Parvoviridae

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Definitions of the virus

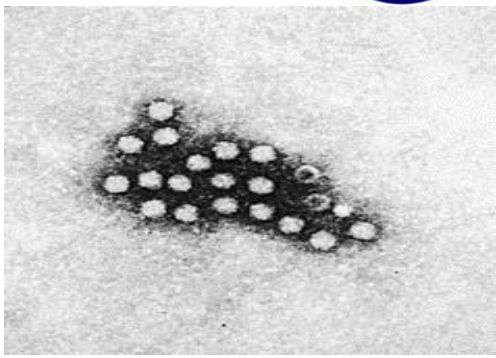
- causative agents of several animal diseases.
- are most severe in fetuses and neonates.
- Parvovirus infections of the fetus or newborn during organogenesis may result in developmental defects.
- Replication of parvovirus is restricted in hemopoietic precursors, lymphocytes, and progenitor cells of intestinal mucosa of older animals.

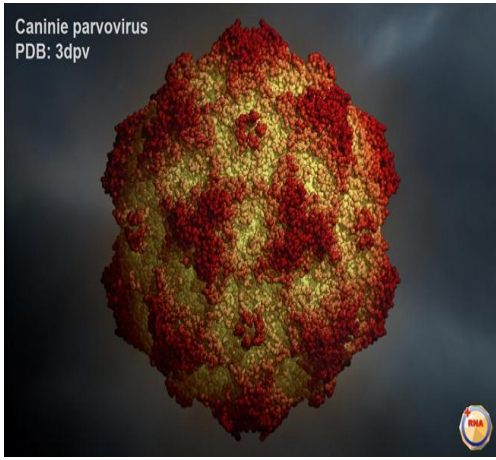
Definitions of the virus

- cause acute infections for a few days,
- others persist for long periods in the feces of apparently robust host immune responses.
- Human Parvovirus B19 replication occurs only in human erythrocyte precursors
- The virus is found to survive in feces and other organic material such as soil for over 10 years.
- It survives extremely low and high temperatures.

Physical Properties of the virus

- Family: Parvoviridae with two subfamilies
  - Parvovirinae. (vertebrate). has 5 genera
  - Densovirinae. (invertebrate). Has3 genera
- non-enveloped, 25 nm in diameter
- Capsid: icosahederal.
- Genome ssDNA





Diseases caused by *parvoviruses*

- As of 2014, there were no known human viruses in the remaining three recognized genera:
- vi) *Amdoparvovirus* (e.g. Aleutian mink disease virus),
- vii) *Aveparvovirus* (e.g. chicken parvovirus) and
- viii) *Copiparvovirus* (e.g. bovine parvovirus 2).
- *Mouse parvovirus 1*, however, causes no symptoms but can contaminate immunology experiments in biological research laboratories.
- *Porcine parvovirus* causes a reproductive disease in swine known as SMEDI, which stands for stillbirth, mummification, embryonic death, and infertility.

Diseases caused by *parvoviruses*

- Many mammalian species sustain infection by multiple parvoviruses.
- Feline panleukopenia is common in kittens and causes fever, low white blood cell count, diarrhea, and death. Infection of the cat fetus and kittens less than two weeks old causes cerebellar hypoplasia.
- *Mink enteritis virus* is similar in effect to feline panleukopenia, except that it does not cause cerebellar hypoplasia. A different parvovirus causes aleutian disease in mink and other mustelids, characterized by lymphadenopathy, splenomegaly, glomerulonephritis, anemia, and death.
- Dogs, cats and swine can be vaccinated against parvovirus.

Viral proteins

- Capsid: Virus outer capsid proteins (VP1, VP2).
- The capsid is composed of VP2 (90%) and approximately 10% being the overlapping but larger VP1 protein.
- The entire sequence of VP2 is encoded within the VP1 gene.

