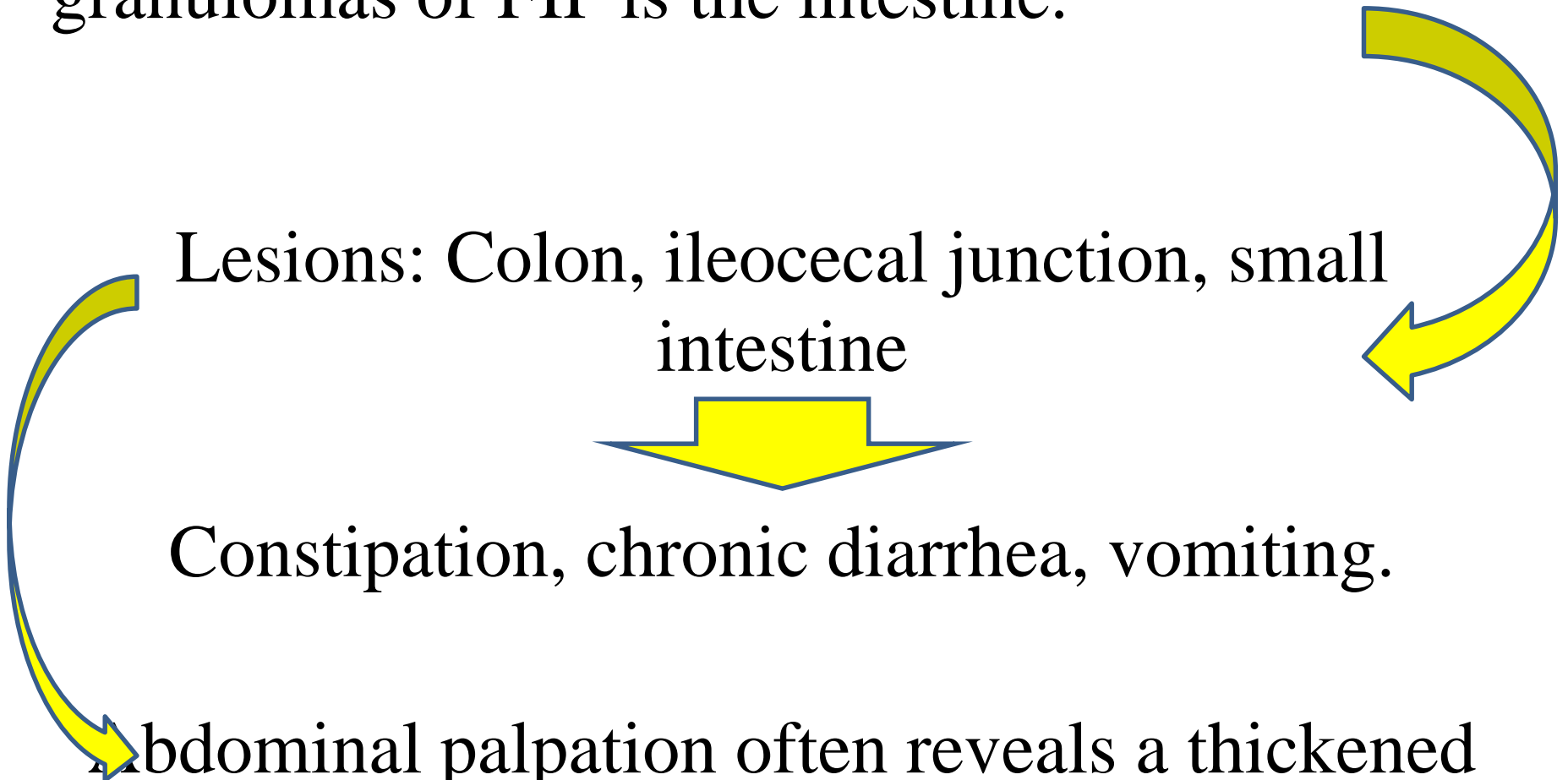
Sometimes, the only organ affected by the granulomas of FIP is the intestine.

Lesions: Colon, ileocecal junction, small intestine




Constipation, chronic diarrhea, vomiting.

Abdominal palpation often reveals a thickened intestine



✓ Frequently, involvement of the central nervous system is manifested by nonspecific symptoms:



Posterior paresis, paralysis, incoordination, nystagmus, hyperesthesia, vestibular disorders, seizures, behavioral disturbances, etc.

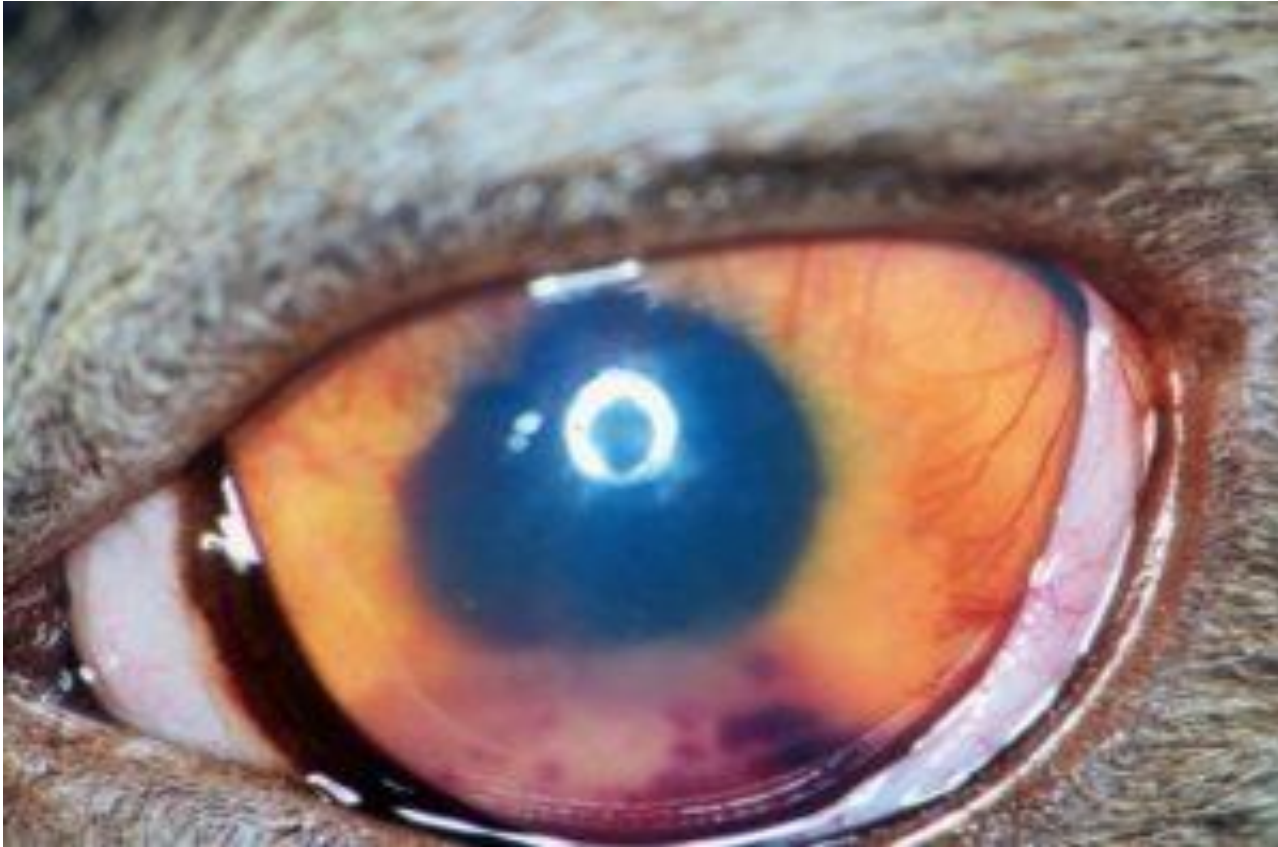
✓ Ocular forms are also very common and often coexist with neurological symptoms:

Chorioretinitis, serous retinal

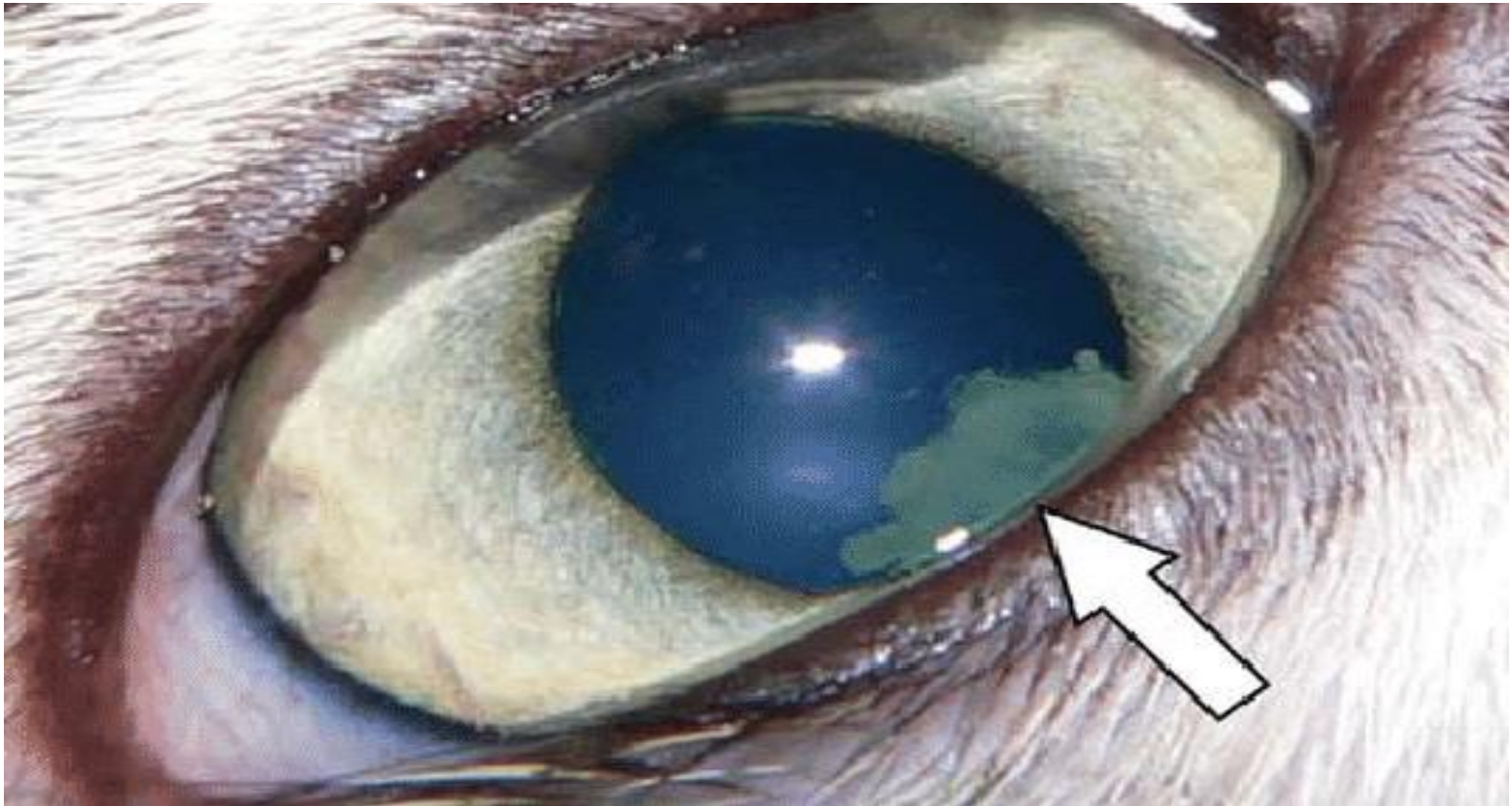
detachment, anterior or posterior uveitis =

