GUIDELINE for Feline Panleukopenia

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The Feline Panleukopenia guidelines were first published by Uwe Truyen et al. in the J Feline Med Surg 2009; 11: 538-546 and updated in J Feline Med Surg 2013; 15: 530-531 and in J Feline Med Surg 2015; 17: 570-582. The present guidelines were updated by Uwe Truyen et al.

Key points

- Feline panleukopenia virus (FPV) and the closely related canine parvovirus 2 (CPV-2) can infect and cause severe disease in cats.
- FPV is shed in high titers in the faeces and the very stable virions stay infectious in the environment for months.
- FPV is very tolerant against many commonly used chemical disinfectants. Efficacy tested disinfectants based on aldehydes, peracetic acid or sodium hypochlorite readily inactivate the virus.
- Very efficacious vaccines are available which protect cats from disease.
- Vaccines provide a long lasting, most likely lifelong, immunity.
- Diseased cats have a poor prognosis and less than 50 % of cats will survive even after intensive care treatment.

Agent properties

Feline panleukopenia virus or feline parvovirus (FPV) is the prototype of closely related parvoviruses isolated from dogs, mink, raccoons, raccoon dogs, foxes and other canids (Parrish, 1990). They were initially named after the hosts from which they had been isolated, e.g., canine parvovirus type 2 (CPV-2), mink enteritis virus, raccoon parvovirus, feline panleukopenia virus (FPV), and others. Current taxonomy defines these viruses as a single entity, the carnivore protoparvovirus 1 (ICTV taxonomy report 2019).

Parvoviruses are, as the name suggests, small, measuring only about 20 nm in diameter, non-enveloped viruses that contain a small single-stranded DNA genome of about only 5,000 nucleotides.

The single stranded DNA is replicated to double stranded DNA by cellular DNA polymerases. Unlike most dsDNA viruses, parvoviruses are unable to activate DNA synthesis in host cells and have to rely on cellular DNA polymerases which are only expressed in cells during mitosis. This is one reason for the restriction of parvovirus replication to mitotically active, i.e., proliferating tissues. The other reason is the cellular receptor that the virus needs to bind to the cell. For FPV the transferrin receptor was identified, a molecule that is highly expressed on many metabolically active cells that need iron ions for their activity. This explains why tissue damage caused by FPV occurs predominantly in rapidly dividing cells, like those in the intestine, bone marrow, and in embryonic tissue.

Parvoviruses replicate in the nucleus of an infected cell, and nuclear inclusion bodies can be demonstrated in infected cells (Figs. 1, 2).

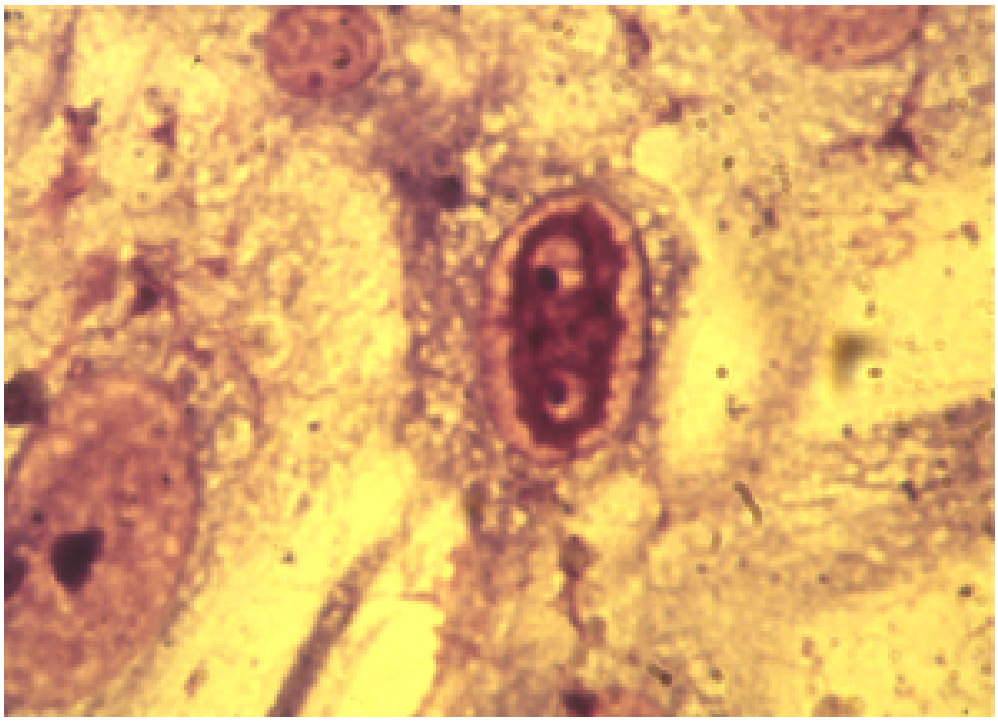


Fig. 1. Nuclear inclusions in cells of the Crandell feline kidney (CrFK) line infected with feline panleukopenia virus; replication of this DNA virus occurs in the nucleus ©Nicola Decaro

