Feline panleukopenia – update on prevention and treatment

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Introduction
Feline panleukopenia is caused by feline parvovirus (FPV), which is a highly contagious virus affecting all members of Felidae. Severity of clinical signs depends on age, immune status, and concurrent infections. Clinical disease ranges from subclinical infection to a peracute syndrome with sudden death. Typical initial signs include fever, depression, and anorexia. Affected cats can initially present for vomiting and, with lower frequency, develop watery to hemorrhagic diarrhea. Atypical presentations are common, especially in adult cats. Infected cats die from complications associated with secondary bacterial infection, sepsis, dehydration, and disseminated intravascular coagulopathy (DIC). Mortality rates of 25%-90% in acute panleukopenia and up to 100% in peracute infections have been reported.

What is the etiology of feline panleukopenia?
Feline panleukopenia is caused by a single-stranded DNA virus, the feline parvovirus (FPV). It is a highly contagious and often lethal disease of cats and other Felidae. FPV, and also strains of the canine parvovirus (CPV), can be isolated from both healthy and diseased cats. CPV was detected in approximately 10% of samples of cats with panleukopenia in Germany; in Southeast Asia, however, an estimate of up to 80% of diseased cats has been reported to be infected with CPV.

Infection spreads rapidly, especially in cells with high mitotic activity, such as bone marrow, lymphoid tissue, and intestinal crypt cells. In clinically affected cats, anorexia, vomiting, diarrhea, neutropenia, and lymphopenia are common. Intrauterine and neonatal infection can result in cerebellar hypoplasia.

Which clinical signs can develop?
Not all cats infected with FPV develop clinical signs, and severity of the disease depends on age, immune status, and concurrent infections. Signs and outcome can vary from subclinical to peracute with sudden death within 12 hours. The acute form is the most common; non-specific signs are observed initially, e.g. fever, depression, and anorexia. Vomiting (unrelated to food intake) is common. Less often, cats develop watery to hemorrhagic diarrhea later in the course of disease. Some cats show serious dehydration, which can lead to progressive weakness and depression when occurring in combination with anorexia, vomiting and diarrhea. Cats typically die due to complications associated with sepsis, dehydration, and disseminated intravascular coagulopathy (DIC). In shelter cats that survived FPV infection, the most commonly observed clinical signs were anorexia, dehydration, fever, and diarrhea. In cats with fatal infections, death was preceded by clinical signs of circulating shock. If infected cats survive for longer than 5 days, they usually recover within days or weeks.

If fetal and neonatal infection (up to 6 weeks of age) occurs, the main clinical signs in infected new-born kittens are neurological, with ataxia, hypermetric movements, and blindness being the predominating hallmarks. In addition, there can be signs of cerebellar dysfunction, such as incoordination or unprogressive tremor with normal mental status. Forebrain damage is much less common, and those kittens present with seizures, behavioral changes and normal gait despite postural reaction deficits. The severity of the disease and of the neurological signs can vary among litters. One study reported that housing litters of kittens with their mother was not associated with an improved outcome in shelter cats with panleukopenia. If a queen becomes infected, she does not have protective antibodies and therefore, is unlikely to provide her kittens with adequate maternally derived antibodies (MDA) to protect them from the FPV that she is shedding.

Cats with mild cerebellar dysfunction can often learn to compensate and retain good quality of life despite residual deficits. FPV can also cause retinal degeneration with or without neurological signs in infected kitten.