Precipitates in the anterior chamber of the

eye, hyphema, etc.



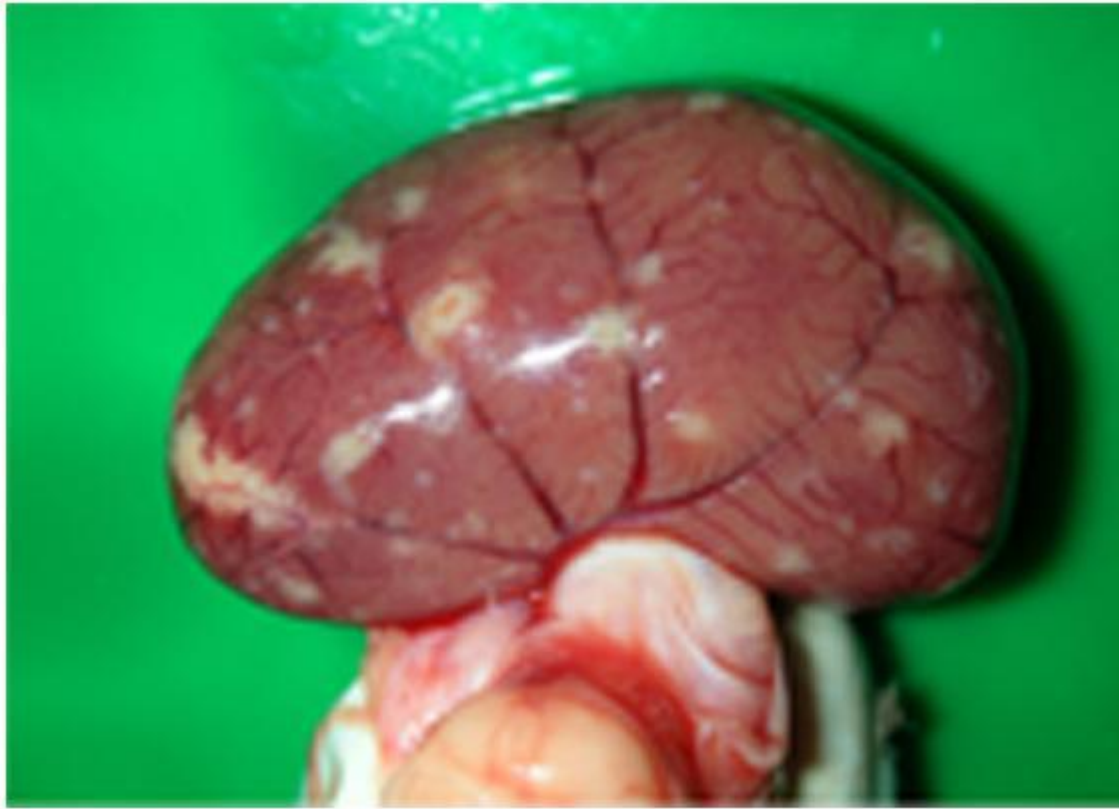
Anterior uveitis associated with FIP can present in various ways, for example with the presence of inflammatory precipitates.



Mild anterior uveitis (FIP). Fibrin formation = hypopyon.

✓ Renal involvement: polyuria, polydipsia
(renal failure).

✓ Liver damage: Liver failure:
Hepatomegaly, jaundice, polydipsia,
vomiting.



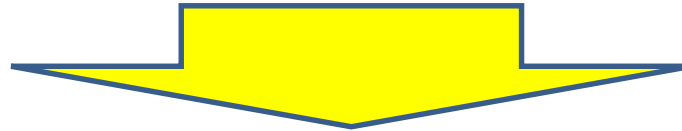
Kidney of a cat affected by dry FIP. Granulomatous lesions may be observed on the capsular surface and in the kidney parenchyma.

➤ Skin lesions

➔ Non-pruritic papules: Slightly elevated intradermal, well-circumscribed, ≈ 2 mm in diameter, on: Neck, forelimbs, and lateral thoracic wall regions.

Skin fragility similar to that associated with Ehlers-Danlos syndrome.

Evolution of the two forms



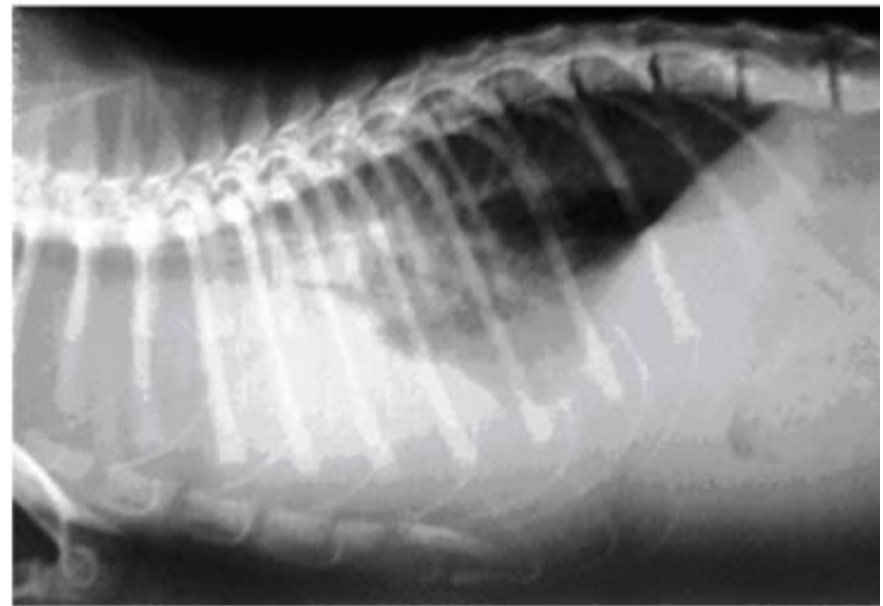
- Cats with the effusive form of FIP generally have a more rapid progression and often die within 2 months of the first clinical signs.
- The non-effusive form may progress more slowly; some cats live several months or even several years.

Lesions

Wet form

Characteristic lesions:

- Abdominal, pleural, or pericardial effusions rich in fibrin.
- Fibrin deposits can be demonstrated on the serous membranes of the abdominal and thoracic cavities.



Forme humide de PIF: abondant liquide d'ascite jaunâtre observable à la palpation. l'abominocentèse. l'autopsie et l'imagerie