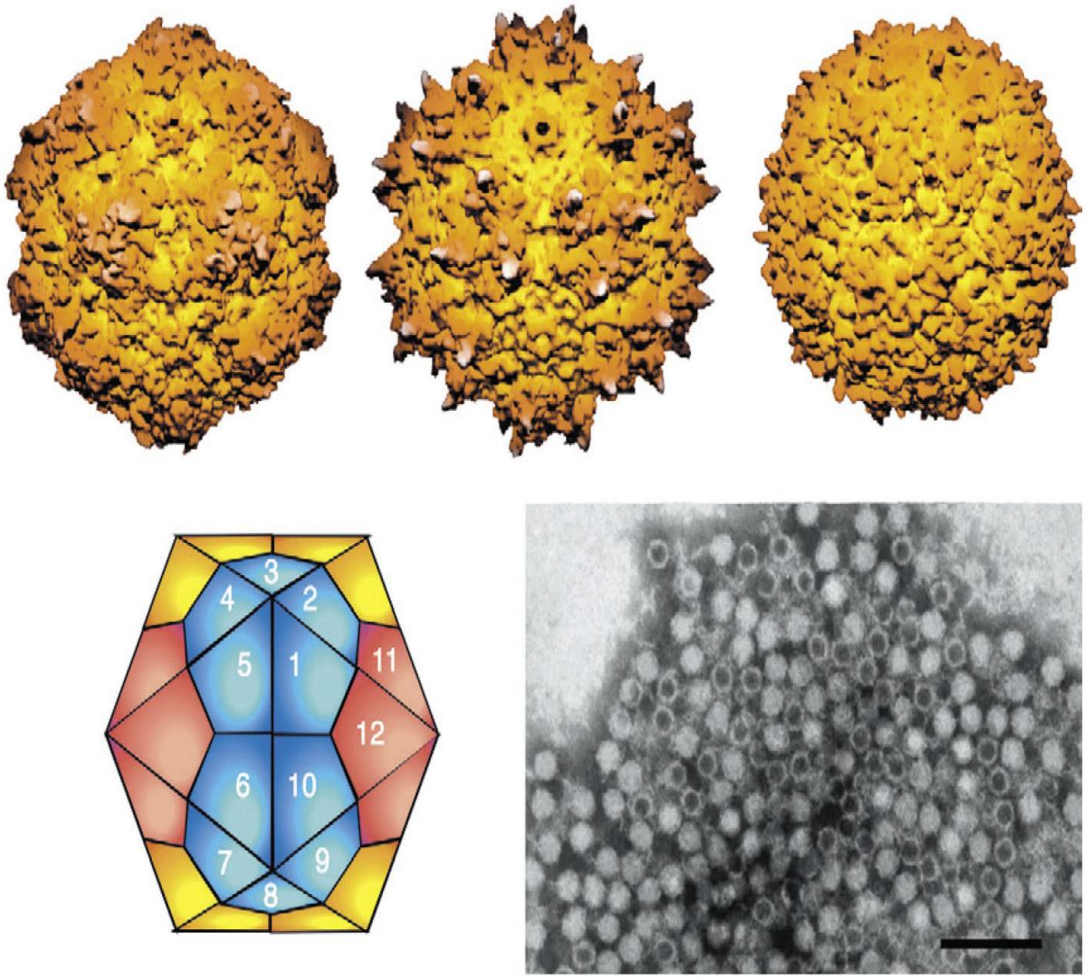
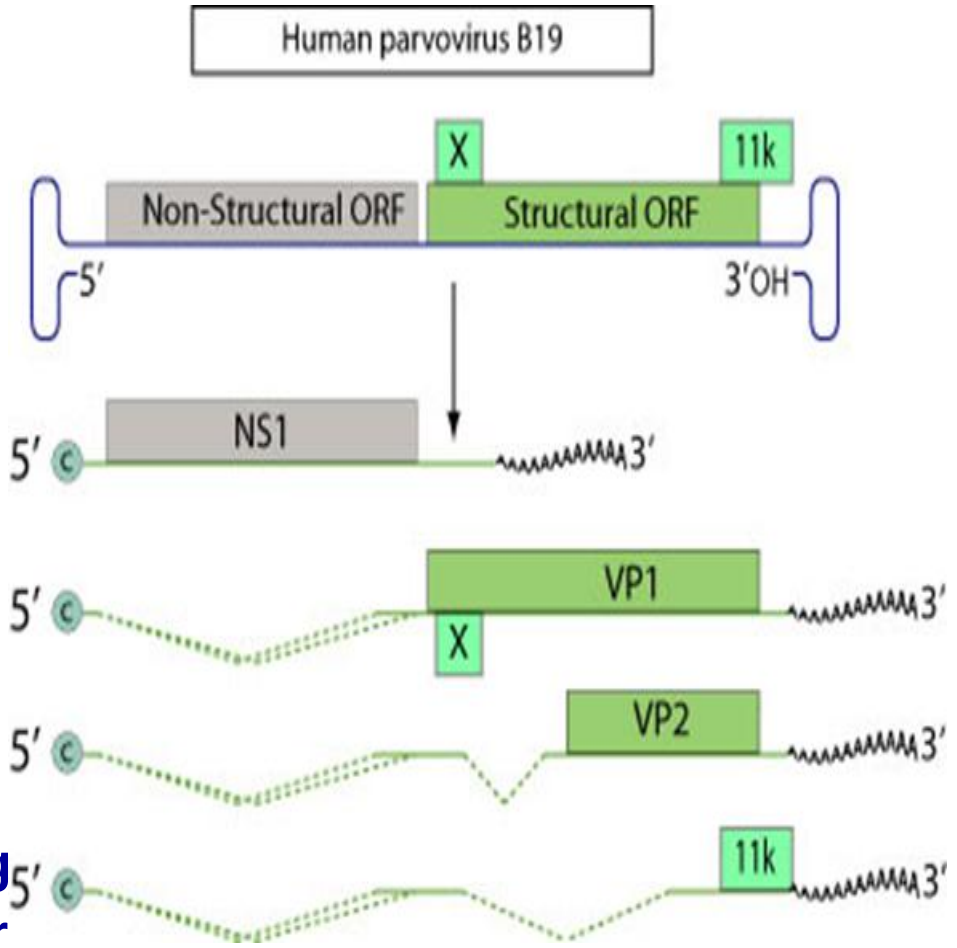


FIGURE 12.1 (Top) Space-filling models of the capsid structures of canine parvovirus (CPV) (left); adeno-associated virus - 2 (AAV-2) (center) and Galleria mellonella densovirus (GmDNV) (right). Each model is drawn to the same scale and is colored according to distance from the viral center. In each case, the view is down a twofold axis at the center of the virus, with threefold axes left and right of center, and fivefold axes above and below (Courtesy of M. Chapman). (Bottom left) Diagram representing a T = 1 capsid structure. (Bottom right) Negative contrast electron micrograph of CPV particles. The bar represents 100 nm. *[From* Virus Taxonomy: Eighth Report of the International Committee on Taxonomy of Viruses *(C. M. Fauquet, M. A. Mayo, J. Maniloff, U. Desselberger, L. A. Ball, eds.), p. 353. Copyright © Elsevier (2005), with permission.]*

Viral genome

- ssDNA (4.5-5.5 kbp) of either polarity.
- The genome contains two ORFs: an ORF in the 3’ half of the genome that encodes the non-structural proteins for DNA transcription and replication;
- another ORF towards 5’ half encodes the structural proteins (VP 1, VP 2, VP 3) of the capsid.
- The genome has terminal palindromic sequences, enabling each end to form hairpin or other complex base-paired structures.



Biological properties

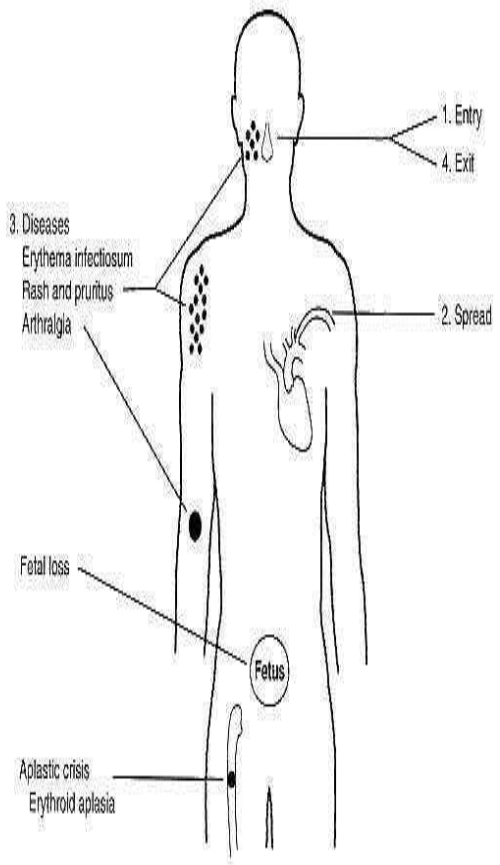
- lack of envelope and the limited DNA content, B19 is extremely resistant to physical inactivation.
- Virus is resistant to:
  - -Heat: 56°C for 60 minutes ,
  - - pH: 3 – 9.
  - -lipid solvents: such as ether and chloroform.
- Virus inactivated by:
  - -Formalin ,
  - -ß- propiolactone ,
  - -Oxidizing agents
- Most parvovoruses agglutinate RBCs
- Transferrin receptor is the receptor for canine parvovirus and feline panleukopenia virus,

REPLICATION

- Attachement to host receptors initiates clathrin-mediated endocytosis of the virion into the host cell.
- The virion penetrates into the cytoplasm via endosomal membrane.
- The viral ssDNA genome penetrates into the nucleus.
- The ssDNA is converted into dsDNA by cellular polymerase.
- dsDNA transcription gives rise to viral mRNAs when host cell enters S phase and translated to produce viral proteins.
- Replication occurs through rolling-hairpin mechanism, with NS1 endonuclease binding covalently to the 5' genomic end.
- These newly synthesized ssDNA can either
  a) be converted to dsDNA and serve as a template for transcription/replication
  b) be encapsidated to form new virions that are released by cell lysis.