What is the best strategy to prevent aneulekopenia?
According to the American Association of Feline Practitioners (AAFP), the European Advisory Board on Cat Diseases (ABCD), and other expert groups, panleukopenia is considered a core vaccine component. One guiding principle of vaccination recommendations is that as many animals of the population as possible should be vaccinated, but in individual cats, vaccines should be administered only as often as regarded necessary. This emphasizes the point that herd immunity is the most important factor for prevention of epidemics. Populations with <70% of animals protected are considered at risk for development of epidemics. There have been several studies on the prevalence of antibodies against parvoviruses in cats. In one US study investigating the prevalence of antibodies in 267 client-owned cats, the critical value of 70% was almost reached (67%). In a study of 350 cats in Germany, prevalence of antibodies against FPV was 71%. In a study from Costa Rica, antibodies were even detected in 93% of cats. This high percentage is probably explained by high environmental contamination due to high infection rates in dogs. Remarkably, relatively low protective antibody rates of 40% were documented in cats entering a Florida animal shelter. Low prevalence
rates were also found in North-Eastern France, with an average antibody prevalence of 25%. Divergent prevalence rates are most likely associated with regionally variable infection pressures and vaccination programs. Inclusion of surviving cats with naturally acquired immunity could be the reason why in the German study, 8/28 (29%) cats were shown to have antibodies against FPV that had never been vaccinated. Interestingly, 11/47 (23%) cats that had been vaccinated according to the current recommendations did not have detectable serum antibodies. This supports another study carried out in Germany in which 37% of kittens did not develop antibodies despite vaccination at 8, 12, and 16 weeks of age.

**Is passive immunization effective?**

In FPV infection, presence of antibodies is a strong predictor of protection. A prophylactic efficacy of passively transferred antibodies has been demonstrated in dogs and is also expected, but has not been proven for cats. Commercial antibody preparations produced in horses are available in some European countries. For prevention of disease due to FPV infection, kitten under 12 weeks of age are given 2 ml SC, cats over 12 weeks of age are administered 4 ml SC. If the commercial product of equine origin is used, repeated administration (at >1 week intervals) is not recommended, as this could lead to potentially fatal anaphylactic reactions. In addition, cats treated with anti-FPV serum should not be vaccinated within 3 weeks following passive immunization, as anti-FPV titers could interfere with vaccination response.

If anti-FPV serum is not commercially available, serum harvested from cats that have survived natural infection or from cats that have recently been vaccinated can also be used. Passive immunization is recommended if rapid protection is important, e.g. in disease outbreaks, or when entering a shelter, where infection pressure is high. Passive immunization can also be used to protect young kittens with incomplete vaccination histories, colostrum-deprived kittens, or unvaccinated adult cats.

**What are the current vaccination recommendations?**

According to current vaccination guidelines worldwide, vaccines against feline panleukopenia are considered core vaccines. In cats <12 weeks of age, complete primary vaccination includes a vaccination series starting at 6 to 8 weeks, then vaccinations every 3 to 4 weeks until 16 weeks of age, followed by revaccination after a longer period (depending in the guideline after 6 months or after 1 year). In cats >12 weeks of age, a complete primary vaccination includes 2 vaccinations at an interval of 3 to 4 weeks, followed by a revaccination after 6 months to 1 year. After this, a booster vaccination is recommended every 3 years.

Cats that respond adequately to primary vaccination against FPV according to current guidelines maintain a solid immunity for 7 or more years. Despite the duration of immunity (DOI) indicated in these studies, experts worldwide recommend a very similar vaccination program, indicating that after the primary series, revaccination at intervals of 3 years or longer are advisable, unless special conditions apply, such as immunosuppression. It is unclear whether a single dose of modified life virus (MLV) FPV vaccine can induce adequate immunity in adult FPV-naive cats. In one experimental study, 8 to 10 weeks old, specific pathogen-free kitten were inoculated once with a multivalent vaccine containing inactivated FPV or MLV FPV. At 14 days after vaccination, 31% of kittens receiving the inactivated vaccines had protective FPV titers, whereas 85% of kittens receiving MLV vaccines had protective titers. Thus, with few exceptions, use of MLV is preferred. One study suggested that, in the absence of MDA, a single dose of a MLV vaccine might be sufficient to provide some protection. However, in a recent field study, these findings could not be confirmed, as 40% of 244 cats with feline panleukopenia had received at least one vaccine dose, but nevertheless developed disease. Possible reasons for this lack of protection by 1 vaccination include the relatively long duration of interference by MDA in kittens, vaccination of immunocompromised cats, vaccination of cats already infected, or administration of less immunogenic inactivated vaccines.