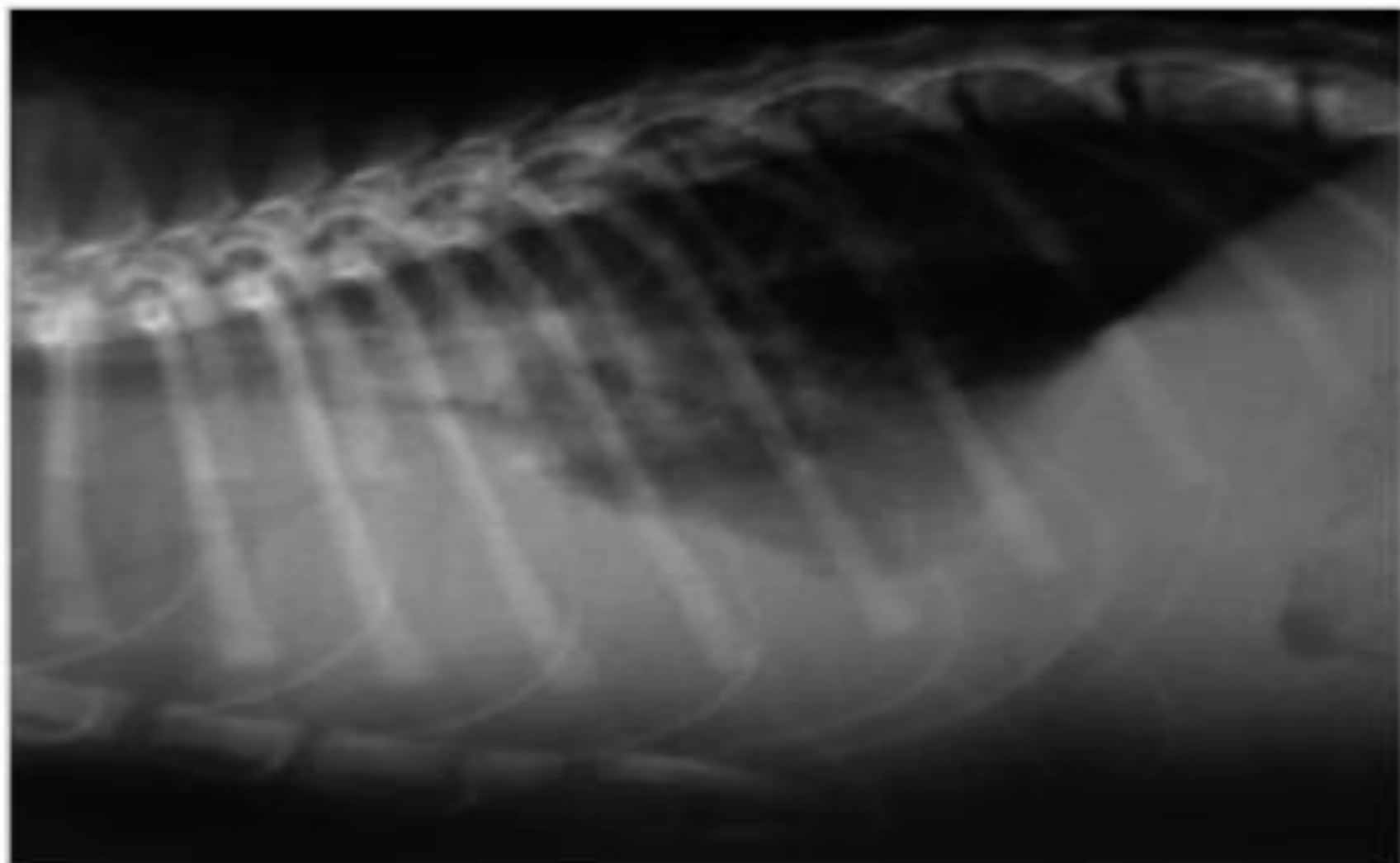


Photo d'Albert Loret

- Radiographie d'un chat atteint de PIF montrant des épanchements thoraciques

A, Gross necropsy findings in a 10-month-old male intact domestic shorthair cat with effusive FIP. Approximately 1.2 liters of yellow fluid was present in the abdomen, and there are abundant fibrin strands adherent to the visceral and parietal peritoneal surfaces.

B, Kidneys of the cat. Multiple, pale tan firm nodules expand the renal cortices and protrude from the cortical surfaces.



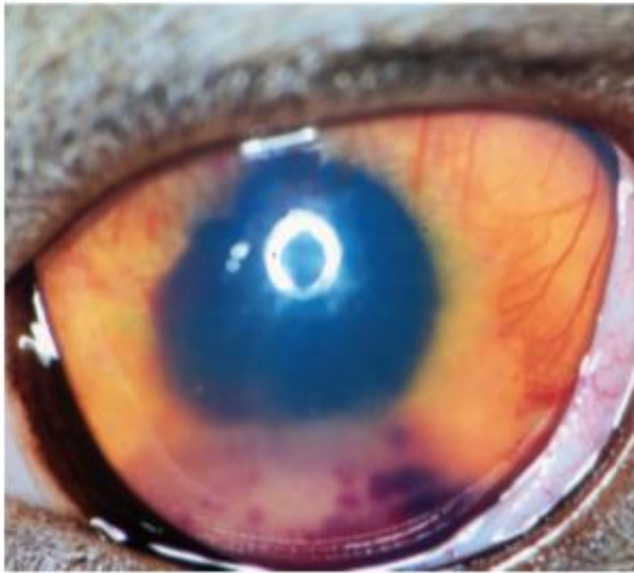
- **Miliary nodules:** Whitish appearance, size of a pinhead, or even a small pea/Perivascular granulomatous lesions.

Clinical examination results of a 4-month-old intact female British shorthair cat with effusive FIP; the surface of the kidney was scattered with miliary white nodules.

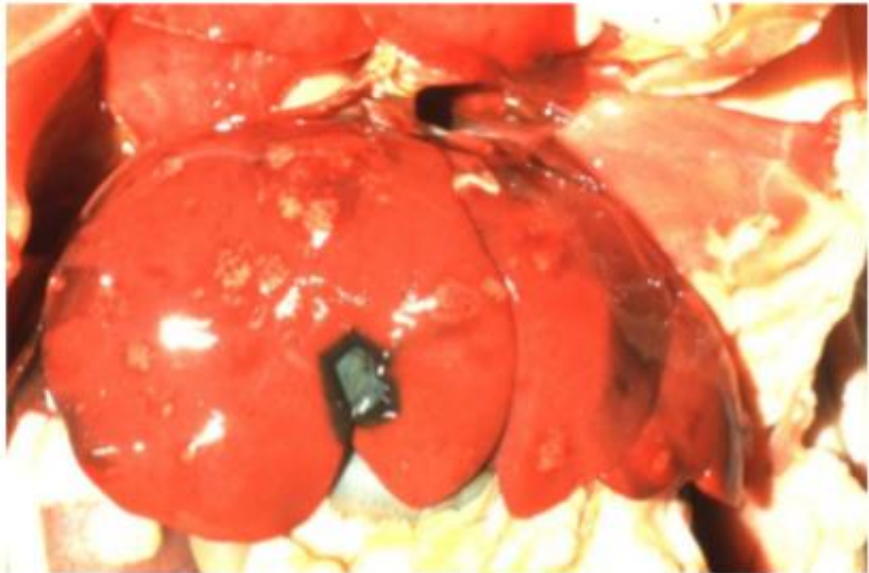


Dry form

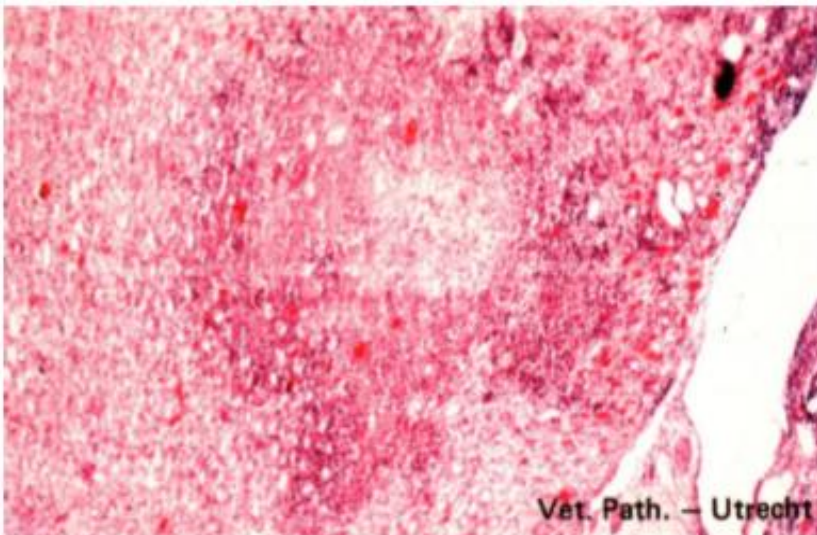
- Granulomatous lesions in the form of pyo-granulomatous foci located around small blood vessels in the various affected organs (intestine, kidney, liver, CNS, etc.).



Uvéite



Granulomes sur le foie



**Granulome dans le rein
(histopathologie)**

Le centre est rempli de cellules
nécrosées et de neutrophiles,
entouré par des phagocytes, des
lymphocytes et des plasmocytes