Pathogenesis

- **Parvovirus B19 was the first pathogenic human parvovirus causing a childhood exanthem called "*fifth disease*" (*erythema infectiosum*) although it is also associated with othe diseases including arthritis**
- **Mood of transmission:**
  1- Horizontally: Infection is spread by a respiratory route.
- **2- Parenteral: blood transfusion or infected blood products.**
- **3- Vertically: trans placental transmission from mother to fetus.**
- **Route of entry:**
- **Respiratory tract. Directly into blood.**
- **Spread:**
  Blood, tropic for human erythroid cells in BM. ، Mitotically active cells for replication).



Target receptor (Cells, tissues)

The cellular receptor for B19 is blood group P antigen (globosids).

P antigen is expressed on:

1- Mature erythrocytes.

2- Erythroid progenitors.

3- Megakaryocytes.

4-Endothelial cells.

5- Placenta, Fetal heart and liver.

<u>Tissue :</u> site of viral replication

1- Adult: bone marrow

2- Fetus: fetal liver.

Mechanism of tissue damage induced by the virus

I. <u>Direct effects:</u>

Viral replication in the erythroid cells cause cell death and interruption of RBC production.

II. <u>Indirect effects:</u>

Antibodies to parvovirus result in formation of immune complex which deposit in tissue and cause damage.

EPIDEMIOLOGY

- Transmission: respiratory or through blood and blood product
- Seasonal:
  commonly as outbreaks of erythema infectiosum in schools during winter and spring months.
- Rate of infection: Common
- 60% of adults possess serum antibodies.
- Prevention:
  1- Interruption of virus transmission (respiratory)
- 2-No vaccine for B19 is currently available.

2.1 Manifestations of Parvovirus Diseases in Animals[a]

Virus	Disease
Feline panleukopenia virus	Generalized disease in kittens, with panleukopenia, enteritis; cerebellar hypoplasia
Canine parvovirus 1 (minute virus of canines)	Minimal
Canine parvovirus 2 (subtypes 2a, 2b, 2c)	Generalized disease in puppies; enteritis, myocarditis (rarely), lymphopenia
Porcine parvovirus	Stillbirth, abortion, fetal death, mummification, infertility.
Mink enteritis virus	Leukopenia, enteritis
Aleutian mink disease virus	Chronic immune complex disease, encephalopathy. Interstitial pneumonia in neonates
Mouse parvoviruses, minute virus of mice, rat parvoviruses, H-1 virus of rats	Subclinical or persistent infection; congenital fetal malformations; hemorrhagic syndrome in rats
Goose parvovirus	Hepatitis, myocarditis, myositis
Duck parvovirus	Hepatitis, myocarditis, myositis

[a] *Parvoviruses have also been detected in a variety of animal species, frequently in the absence of obvious clinical disease.*

Canine parvovirus

Canine Parvovirus

- *Canine parvovirus* is a particularly deadly disease among young puppies, about 80% fatal, causing gastrointestinal tract damage and dehydration as well as a cardiac syndrome in very young animals
- Symptoms include lethargy, severe diarrhea, fever, vomiting, loss of appetite, and dehydration.

Canine parvovirus (CPV-2) appears to be a mutant strain of feline parvovirus

- All isolates of canine parvovirus affect dogs, wolves, and foxes, but only some of them will infect cats.

Some breeds are more sensitive to CPV infection

- It is a hardy virus resist in the environment condition
- Vaccine is available

- Canine parvovirus type 2 (CPV2) is a contagious virus mainly affecting dogs, and thought to originate in cats.
- the feline panleukopenia mutated into CPV2.
- two forms of CPV2: intestinal and cardiac.
- . Dogs who catch Parvovirus usually die from the dehydration it causes or secondary infection rather than the virus itself.
- Vaccines can prevent this infection, but mortality can reach 91% in untreated cases.
- Treatment often involves veterinary hospitalization.
- Canine parvovirus may infect other mammals including foxes, wolves, cats, and skunks; however, it will not infect humans.

Viral characters

- CPV2 is a non-enveloped single-stranded DNA virus. The name comes from the Latin *parvus*, meaning small, as the virus is only 20 to 26 nm in diameter.
- It has an icosahedral symmetry. The genome is about 5000 nucleotides long
- CPV2 continues to evolve, and the success of new strains seems to depend on extending the range of hosts affected and improved binding to its receptor, the canine transferrin receptor.
- CPV2 has a high rate of evolution, possibly due to a rate of nucleotide substitution that is more like RNA viruses such as Influenzavirus A.
- In contrast, FPV seems to evolve only through random genetic drift.

Canine and feline parvovoruses

- Canine parvovirus is a mutant strain of feline parvovirus.
- A very specific mutation is necessary for the virus to change species of infection.
- The mutation affects capsid proteins of feline parvovirus giving it the ability to infect dogs
- Both forms of the virus are very similar, so once the mutation has occurred, canine parvovirus is still able to infect cats.
- The canine parvovirus has the trade off of gaining the ability to infect canine cells while becoming less effective at infecting feline cells.

- Both feline parvovirus and canine parvovirus bind to and infect the transferrin receptors, but both have different sequences in the cells and animals.
- Infection by both feline parvovirus and canine parvovirus are relatively quick; but because of constant mutation of canine parvovirus, canine parvovirus has a slower infection time than feline parvovirus
- Studies of other strains of mutated canine parvovirus have revealed that changes in the viral capsid by just one protein can be fatal to the virus.
- Deleterious mutations have been noted to lead to inability to bind to transferrin receptors, bind to non-receptive parts of the cell membrane, and identification of the virus by the host's antibody cells

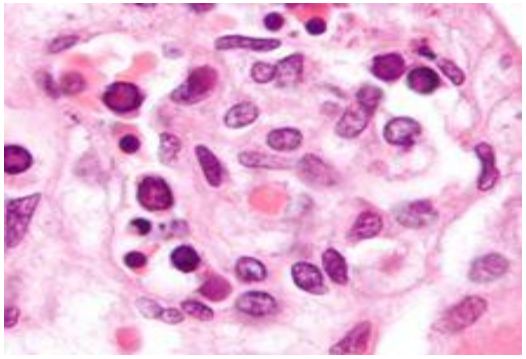
- CPV2 affects dogs, wolves, foxes, and other canids.
- CPV2a and CPV2b have been isolated from a small percentage of symptomatic cats and is more common than feline panleukopenia in big cats.
- However studies in Vietnam have shown that CPV2 can undergo minor antigenic shift and natural mutation to infect felids.
- Analyses of feline parvovirus (FPV) isolates in Vietnam and Taiwan revealed that more than 80% of the isolates were of the canine parvovirus type, rather than feline panleukopenia virus (FPLV).
- CPV2 may spread to cats easier than dogs and undergo faster rates of mutation within that species

Pathogenesis of canine parvovirus

- Both feline parvovirus and canine parvovirus enter their hosts, follow specific pathways, and infect at certain parts of cells before infecting major organs.
- Parvovirus infects carnivorous animals through the oropharyngeal pathway.
- Parvovirus infects the oropharyngeal cells that come in immediate contact with the virus.
- It contains a plasmid that infects and binds to transferrin receptors, a glycoprotein, on the plasma membrane
- The parvovirus plasmid is stored in a small non-enveloped capsid
- Once oropharyngeal cells become infected the virus spreads to dividing lymph cells and continues to work to the bone marrow and spread to target organs through blood.