**Are there risk factors for lack of protection?**

In many countries, feline panleukopenia is still commonly diagnosed despite widespread vaccination. Clinical disease has been described in both vaccinated and non-vaccinated cats. Thus, a lack of immunity can occur even when current recommended vaccination guidelines are followed. In a German study, 25% of cats diagnosed with feline panleukopenia were older than 1 year, and 11% were older than 5 years. The relatively high infection rate in older cats in the German study might be explained by a lack of environmental virus exposure, since indoor cats were overrepresented in this study. As natural contact with parvoviruses is less likely in indoor cats, there is reduced opportunity to build protective immunity following subclinical infection. In addition, indoor cats are less commonly vaccinated, due to the misconception by their owners that vaccination is unnecessary.

It is well known that MDAs interfere with development of active immunity after vaccination. MDAs to FPV have a half-life of about 9 days. Until a few years ago, MDAs were considered to decline to a level that could be overcome by MLV at 12 weeks of age. This however, Is not true, and current guidelines recommend vaccinations every 3 to 4 weeks until an age of 16 weeks. In 2008 and 2009, several outbreaks of panleukopenia in Norwegian Forest cats were reported in Germany. Subsequently, a field study revealed that 37% of kittens did not develop antibodies despite 3 vaccinations at 8, 12, and 16 weeks of age. MDAs were found in most kittens beyond 12 weeks of age; in some cats, MDAs interfering with primary vaccination and preventing antibody development were detected until 20 weeks of age. Thus, even if a course of vaccination is
continued until 16 weeks of age, this is not sufficient to protect all kittens. Evaluation of the best starting point for primary vaccination by antibody testing in individual kittens could be helpful to reduce incidence of feline panleukopenia. The optimum starting point is defined as the age when MDAs have dropped below a certain level. Alternatively, future recommendations for primary vaccination might include continuing kitten vaccination series until 20 weeks of age, or revaccinating at 6 months of age after the kitten vaccination series has been completed.

Is antibody testing useful to predict vaccination necessity?
Although rare in cats, mild to severe adverse reactions can occur after vaccination. Adverse reactions include feline injection site sarcomas, which have a guarded prognosis because of frequent recurrence after surgical excision. In previously vaccinated cats, detection of FPV-specific antibodies above certain pre-determined levels is predictive of protection, regardless of vaccine type or vaccination interval. Therefore, yearly FPV antibody titer testing can be helpful in determining the susceptibility of individual cats and the response to vaccination before a decision is made regarding the need for booster vaccination. However, in the interpretation of antibody test results, it should be remembered that while a protective titer against FPV denote immunity, cats with negative or low antibody titers might still be protected. Studies have been conducted to investigate whether point of care tests can also be used for the detection of antibodies. One study investigated the accuracy the ImmunoComb Feline VaccCheck antibody test kit (Biogal, Israel) in young (probably unvaccinated) cats entering a shelter in Florida. Subsequently, the test was modified to increase its sensitivity. In a German study investigating the modified test, sera from 347 cats were evaluated using haemagglutination inhibition (HI) as reference method. Sensitivity was 87%, and specificity was 81%. It can be concluded, that these point of care tests can be useful in the decision whether panleukopenia vaccination is necessary in an adult cat or not.

How should cats with panleukopenia be managed and treated?
Mortality of panleukopenia is 25%–90% in cats with the acute form of the disease and up to 100% in cats with peracute disease. The prevalence of subclinical infections is unknown. Kittens up to 12 months of age were once considered to have the highest morbidity and mortality. However, one German study reported no significant correlations between age and severity of clinical signs or outcome in 244 cats with panleukopenia. In this study, 57% of cats were less than 6 months of age, confirming that young cats are more susceptible to feline panleukopenia than older cats, but do not have an increased mortality. No significant correlation was found between outcome and living conditions, vaccination status (unvaccinated versus 1 or more vaccines administered) or severity of clinical signs. In contrast, white blood cell and platelet counts at the time of presentation, as well as albumin and potassium serum concentrations were prognostic markers.

What are adequate measures to avoid transmission?
Cats diagnosed with feline panleukopenia should be hospitalized and kept in isolation for at least 2 weeks to avoid viral transmission. Intensive care and strict hygiene to prevent fomite transmission are essential. Due to the extreme stability of FPV, contaminated cages, litter trays, food dishes, water bowls, shoes and clothing of caregivers and visitors can play a role in transmission; therefore, proper sanitization measures are of utmost importance. FPV is resistant to many commonly used disinfectants, but is inactivated by products containing potassium peroxymonosulfate, accelerated hydrogen peroxide, peracetic acid, formaldehyde, sodium hypochlorite, or sodium hydroxide, provided thorough cleaning is performed first to remove organic matter and recommended contact times are guaranteed. Sodium hypochlorite (household bleach, 1:30 dilution) can be used on surfaces, such as litter trays, and formaldehyde gas can be used for room disinfection.