Lésions – forme sèche de la PIF

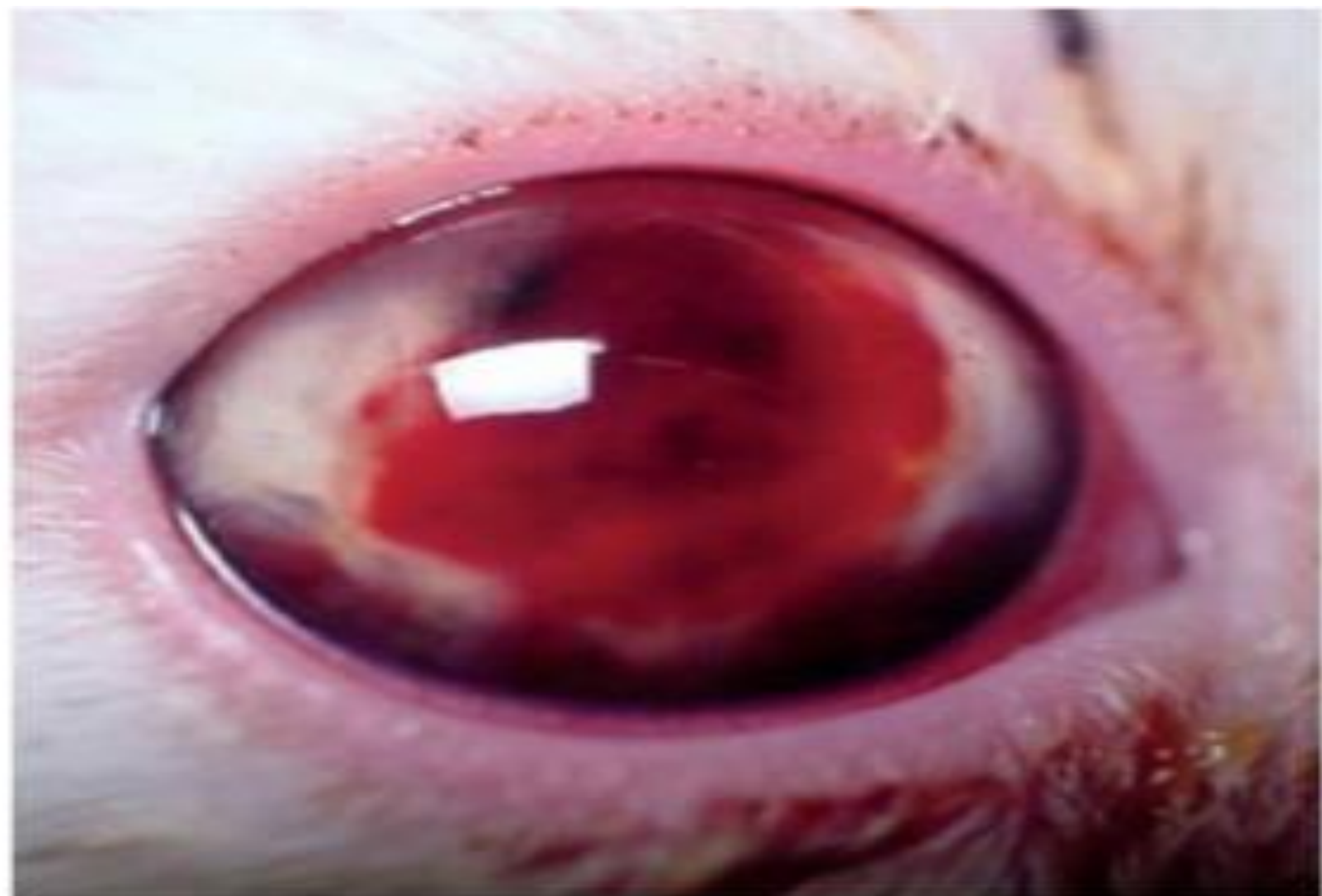


Photo d'Alhart / Inrat

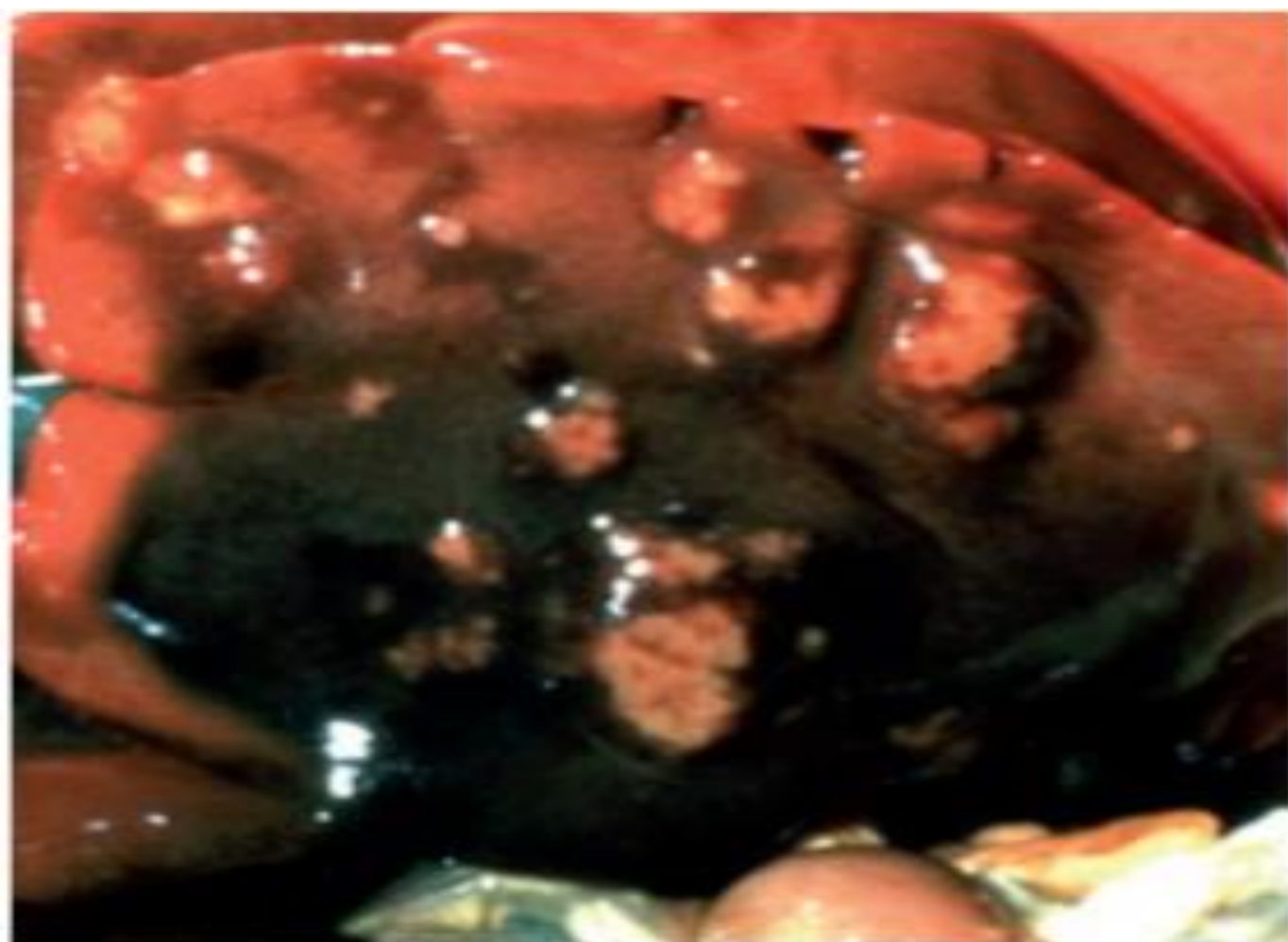
■ Hyphéma chez un chat atteint de PIF.

Kidney of a kitten
with a dry form of
FIP: Presence of
numerous granulomas
on the capsule.



Detail of a
pyogranulomatous
lesion of the kidney





- **Forme sèche de PIF : lésions granulomateuses hépatiques.**

Diagnostic

Differential clinical diagnosis

- Difficult: No pathognomonic signs of FIP.
- In exudative forms, the differential diagnosis aims not to confuse this viral effusion with other causes of thoracic and/or abdominal effusions.

➤ In dry forms, the differential diagnosis is even more difficult given the wide variety of potentially observable symptoms.

Épanchements thoraciques	Pleurésies bactériennes Insuffisance cardiaque Tumeur (lymphosarcome) Chylothorax
Épanchements abdominaux	Péritonites bactériennes Ascite d'origine cardiaque, hépatique, rénale Tumeur Épanchements chyliformes
Fièvre d'origine indéterminée	FeLV, FIV Toxoplasmose Abscess
Hyperglobulinémie	Infection bactérienne chronique Gammopathie monoclonale (lymphosarcome)
Insuffisance hépatique	Anémie hémolytique (hémobartonellose, FeLV, toxique, auto-immune) Complexe cholangiohépatite Infiltration néoplasique Obstruction biliaire
Insuffisance rénale	Insuffisance rénale chronique idiopathique Toxicité (anti-inflammatoire non stéroïdien) Maladie kystique Pyélonéphrite Obstruction des voies urinaires Infiltration néoplasique
Lésions oculaires	FeLV, FIV, Toxoplasmose
Troubles neurologiques	FeLV, FIV Toxoplasmose Encéphalopathies métaboliques Ischémie Infiltration néoplasique

FeLV : virus leucémogène félin ; FIV : virus de l'immunodéficience féline.

➤ In summary, clinical elements only help to direct suspicion and it is important to rely on:

- Epidemiological elements (especially the age of the cat, origin, and known epidemiological contacts).
- Additional laboratory tests.

Laboratory diagnosis

□ Analysis of effusion fluid

➤ Wet form = Effusion fluid:

- ✓ High density > 1.017 (1.030–1.040).
- ✓ Rich in protein (> 3.5 g/dL) ($>50\%$ globulins).
- ✓ Low nucleated cell count (< 5000 cells/ μL), in contrast with effusions related to septic peritonitis.

Composition of Body Cavity Effusions from 21 Cats with Necropsy-Confirmed Feline Infectious Peritonitis at the UC Davis VMTH

Test	Range	Mean \pm SD	Number of Cats Tested
Total protein (g/dL)	2.9-8.1	5.1 \pm 1.8	21
RBC (cells/ μ L)	<100-38,600	ND	18
TNC (cells/ μ L)	200-13,200	3683 \pm 3474	19
Neutrophils (%)	3-97	61 \pm 28	21
Lymphocytes (%)	0-22	6 \pm 6	21
Monocytes (%)	1-96	33 \pm 26	21

Nineteen specimens were abdominal and two were pleural effusions. ND, Not determined; SD, standard deviation; TNC, total neutrophil count.

Red blood cells (RBC)

The high protein content of the effusion parallels increased gammaglobulin levels; thus, a low albumin/globulin (A:G) ratio in an effusion is highly predictive of PIF.

- An A:G ratio > 0.8 almost certainly excludes PIF.
- With values between 0.45 and 0.8, PIF remains a possibility.
- An A:G ratio < 0.45 + [proteins] > 3.5 g/dl + low cellularity (mainly consisting of neutrophils and macrophages) = is highly predictive of wet PIF.

▪ Rivalta Test

The Rivalta test is a relatively easy test to implement = It can contribute to the diagnosis of wet FIP.



**To differentiate a Transudate from an
Exudate (FIP)**

Exudate

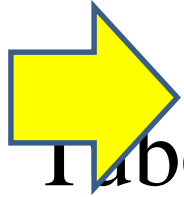
Fluid accumulation of serous nature due to a modification of the permeability of the membrane resulting from inflammation, containing a high concentration of leukocytes.

Transudate

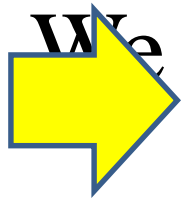
Extracellular fluid obtained by transudation from blood vessels and mechanically secreted from a non-inflamed surface of the organism through an epithelium (mucous or serous), by osmotic pull or by pressure during vascular stasis.