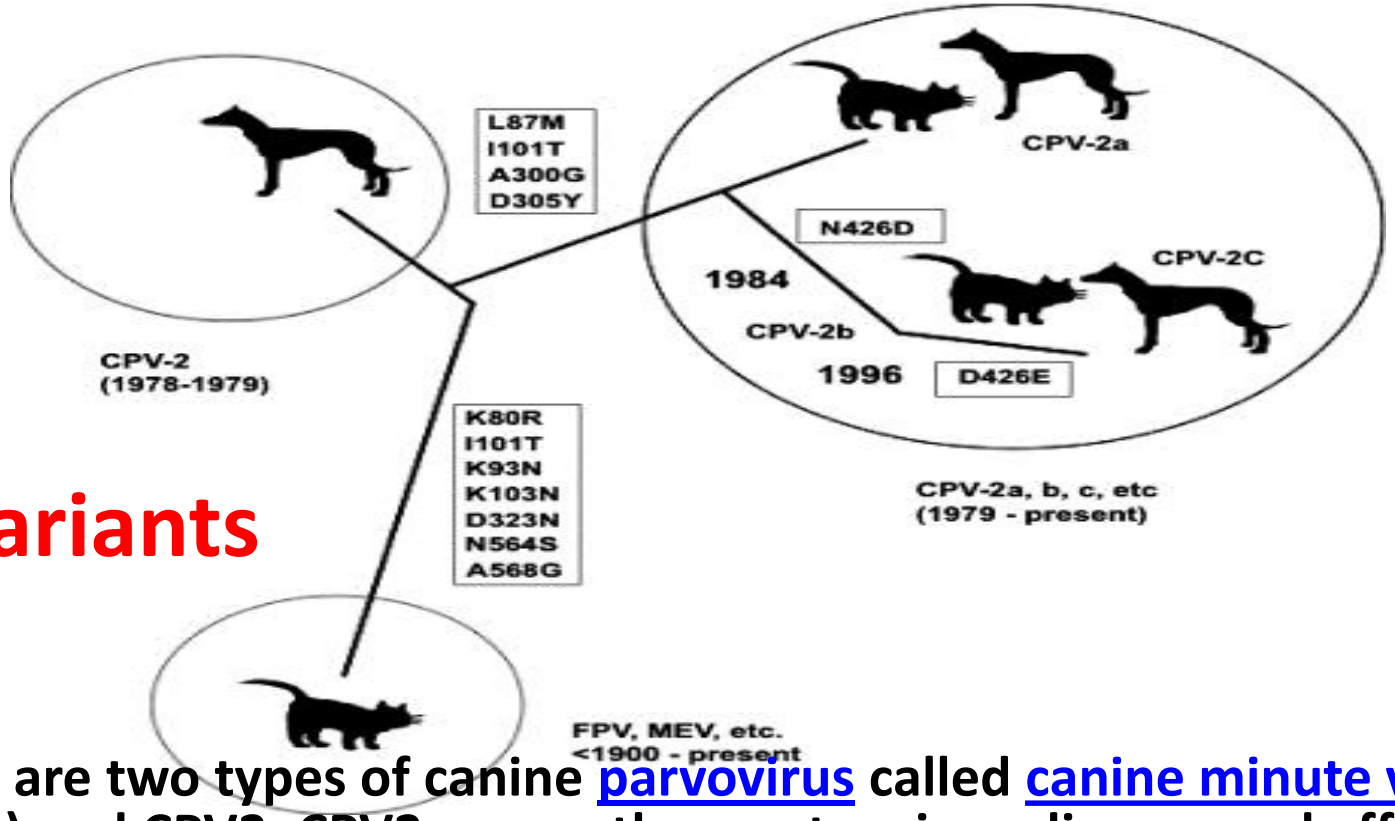
Host suscptibility

- Certain breeds, such as Rottweilers, Doberman Pinschers, and Pit bull may be more susceptible to CPV2
- Along with age and breed, factors such as a stressful environment, concurrent infections with bacteria, parasites, and canine coronavirus increase a dog's risk of severe infection
- Puppies are most susceptible, but 80% of adult dogs show no symptoms
- With severe disease, dogs can die within 48 to 72 hours without treatment by fluids.
- less severe form, mortality is about 10 percent



Micrograph showing parvovirus infected nucleated (fetal) red blood cells. H&E stain

CPV Variants



- There are two types of canine parvovirus called canine minute virus (CPV1) and CPV2. CPV2 causes the most serious disease and affects domesticated dogs and wild canids. There are variants of CPV type 2 called CPV-2a, CPV-2b and CPV-2c. The antigenic patterns of 2a and 2b are quite similar to the original CPV type 2. Variant 2c however has a unique pattern of antigenicity.This has led to claims of ineffective vaccination of dogs but studies have shown that the existing CPV vaccines based on CPV type 2b, provide adequate levels of protection against CPV type 2c.

The virus is very similar to feline panleukopenia (also a parvovirus); they are 98% identical, differing only in two amino acids in the viral capsid protein VP2.