Which supportive treatment is useful?
Supportive therapy and good nursing care are important to decrease mortality in cats with feline panleukopenia. Parenteral fluid therapy to restore hydration, electrolyte and acid base balance is most important. Fluids are preferably administered IV as continuous rate infusion. Vitamin B complex can be added to prevent thiamine deficiency, but this complication occurs infrequently. Hypoproteinemic cats sometimes require plasma or whole blood transfusions to improve oncotic pressure. Plasma transfusions in combination with heparin can control DIC, as they supplement anti-thrombin III and other important plasma proteins. In anorectic cats, those with severe vomiting and/or diarrhea or with persistent hypoproteinemia, parenteral nutrition is required, preferably via a central venous catheter in the jugular vein. As the gastrointestinal barrier is often destroyed, intestinal bacteria can invade the blood stream, and bacteraemia combined with neutropenia can lead to sepsis in these immunocompromised animals. Thus, prevention of sepsis is essential for all cases, and a broad-spectrum antibiotic with proven efficacy against Gram-negative and anaerobic bacteria is recommended. A good combination for cats with panleukopenia is amoxicillin/clavulanic acid in combination with a third generation cephalosporin. Due to renal toxicity, gentamycin should only be used in well hydrated cats. A broad spectrum can also be provided by combining amoxicillin/clavulanic acid with fluoroquinolones. It has to be considered, however, that fluoroquinolones, with the exception of pradofloxacin (which only can be given orally), have been associated with retinal toxicity in cats and should therefore be avoided. Antibiotics should be administered parenterally (preferably IV), but...
pradofloxacin is not currently available for parenteral use.

Antiemetics might be required to control persistent vomiting. Maropitant is the drug of choice. Gastrointestinal protectants are also commonly administered. The use of anticholinergic medications is not indicated as these can produce sustained intestinal ileus and can lead to intussusception.

Oral caloric intake and water should only be withheld while cats are severely vomiting, but should recommence as soon as possible, starting with frequent feeding of small amounts. In dogs with parvovirosis, beneficial effects of early enteral nutrition have been demonstrated. A highly digestible diet is preferred for cats recovering from feline panleukopenia, but if the cat does not accept it, any diet is better than no food intake at all. Semi-moist foods with low fiber content can help firm the feces of cats with diarrhea. Glucocorticoids should not be administered because of their immunosuppressive effects.

**Is antiviral chemotherapy effective?**

There are only few antiviral compounds that can be used in cats with panleukopenia.

**Feline interferon-ω:** In dogs, feline interferon-ω (IFN-ω) has been successfully used to treat CPV infection in experimental studies and field trials. In one study, treatment reduced mortality of CPV infection by about 5-fold. IFN-ω also inhibits replication of FPV in cell culture, but the efficacy of IFN-ω as a treatment for feline panleukopenia has not been confirmed. IFN-ω was administered to cats in a cattery before an outbreak of panleukopenia in order to investigate a possible prophylactic effect. Twenty-three kittens were injected with IFN-ω (10^6 U/kg SQ q 24 h for 3 days), and survival and blood parameters were compared to those of 17 untreated cats; however, no significant difference in survival between the groups was found. Treated kittens displayed lower levels of α1-globulins and higher values of γ-globulins and immunoglobulins, suggesting that IFN-ω might have stimulated antibody production. However, this did not lead to a better outcome. **Immunoglobulins:** Specific immunoglobulins are also being used to treat cats with FPV infection. Concentrated immunoglobulin preparations containing FPV antibodies are commercially available in some countries and are used to treat and prevent infection in susceptible animals. In a recent study in which dogs with CPV infection received specific immunoglobulins, this treatment was, however, not successful. There are no studies in cats with panleukopenia so far.

**Suggested Reading References**


**Other references can be provided by the author on request.**