It is differentiated from exudate by its low protein content ($< 30 \text{ g/l}$) and leukocytes ($< 300/\text{mm}^3$), as well as by its origin, which is inflammatory

Method and interpretation



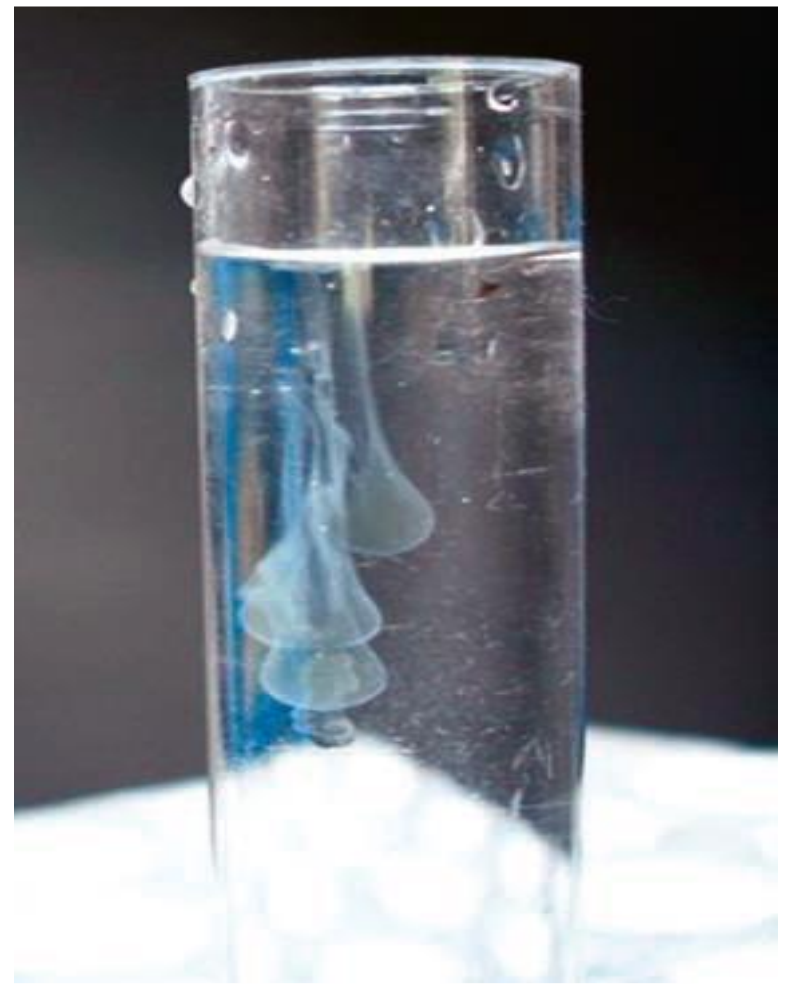
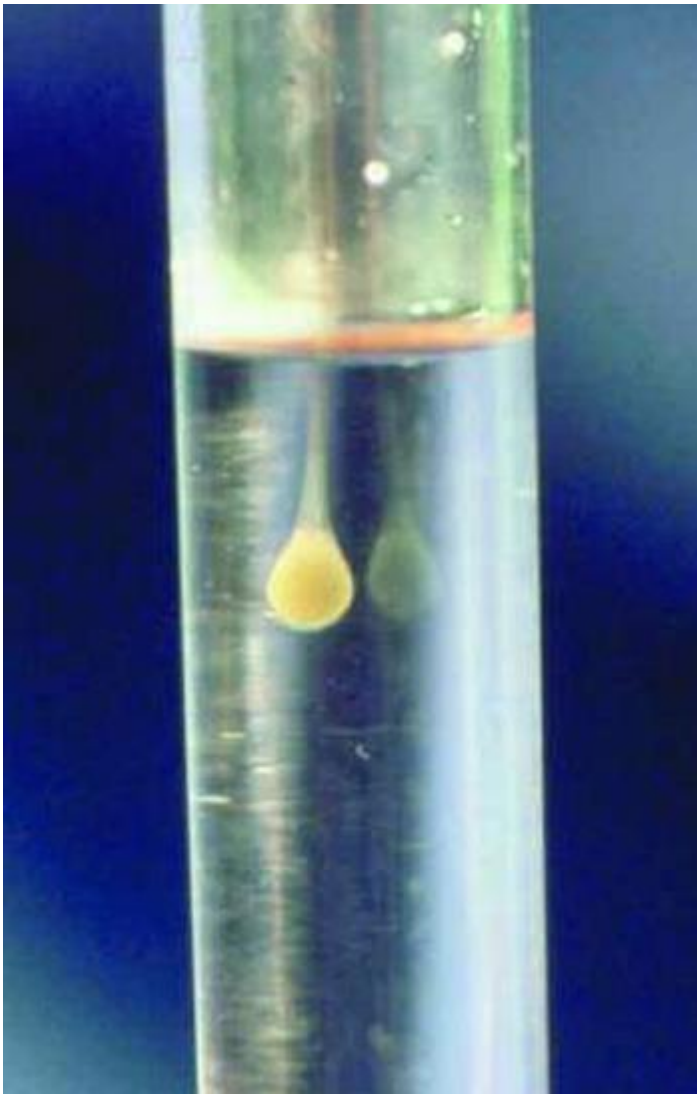
Tube filled with distilled water (5ml) + 1 drop of 98% acetic acid (white vinegar).



We add a drop of abdominal or pleural effusion taken from the sick cat.

○ **Positive test (Exudate = PIF):** The drop remains attached to the surface of the liquid, retains its shape with a connection to the surface (floats); or sediment slowly at the bottom of the tube in the form of a drop or jellyfish.

○ **Negative test (Transudate = No PIF):** Indicated by the disappearance of the drop = the solution remains clear.



Positive Rivalta test

❖ **Result + :**

Is not specific to PIF. Positive results have been reported in cats without PIF; also in cases of septic peritonitis and lymphoma.

A positive result requires confirmation of PIF with other tests.

❖ Negative Rivalta test :

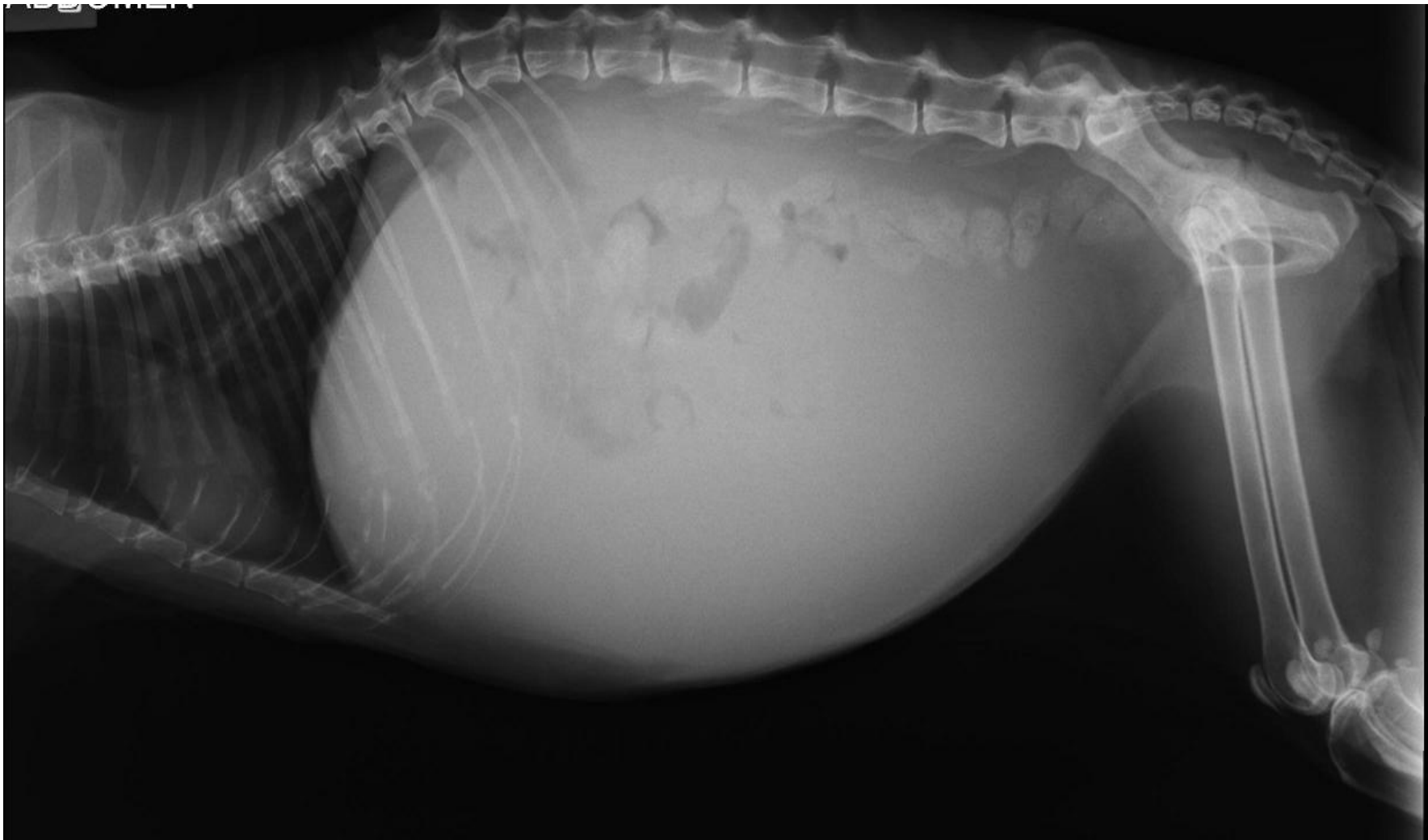
PIF can be excluded quickly and at low cost.