It is also highly similar to mink enteritis, and the parvoviruses of raccoons and foxes

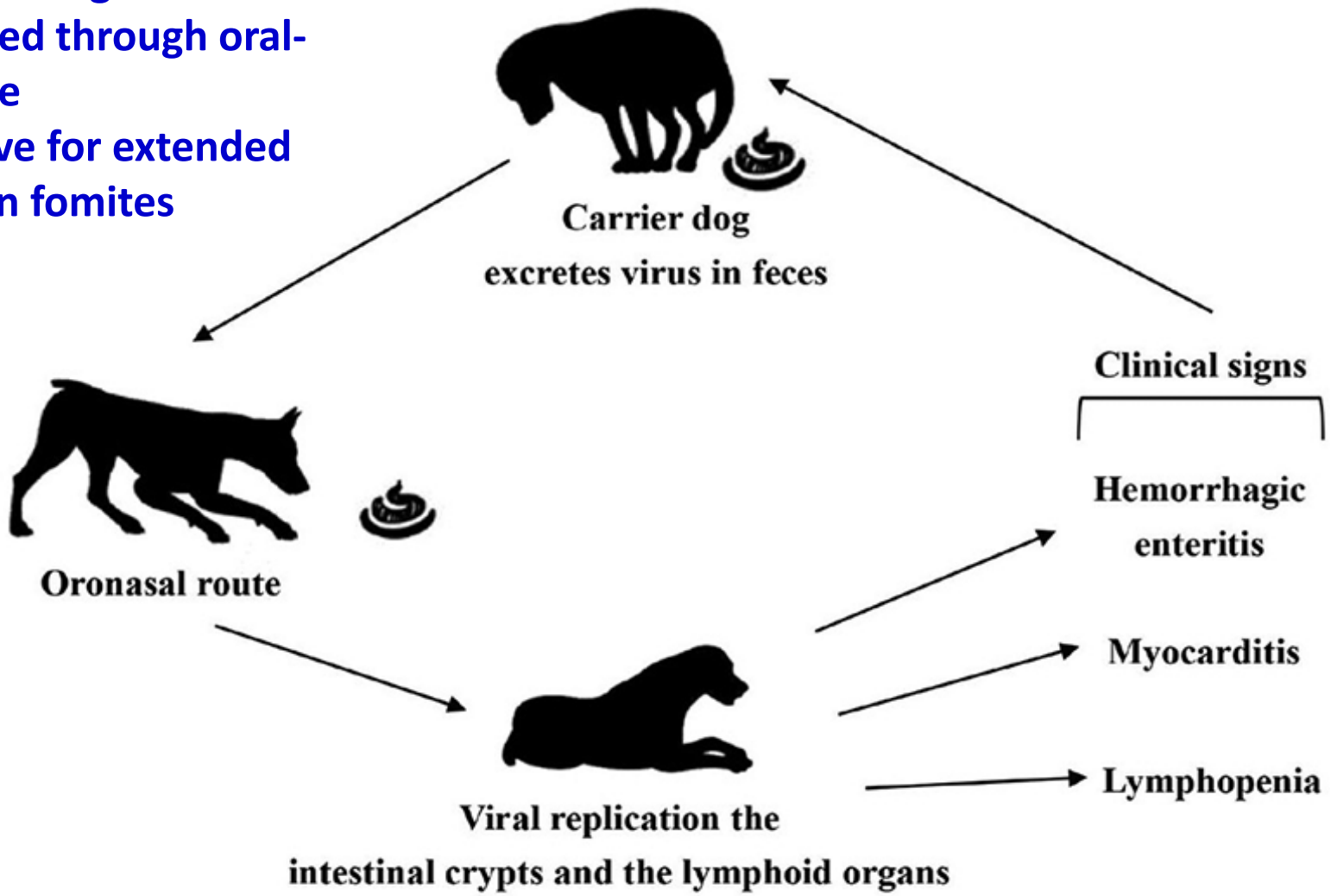
It is possible that CPV2 is a mutant of an unidentified parvovirus (similar to feline parvovirus (FPV)) of some wild carnivore

A strain of CPV2b (strain FP84) has been shown to cause disease in a small percentage of domestic cats, although vaccination for FPV seems to be protective

CPV2, however, does not cause disease in cats and does so only mildly in mink and raccoons, and is a virus almost exclusively affecting canines.

Transmission

- It is spread by contact with an infected dog's feces.
- Transmitted through oral-fecal route
- Can survive for extended periods on fomites



Pathogenesis

Dogs become infected through oral contact with CPV2 in feces, infected soil, or fomites that carry the virus.

Following ingestion, the virus replicates in the lymphoid tissue in the throat, and then spreads to the bloodstream.

From there, the virus attacks rapidly dividing cells, notably those in the lymph nodes, intestinal crypts, and the bone marrow.

Infection of the fetus

- This type of infection can occur when a pregnant female dog is infected with CPV2.
- The adult may develop immunity with little or no clinical signs of disease.
- The virus may have already crossed the placenta to infect the fetus.
- This can lead to several abnormalities.
- In mild to moderate cases the pups can be born with neurological abnormalities such as cerebellar hypoplasia

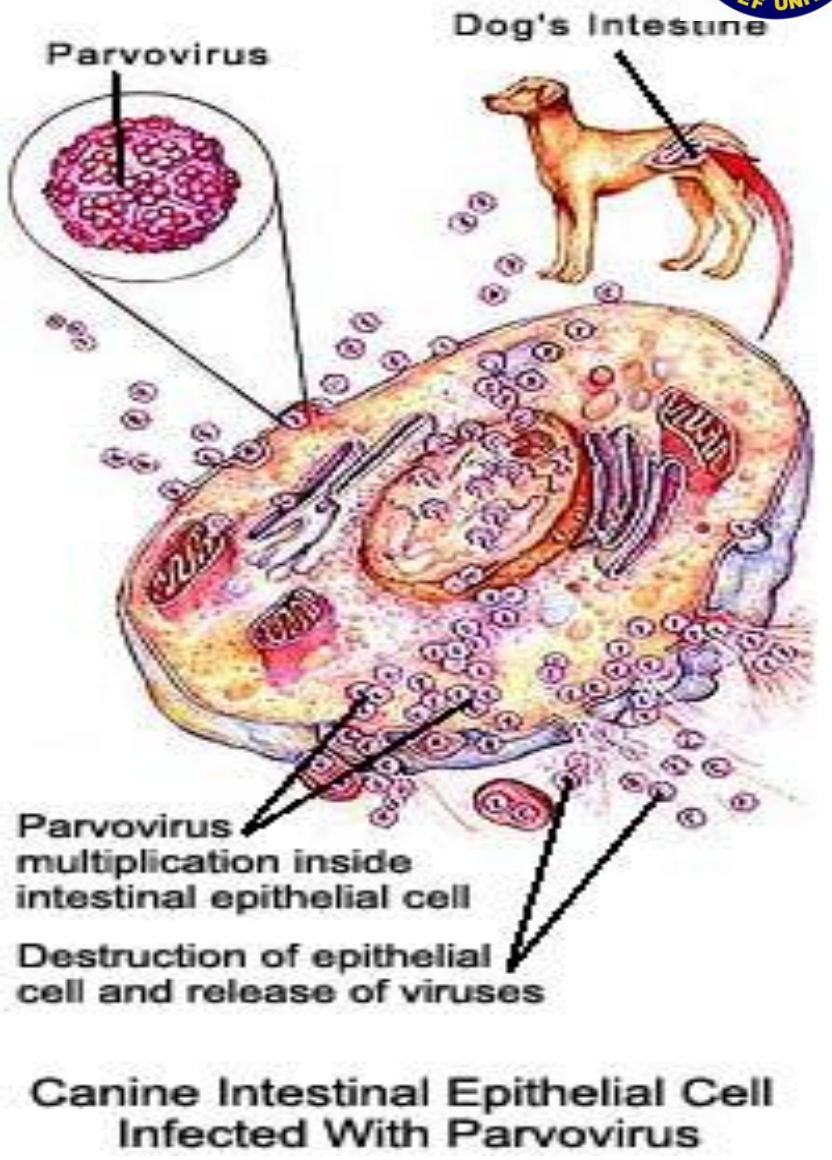
Clinical signs

. The infection manifests itself in 2 different types. The more typical kind is the intestinal

- Dogs that develop the disease show signs of the illness within 3 to 7 days.
- The signs may include lethargy, vomiting, fever, and diarrhea (usually bloody).
- Generally, the first sign of CPV is lethargy.
- Secondary signs are loss of weight and appetite or diarrhea followed by vomiting.
- Diarrhea and vomiting result in dehydration that upsets the electrolyte balance and this may affect the dog critically.
- Secondary infections occur as a result of the weakened immune system.
- Because the normal intestinal lining is also compromised, blood and protein leak into the intestines leading to anemia and loss of protein, and endotoxins escaping into the bloodstream, causing endotoxemia.
- Dogs have a distinctive odor in the later stages of the infection.
- The white blood cell level falls, further weakening the dog. Any or all of these factors can lead to shock and death.[2]

Intestinal form

- There is depletion of lymphocytes in lymph nodes and necrosis and destruction of the intestinal crypts
- Anaerobic bacteria that normally reside in the intestines can then cross into the bloodstream, a process known as translocation, with bacteremia leading to sepsis.
- The most common bacteria involved in severe cases are *Clostridium*, *Campylobacter* and *Salmonella* species. This can lead to a syndrome known as systemic inflammatory response syndrome (SIRS).
- SIRS leads to a range of complications such as hypercoagulability of the blood, endotoxaemia and acute respiratory distress syndrome (ARDS). Bacterial myocarditis has also been reported secondarily to sepsis
- Dogs with CPV are at risk of intussusception, a condition where part of the intestine prolapses into another part.
- Three to four days following infection, the virus is shed in the feces for up to three weeks, and the dog may remain an asymptomatic carrier and shed the virus periodically.[1]
- The virus is usually more deadly if the host is concurrently infested with worms or other intestinal parasites

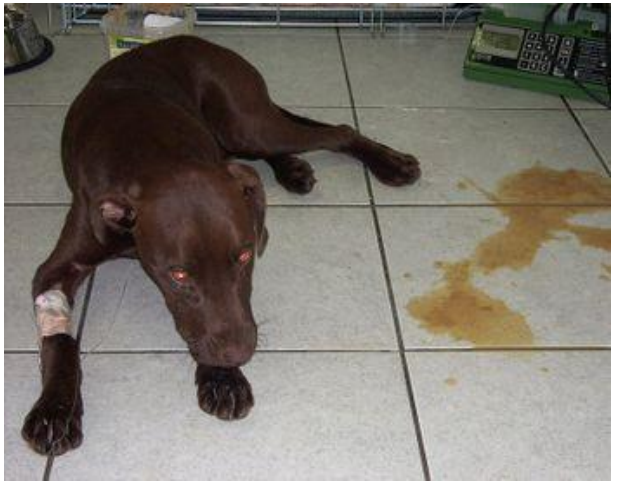


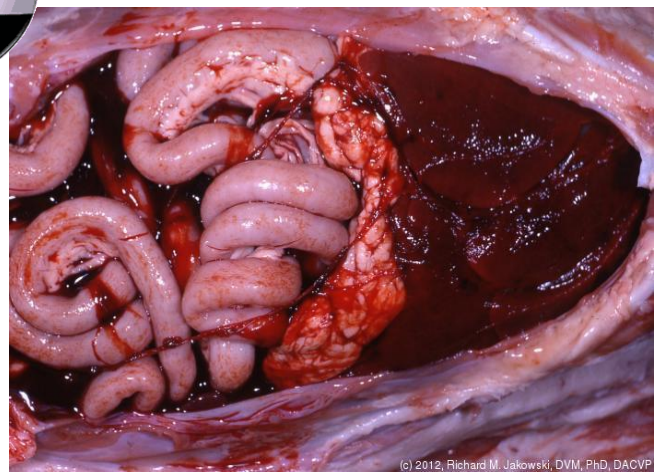
Canine Intestinal Epithelial Cell Infected With Parvovirus

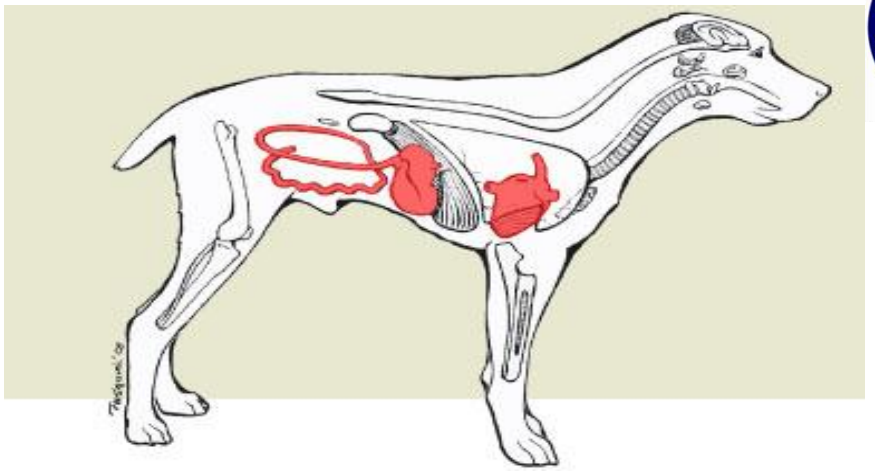
Cardiac form

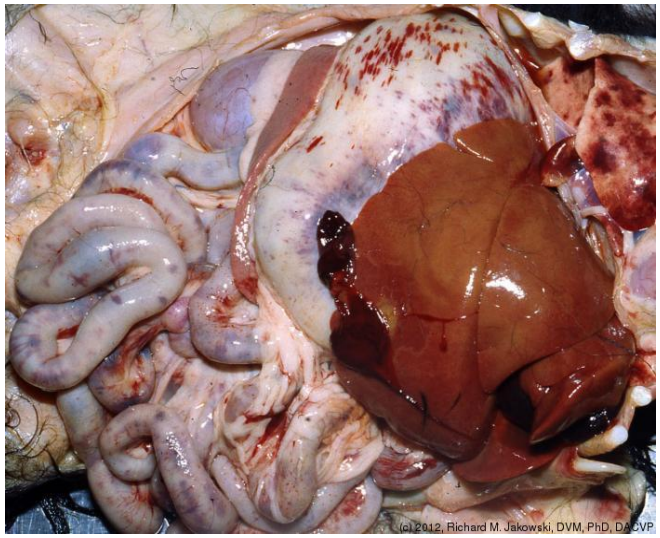
- This form is less common and affects puppies infected in the uterus or shortly after birth until about 8 weeks of age
- The virus attacks the heart muscle and the puppy often dies suddenly or after a brief period of breathing difficulty due to pulmonary edema.
- The disease may or may not be accompanied with the signs and symptoms of the intestinal form.
- Even less frequently, the disease may also lead to a generalized infection in neonates and cause lesions and viral replication and attack in other tissues other than the gastrointestinal tissues and heart, but also brain, liver, lungs, kidneys, and adrenal cortex. The lining of the blood vessels are also severely affected, which lead the lesions in this region to hemorrhage.