□ Imaging

Most commonly used techniques:
Radiography, Ultrasound

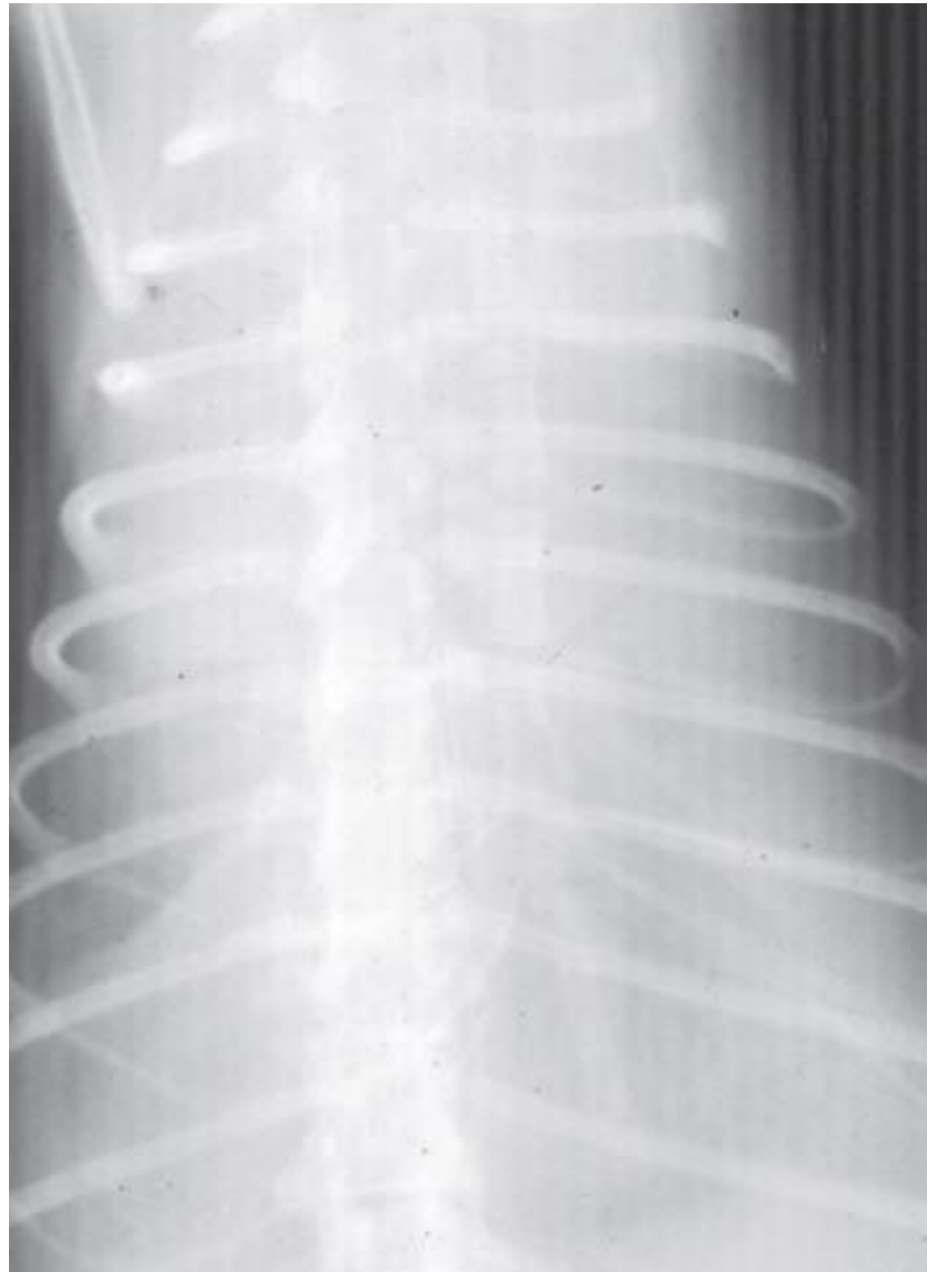


Confirmation: Ascites, granulomas.

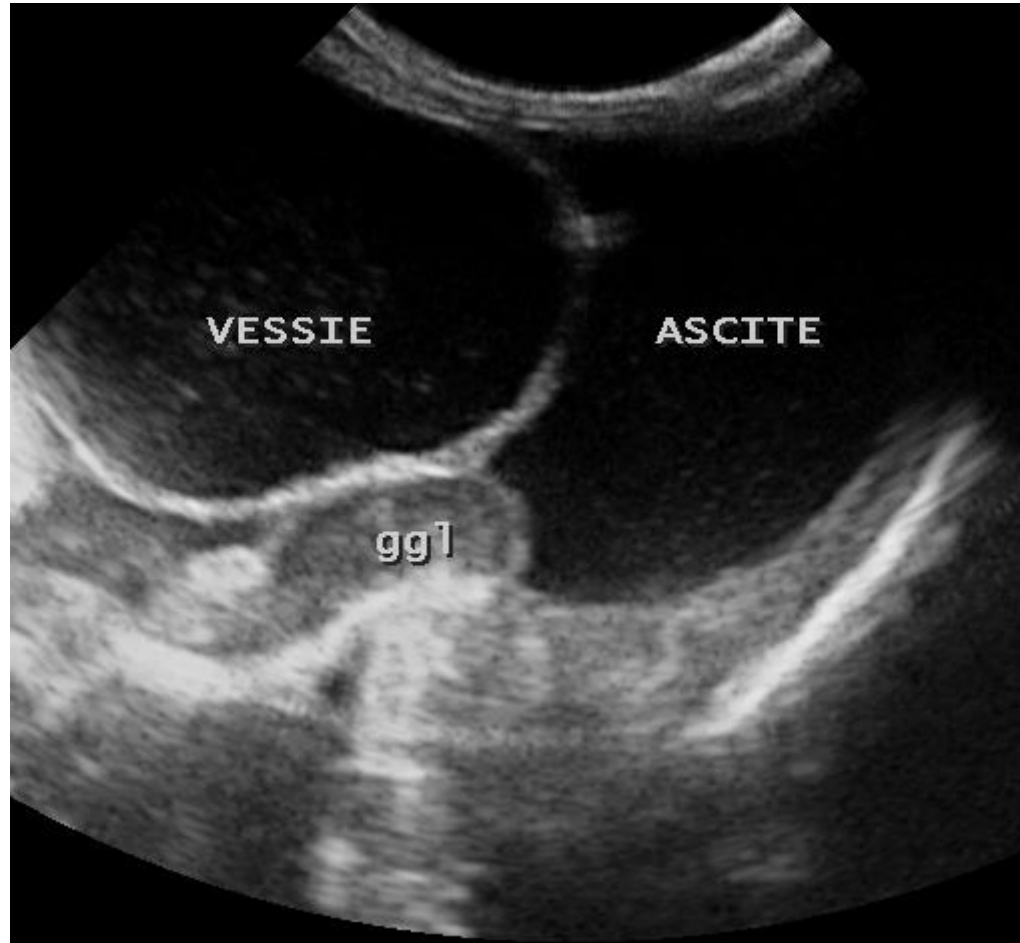
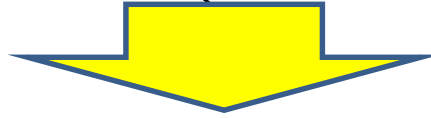


Confirm the presence of abdominal fluid through radiography

Radiograph of a
cat with FIP and
thoracic effusion.



Ascites (wet FIP)





Lateral thoracic radiograph from a 9-month-old male neutered domestic shorthair cat with FIP and pyogranulomatous pneumonia. There is a severe, diffuse, patchy alveolar and nodular interstitial pattern with thickening of the bronchial walls and mild pleural effusion.

■ **Biochemical tests**

- Serum biochemical profile: Variety of possible abnormalities depending on the organ involvement.
- Liver lesions: Hyperbilirubinemia, Hyperbilirubinuria; Increased alkaline phosphatase and alanine aminotransferase.

➤ Elevation of urea and creatinine concentrations reflects renal involvement.

➤ Increase in total proteins
(hypergammaglobulinemia): >78 g/l

In:

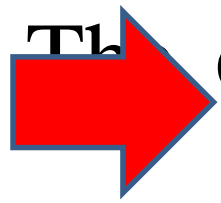
50% of cats affected by the wet form.

75% of cats affected by the dry form.

➤ Electrophoresis



Hyperproteinemia (hyperglobulinemia)



The electrophoretic pattern of proteins shows

that there is particularly an increase in the

fractions:

Alpha-2, Beta, and Gamma globulins

Findings on Serum Biochemistry Analysis in 36 Cats with Necropsy-Confirmed Feline Infectious Peritonitis at the UC Davis VMTH

Test	Reference Range	Percent below the Reference Range	Percent within the Reference Range	Percent above the Reference Range	Range for cats with FIP	Number of Cats Tested
Sodium (mmol/L)	151-158	94	6	0	129-152	35
Potassium (mmol/L)	3.6-4.9	26	74	0	2.2-5.4	35
Chloride (mmol/L)	117-126	91	9	0	94-121	35
Bicarbonate (mmol/L)	15-21	8	75	17	12-25	36
Calcium (mg/dL)	9.0-10.9	56	44	0	6.6-10.6	36
Phosphorus (mg/dL)	3.2-6.3	8	69	22	1.9-8.4	36
Creatinine (mg/dL)	1.1-2.2	69	28	3	0.4-2.8	36
BUN (mg/dL)	18-33	56	31	14	10-58	36
Glucose (mg/dL)	63-118	0	47	53	63-381	36
Total protein (g/dL)	6.6-8.4	31	28	42	4.1-11.9	36
Albumin (g/dL)	2.2-4.6	50	50	0	0.9-3.6	36
Globulin (g/dL)	2.8-5.4	3	42	56	2.5-9.4	36
Cholesterol (mg/dL)	89-258	17	83	0	56-247	36
Total bilirubin (mg/dL)	0-0.2	0	40	60	0-5.3	36
ALT (U/L)	27-101	50	25	25	18-648	36
AST (U/L)	17-58	6	43	51	0-1554	36
ALP (U/L)	14-71	28	61	11	0-161	36
GGT (U/L)	0-4	0	96	4	0-5	23

FIP, feline infectious peritonitis.

- **Complete blood count:**

Half of the cats affected by FIP gradually develop a non-regenerative anemia, frequently associated with leukocytosis with neutrophilia and lymphopenia in the terminal stages.