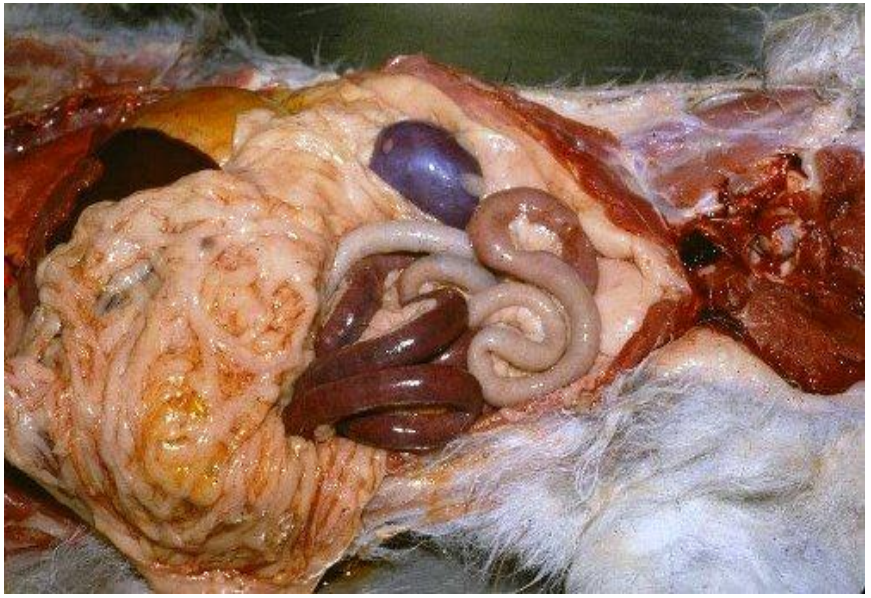










Necropsy of CPV2 infected canine shows signs of small intestine dilatation and luminal hemorrhage

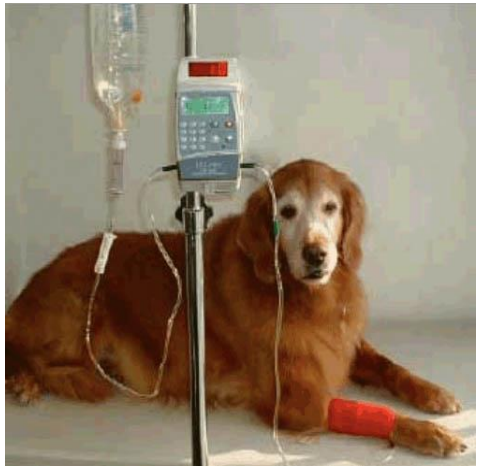
Diagnosis

- Diagnosis is made through detection of CPV2 in the feces by ELISA or a hemagglutination test, or by electron microscopy.
- PCR has become available to diagnose CPV2
- Clinically, the intestinal form of the infection can sometimes be confused with coronavirus or other forms of enteritis.
- Parvovirus, however, is more serious and the presence of bloody diarrhea, a low white blood cell count, and necrosis of the intestinal lining also point more towards parvovirus, especially in an unvaccinated dog.
- The cardiac form is typically easier to diagnose because the symptoms are distinct.

- Treatment ideally also consists of crystalloid IV fluids and/or colloids (e.g., Hetastarch), antinausea injections (antiemetics) such as maropitant, metoclopramide, dolasetron, ondansetron and prochlorperazine, and broad-spectrum antibiotic injections such as cefazolin/enrofloxacin, ampicillin/enrofloxacin, metronidazole, timentin, or enrofloxacin.
- IV fluids are administered and antinausea and antibiotic injections are given subcutaneously, intramuscularly, or intravenously. The fluids are typically a mix of a sterile, balanced electrolyte solution, with an appropriate amount of B-complex vitamins, dextrose and potassium chloride. Analgesic medications can be used to counteract the intestinal discomfort caused by frequent bouts of diarrhea; however, the use of opioid analgesics can result in secondary ileus and decreased motility.

Treatment

- A blood plasma transfusion from a donor dog that has already survived CPV is sometimes used to provide passive immunity to the sick dog.
- Some veterinarians keep these dogs on site, or have frozen serum available. There have been no controlled studies regarding this treatment
- Additionally, fresh frozen plasma and human albumin transfusions can help replace the extreme protein losses seen in severe cases and help assure adequate tissue healing. However, this is controversial with the availability of safer colloids such as Hetastarch, as it will also increase the colloid osmotic pressure without the ill effect of predisposing that canine patient to future transfusion reaction.



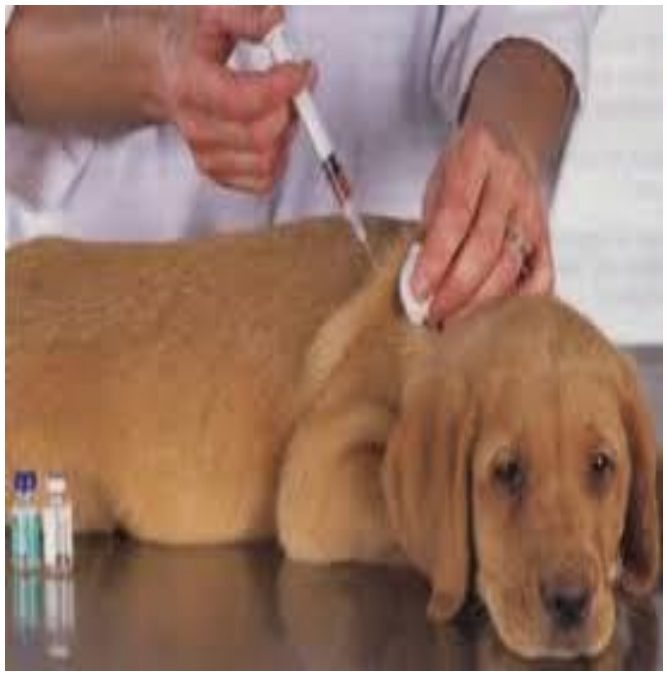
Once the dog can keep fluids down, the IV fluids are gradually discontinued, and very bland food slowly introduced.