Complete Blood Count Findings at Admission in 38 Cats with Necropsy-Confirmed Feline Infectious Peritonitis at the UC Davis VMTH

Test	Reference Range	Percent below the Reference Range	Percent within the Reference Range	Percent above the Reference Range	Range for Cats with FIP	Number Tested
Hematocrit (%)	30-50	68	32	0	17-53	38
MCV (fL)	65-75	18	82	0	36-52	38
MCHC (g/dL)	33-36	5	58	37	28-36	38
RDW (%)	14-18	0	30	70	14-33	27
Neutrophils* (cells/ μ L)	2000-9000	3	26	71	416-49,313	38
Band neutrophils* (cells/ μ L)	0-rare	0	50	50	0-3251	38
Metamyelocytes (cells/ μ L)	0	0	95	5	0-276	38
Monocytes (cells/ μ L)	50-600	5	71	24	0-820	38
Lymphocytes (cells/ μ L)	1000-7000	58	42	0	89-6886	38
Eosinophils (cells/ μ L)	150-1100	71	29	0	0-770	38
Platelets (cells/ μ L)	180,000-500,000	37	44	19	30,000-874,000	27 [†]

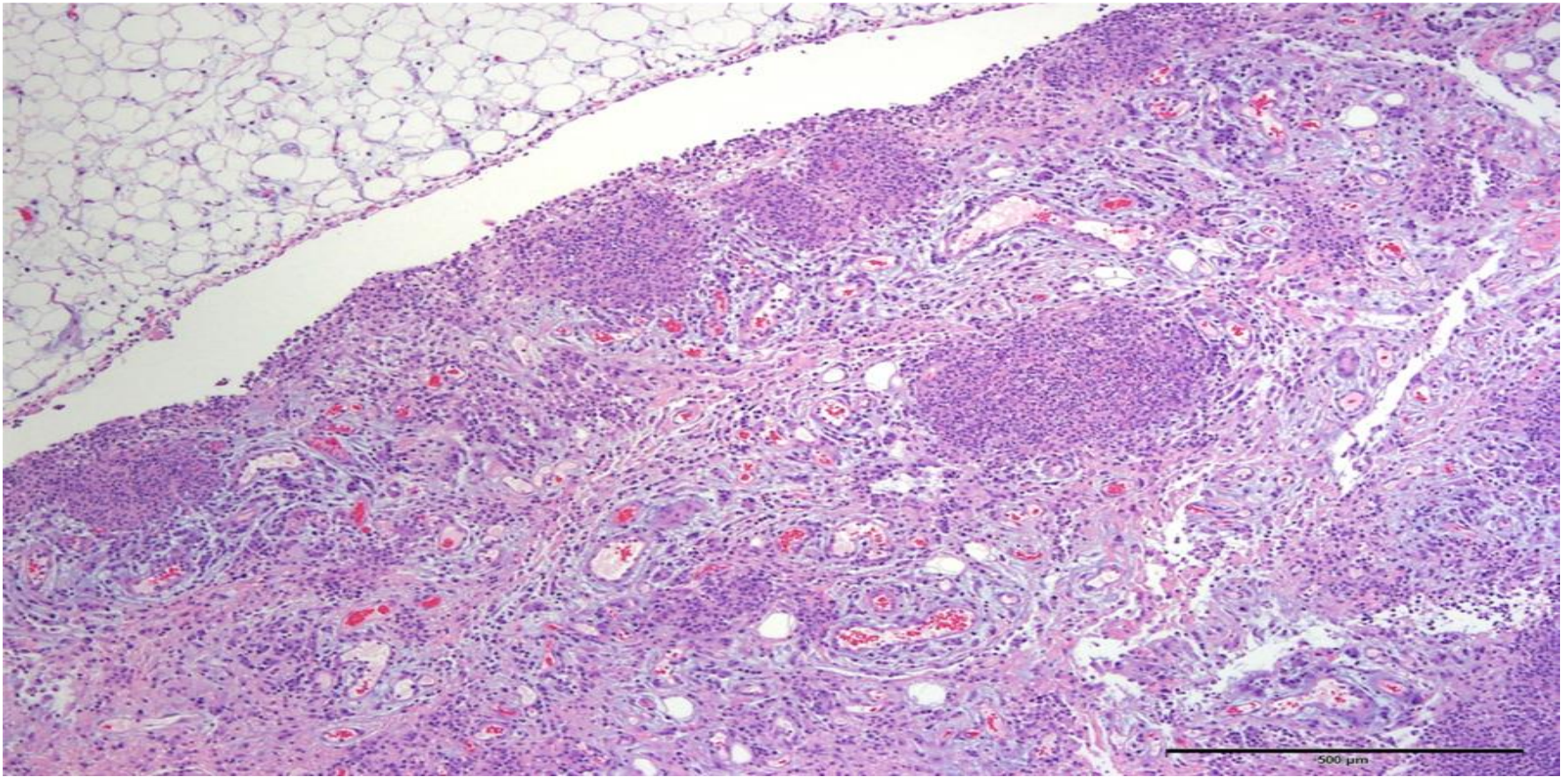
FIP, Feline infectious peritonitis; RDW, red cell distribution width.

*22 (58%) had evidence of toxic neutrophils.

■ **Histology**

➤ The specimens to prioritize: Kidney, liver, spleen, mesentery, and the mesenteric lymph node.

Histological analysis: Lesions of vasculitis, peri-vasculitis, necrotizing pyogranulomatous inflammation, fibrino-necrotizing inflammation of the serosa, and mesothelial hyperplasia.



The omentum is significantly dilated by pyogranulomatous inflammatory nodules. Blood vessels are prominent (H & E stain).

▪ **Detection of FCoV antibodies (rapid test)**

➤ ELISA

➤ Indirect immunofluorescence.

➤ Antibodies can be sought in the serum, but also in the effusion fluid.

Speed F-Corona (Virbac)

Rapid detection of feline anti-Coronavirus antibodies.

Method: Membrane
Immunochromatography

Analysis: Search for specific antibodies directed against feline coronavirus (FCoV)

Sample: Whole blood with anticoagulant, plasma or serum, and ascitic fluid

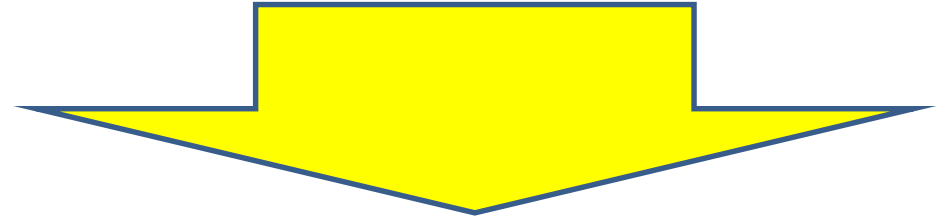
Handling: 2 minutes

Reading: 15 minutes



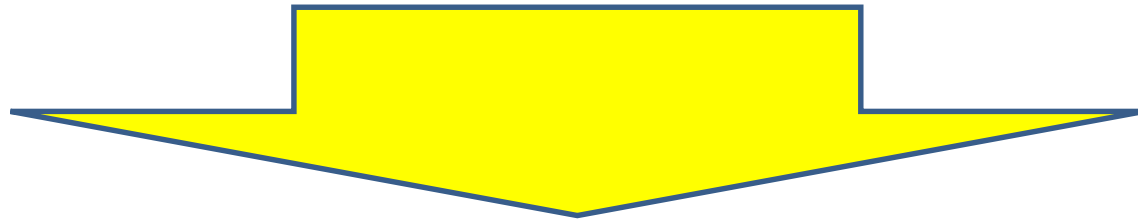
➤ Result + (only: clinically healthy cat) =

Not a diagnosis for FIP:



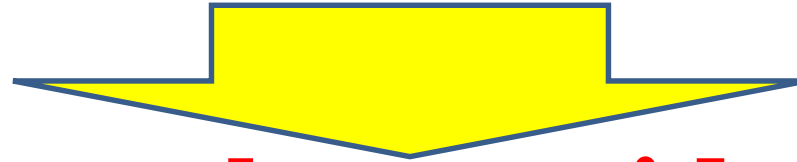
Unable to differentiate antibodies induced
by benign strains from those induced by
strains responsible for FIP.

➤ Result + with clinically ill Animal
(Clinical chart) with Confirmation by
other complementary examinations



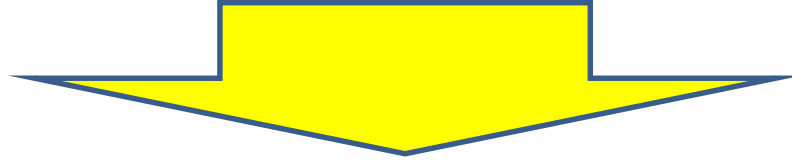
FIP

➤ Result - (only: clinically healthy cat)



**Chat can be considered as
unaffected**

➤ Result - (Sick cat): Does not exclude the PIF



NB:

Approximately 10% of cats with advanced stages of the disease do not produce antibodies, due to severe immunosuppression.

■ PRC

- Very sensitive, specific.
- Detect the genome of feline coronaviruses in samples: blood, effusion fluid, cerebrospinal fluid, feces.
- The test for effusions is more sensitive than that of blood.
- PCR targeting FCoV cannot differentiate between benign and virulent strains.

➤ **Real-time PCR test for messenger RNA has been developed to detect a specific mutation in the 'Spike' protein that leads to the virus's inability to replicate in enterocytes.**

The test detects mutated virus.



- **Immunostaining of the antigen (FCoV)**

- The FCoV antigen can be detected in the effusion or tissue macrophages in biopsy samples.

- A positive test confirms a diagnosis of FIP (effusion, tissues).

Assays Available for Diagnosis of Feline Infectious Peritonitis

Assay	Specimen Type	Target	Performance
Fluorescent or immunoperoxidase antibody staining	Wash or effusion specimens, tissue aspirates, tissues obtained at biopsy or necropsy	FCoV	Gold standard for diagnosis. False negatives can occur in specimens that contain low numbers of macrophages or virus particles, or when virus is complexed by antibody. Immunofluorescence is more sensitive than immunoperoxidase methods. Non-specific staining may be interpreted as positive results by untrained personnel.
Serology	Blood, CSF, aqueous humor, effusion fluid	FCoV antibody	Positive antibody titers reflect only antibodies to a coronavirus and are not specific for a diagnosis of FIP. Most cats in multicat households test positive. Negative titers can occur in cats with advanced FIP. High titers in cats that do not reside in multicat households and that have signs suggestive of FIP may support the diagnosis. Interlaboratory variation in methodology and titer reporting occurs.
RT-PCR	Blood, wash or effusion specimens, tissue aspirates, tissues obtained at biopsy or necropsy	FCoV RNA	Does not differentiate between virulent and avirulent FCoV strains, and avirulent strains may be found in tissues and blood. Sensitivity and specificity can vary depending on assay design. False negative results occur when virus levels are low, when variant virus strains are present, or as a result of degradation of viral nucleic acid during specimen transport.
Histopathology	Usually necropsy specimens, but also biopsies	Inflammatory lesions induced by FCoV (pyogranulomatous vasculitis)	Biopsy is often not feasible antemortem as a result of critical illness and coagulopathies.