Oral antibiotics are administered for a number of days depending on the white blood cell count and the patient's ability to fight off secondary infection

A puppy with minimal symptoms can recover in 2 or 3 days if the IV fluids are begun as soon as symptoms are noticed and the CPV test confirms the diagnosis

If more severe, depending on treatment, puppies can remain ill from 5 days up to 2 weeks. However, even with hospitalization, there is no guarantee that the dog will be cured and survive.


PARVO KILLS
vaccinate your dog




Parvovirus Vaccine
Modified Live Virus
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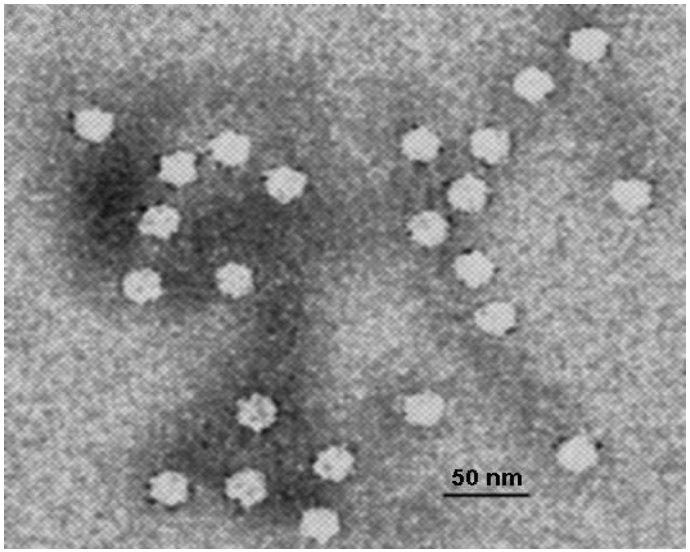
Feline panleukopenia

- Feline panleukopenia virus (FPV), also known as feline infectious enteritis, feline parvo viral enteritis, feline distemper, feline ataxia, or cat plague, is a viral infection affecting cats, both domesticated and wild feline species.
- It is caused by feline parvovirus, a close relative of both type 2 canine parvovirus and mink enteritis. Once contracted, it is highly contagious and can be fatal to the affected cat
- The name panleukopenia comes from the low white blood cell count (leucocytes) exhibited by affected animals

Virus classification and physical characters



- (ssDNA) genome
- Family:*Parvoviridae*
- Subfamily:*Parvovirinae*
- Genus:*Protoparvovirus*
- Species:*Feline panleukopenia virus*
- *Nacked virus*
- *Icosahedral capside*
- *25-28 nm diameter*
- *Replicate in the nuclus*

Transmission

- Panleukopenia is primarily spread through contact with an infected animal's bodily fluids, feces, or other fomites, as well as by fleas
- It may be spread to and by cats, minks and ferrets and can be spread long distances through contact with bedding, food dishes, or even by clothing and shoes of handlers of infected animals.
- It is not, however, contagious or contractable by humans.
- Like all parvoviruses, FPV is extremely resistant to inactivation and can survive for longer than one year in a suitable environment.

Clinical signs

- The virus primarily attacks the lining of the gastrointestinal tract, causing internal ulceration and, ultimately, total sloughing of the intestinal epithelium. This results in profuse and usually bloody diarrhea, severe dehydration, malnutrition, anemia, and often death. It causes a decrease in the cat's white blood cells, thus compromising its immune system.
- Typically, it also causes a decrease in hematocrit and platelet counts on a complete blood count. This is often key in diagnosing panleukopenia.
- depression, lethargy, loss of appetite, fever, vomiting, loss of skin elasticity due to dehydration, and self-biting in the tail, lower back and back legs.
- Terminal cases are hypothermic and may develop septic shock and disseminated intravascular coagulation.
- Most panleukopenia deaths are due to secondary infections or dehydration resulting from diarrhea.
- If a cat is exposed during pregnancy, the virus can cause cerebellar hypoplasia in her offspring. Therefore modified live feline panleukopenia vaccine during pregnancy is discouraged.

Diagnosis

- A presumptive diagnosis is usually based on compatible clinical signs in an inadequately vaccinated cat and the presence of leukopenia (nadir 50–3,000 WBC/µL).
- Neutropenia is a more consistent finding than lymphopenia. Total WBC counts <2,000 cells/µL are associated with a poorer prognosis.
- During recovery from infection, there is typically a rebound neutrophilia with a marked left shift. Diagnosis can sometimes be confirmed using an in-office immunochromatographic test kit intended for detection of fecal CPV antigen. However, fecal antigen is detectable only for a short time after infection. False-negative results are common.
- Differential diagnoses include other causes of profound depression, leukopenia, and GI signs. Salmonellosis (see Salmonellosis) and infections with feline leukemia virus (FeLV, see Feline Leukemia Virus and Related Diseases) and feline immunodeficiency virus (see Feline Immunodeficiency Virus (FIV)) should be considered. Concurrent infection with FeLV and FPV can cause a panleukopenia-like syndrome in adult cats.

Treatment

- blood transfusion to improve pancytopenia,
- injections of vitamins A, B, and C
- IV antibiotics to prevent septicemia,
- *Supportive Therapy*. Intravenous fluid therapy is important to prevent dehydration
- if vomiting persists, anti-emetics should be applied.
- *Antiviral therapy tamiflu*.
- Feline recombinant interferon-omega is effective in dogs and also inhibits FPV replication in cell culture

Complications

- Hyponatremia and other electrolyte disturbances are also quite common, as is hypotension, hyperpyrexia
- The patients' severe leukocytopenia predispose them to secondary infections, especially bacterial and fungal, though secondary viral infections also occur with some frequency.
- Disseminated intravascular coagulation may also occur, and is often fatal. Extreme thrombocytopenia may also occur, and can lead to severe hemorrhagic complications.
- Even if a cat survives acute FPL, late complications such as cardiomyopathy and myocarditis can occur

Prognosis

- Of affected kittens that are two months or less of age, 90–95% die regardless of treatment.
- Kittens that are more than two months old have a 60–70% mortality rate with treatment and a nearly 100% mortality rate if not treated.
- Adult cats have a 10–20% mortality rate if treated, and an 85% mortality rate if not treated.
- Elderly cats have a 20–30% mortality rate if treated and a 90% mortality rate if not treated

Vaccination

- Protection is offered by commercial feline distemper vaccines
- A number of combination vaccines for several different diseases, including panleukopenia, are also available.
- Because of the serious disease and ubiquity of the virus vaccination is recommended for every cat.
- Even cats kept indoors can be infected since the virus is so stable that it can be transmitted on fomites
- In a disease outbreak, unvaccinated kittens or adults can be given anti-FPV serum containing FPV antibodies subcutaneously or intraperitoneally, which may protect for 2–4 weeks