FCoV, feline coronavirus; FIP, feline infectious peritonitis; RT-PCR, reverse transcriptase–polymerase chain reaction.

Treatment

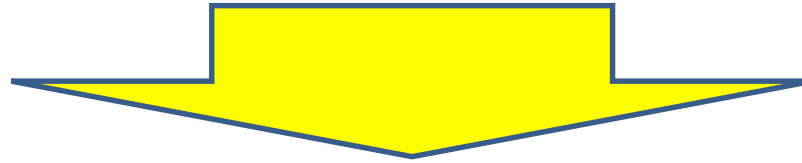
- There are currently no therapeutics with demonstrated efficacy.
- Treatments only aim to improve the comfort of the animal = Symptomatic treatment.

➤ *Correct dehydration = Fluid therapy*

(IV; SC).

➤ *Nutritional support (IV; SC).*

➤ Anti-inflammatory and immunosuppressive.



Decrease inflammation = vasculitis

- Corticosteroids: Prednisolone (2–4 mg/kg/Day PO). The dose is gradually reduced every 10 to 14 days until the optimal dosage for the cat is determined.
- Chlorambucil (2 mg/cat PO every 48–72h).

➤ *Antivirals*


- Ineffective and may cause serious side effects.

- Example:

Zidovudine (AZT); Foscarnet; Ribavirin (16.5 mg/kg/24 h for 10 to 14 days; PO, IV or IM. Ribavirin is a nucleoside analogue that prevents the formation of viral proteins); GC376 (promising results).

➤ Immuno-modulators

Interferon (feline IFN, human IFN)

Effective in vitro; limited success in vivo.

Immunomodulator drugs that can be used for the treatment of FIP

DRUG	DOSE
Human interferon alfa-2b	30 units/cat PO q24h on alternating weeks
Feline interferon-omega	Non-effusive form: 50,000 U/cat PO q24h until albumin, globulins, hematocrit and lymphocyte count return to within normal limits and there is improvement in clinical signs Effusive form: 1 mega-unit/kg injected into the cavity site of effusion. If the latter is not possible, SC administration every other day, then once a week, once in clinical remission
Polyprenyl immunostimulant	3 mg/kg PO 2–3 times a week for non-effusive FIP

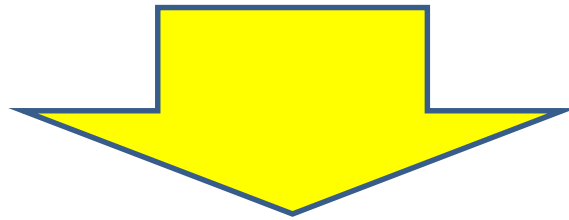
➤ Antibiotic therapy

○ Ineffective as they are generally not associated with secondary bacterial infections.

○ Moraillon et al., 1997 propose Tylosin (160mg/kg in 2 doses).

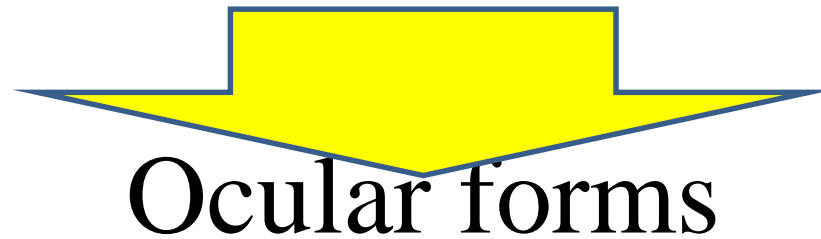
➤ Other symptomatic treatments for renal or hepatic failure must be implemented.

➤ Abdominocentesis: Removal of the effusion fluid allows relief from respiratory discomfort caused by diaphragmatic compression.



In exudative forms

- Ocular topical treatment based on glucocorticoids
(or subconjunctival injection)



Treatment Protocols For Effusive and Noneffusive Feline Infectious Peritonitis

Effusive FIP

Glucocorticoids:

Dexamethasone: 1 mg/kg intrathoracic or intraperitoneal injection once only, AND:

Prednisolone sliding dose: 4 mg/kg/day, PO, for 10–14 days reducing to 2 mg/kg/day for 10–14 days, then 1 mg/kg/day for 10–14 days, then 0.5 mg/kg/day for 10–14 days, then 0.25 mg/kg/day for 10–14 days, then 0.25 mg/kg/e.o.d. and so on, ceasing after complete remission of clinical signs. If, at any point, the cat's condition regresses, go back to the previous dose.

Feline interferon- ω : 1 MU/kg into the site of the effusion—the abdominal or thoracic cavity or (if not possible) SC, every other day, reducing frequency of treatment to once weekly if remission occurs.

Polyprenyl immunostimulant: Not advised.

Noneffusive FIP

Polyprenyl immunostimulant: 3 mg/kg every other day

If Polyprenyl immunostimulant is not available: Glucocorticoids:

Prednisolone sliding dose: As for effusive FIP. In addition, for FIP-related uveitis, topical glucocorticoids will be used.

Feline interferon- ω : 50,000 U per cat PO q 24 hr until AGP, globulins, HCT, lymphocyte count, and clinical signs return to normal.

Diluting feline interferon ω : Feline interferon ω (Virbagen Omega, Virbac) comes in vials of 10 million units (MU). It is reconstituted with 1 mL of diluent. Ten aliquots of 0.1 mL (1 MU per syringe) are prepared in insulin syringes. Nine of the 10 syringes are placed in the freezer (can be stored up to 6 months). The 10th syringe is diluted with 9.9 mL of sterile 0.9% saline solution to obtain 10 mL of a solution containing a total of 1 MU (100,000 U/mL) of feline interferon- ω . This syringe is stored in the refrigerator at +4°C where it will last up to 3 weeks^{3a} (do not freeze diluted interferon- ω ; it is unstable). Dose: 0.5–1 mL of this diluted solution (containing 50,000–100,000 units) orally daily, using the syringe without the needle.

Prognosis

➤ **Very dark.**

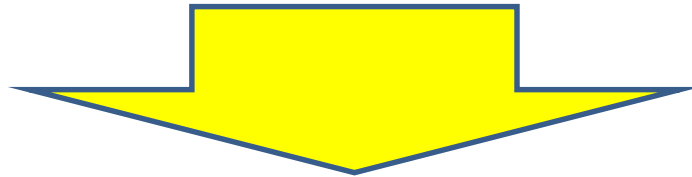
- Most cats are euthanized or die a few days to a few weeks after diagnosis.
- Cats without effusion tend to survive longer (weeks to several months): Clinical deterioration occurs rapidly once neurological signs develop.

Prophylaxis

Sanitary prophylaxis

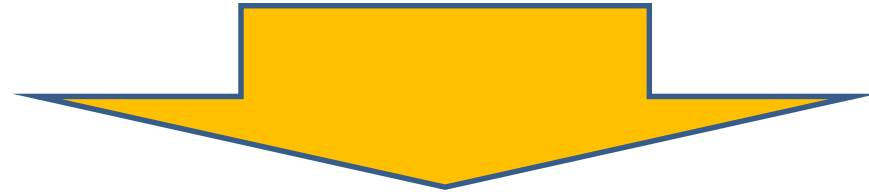
➤ Prophylactic measures primarily concern

breeding farms and catteries:



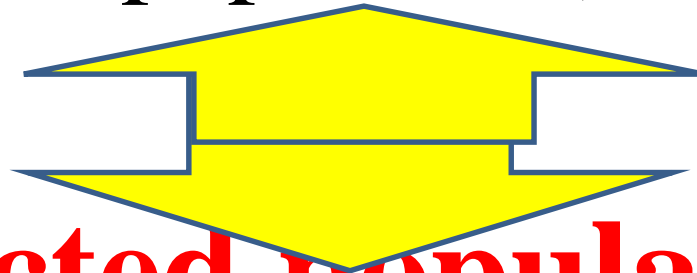
Very difficult

Healthy populations



Quarantine of 2 months for any new animal with serological control at the entrance and exit of the quarantine

Isolation of the kitten from weaning (4th-5th week) without contact with the infected population with serological control (If they remain uninfected = allows for the return of a healthy population)



Infected populations

Isolate infected cats.

Medical prophylaxis

➤ FIP is a non-essential vaccine valence.

Primucell® FIP (ZOETIS): containing a live attenuated strain of feline coronavirus

- Vaccin atténué par voie intranasale
- Taux d'efficacité (fraction évitable) : 75 %
- Primo-vaccination
 - À partir de 16 semaines
 - 2 injections à 3-4 semaines d'intervalle
- Rappel annuel



- Marketed in the United States and in some European countries.
- This vaccine is ineffective in cats that have already been infected with FCoV.
- Useful in seronegative kittens before their introduction into an endemic environment.

Guidelines for Vaccination of Individual Pet Cats—cont'd

Vaccine	Initial Vaccination		Booster Schedule	Comments
	Age ≤ 16 Weeks	Age > 16 Weeks		
FIP (A, IN)	Two doses, 3-4 weeks apart, starting at 16 weeks of age	Two doses, 3-4 weeks apart	Annual	Not generally recommended. Only seronegative cats have the potential to be protected. Benefit and risks currently unclear

A, attenuated live; IN, intranasal.

Public health aspects

- ❑ There is no evidence that humans can be infected by FCoV.
- ❑ Other coronaviruses cause a PIF-like disease in non-felids such as ferrets and mice.
- ❑ If a coronavirus were to emerge that could cause clinical manifestations and consequences in humans similar to those of PIF in cats, it would represent a major threat to humans.