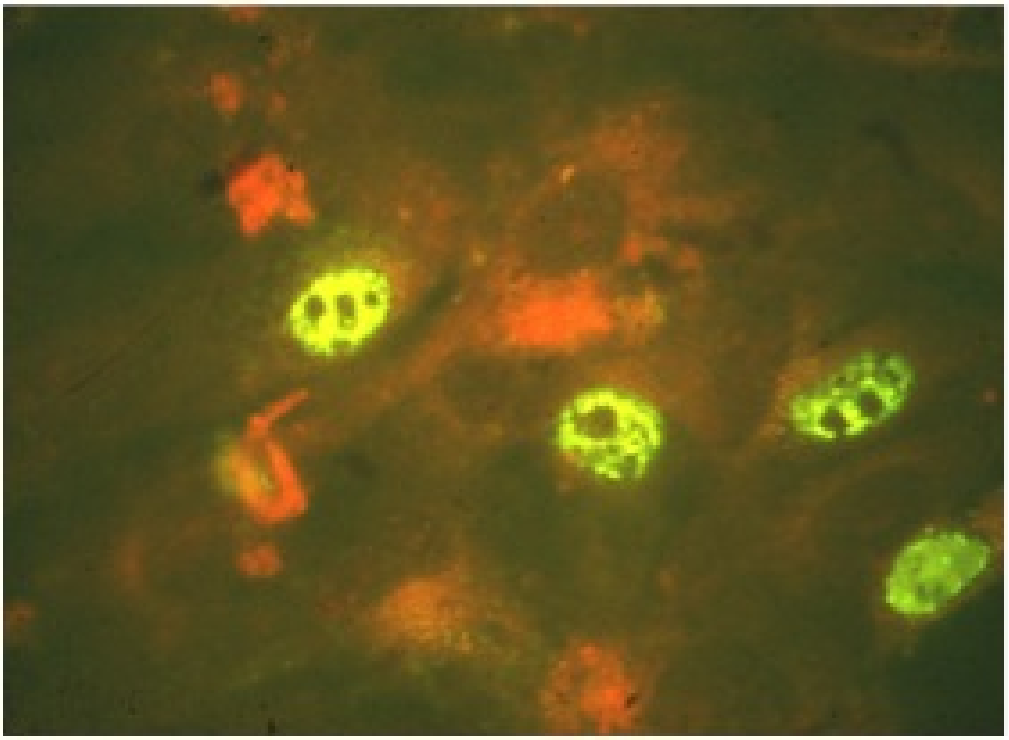


Fig. 2. Nuclear immunofluorescence of Crandell feline kidney (CrFK) line cells infected with feline panleukopenia virus; note absence of viral antigen in the cytoplasm. Not every cell is infected – the shadow of a nucleus is visible ©Nicola Decaro

FPV infects cats and other members of the *Felidae*, as well as raccoons, mink, and foxes (Steinel et al., 2001). FPV also can infect dogs,

and FPV replication occurs in the lymphoid tissues (thymus, spleen, bone marrow) but not in the gut of dogs; FPV is not shed in the faeces of dogs infected with FPV, and dogs do not develop disease (Truyen and Parrish, 1992).

In 1978, a new parvovirus, closely related to the long known FPV, was first described in dogs (Carmichael, 2005). It was named canine parvovirus type 2 (CPV-2) to distinguish it from another, only distantly related, parvovirus isolated from dogs in 1970 which was first named CPV-1 but which is now called "canine minute virus" and grouped within the genus *Bocaparvovirus*. CPV-2 has evolved from FPV by acquiring 5 or 6 amino acid changes in the capsid protein gene (Parrish, 1990; Truyen, 1999), which enabled the virus to bind to the canine transferrin receptor and thus infect canine cells, but at the same time CPV-2 lost its ability to replicate in cats. However, during a parallel evolution the ancestor viruses of CPV-2, which were most likely infecting raccoons, retained their ability to infect cats but acquired further amino acid changes that enabled the new virus to better bind to the canine cellular receptor (Hueffer and Parrish, 2003; Allison et al., 2012). This led to the generation of the new type CPV-2a, that subsequently acquired further mutations including those at amino acid 426 of the capsid protein VP2, which as a polymorphism determines the different antigenic types 2a, 2b, and 2c (Fig. 3). The original virus from 1978, the CPV-2 became extinct. Analyses of genomic full-length CPV sequences revealed various genotypes independent of the antigenic characterization of the viruses in CPV-2a, CPV-2b or CPV-2c viruses (Chung et al., 2020; Voorhees et al., 2020).

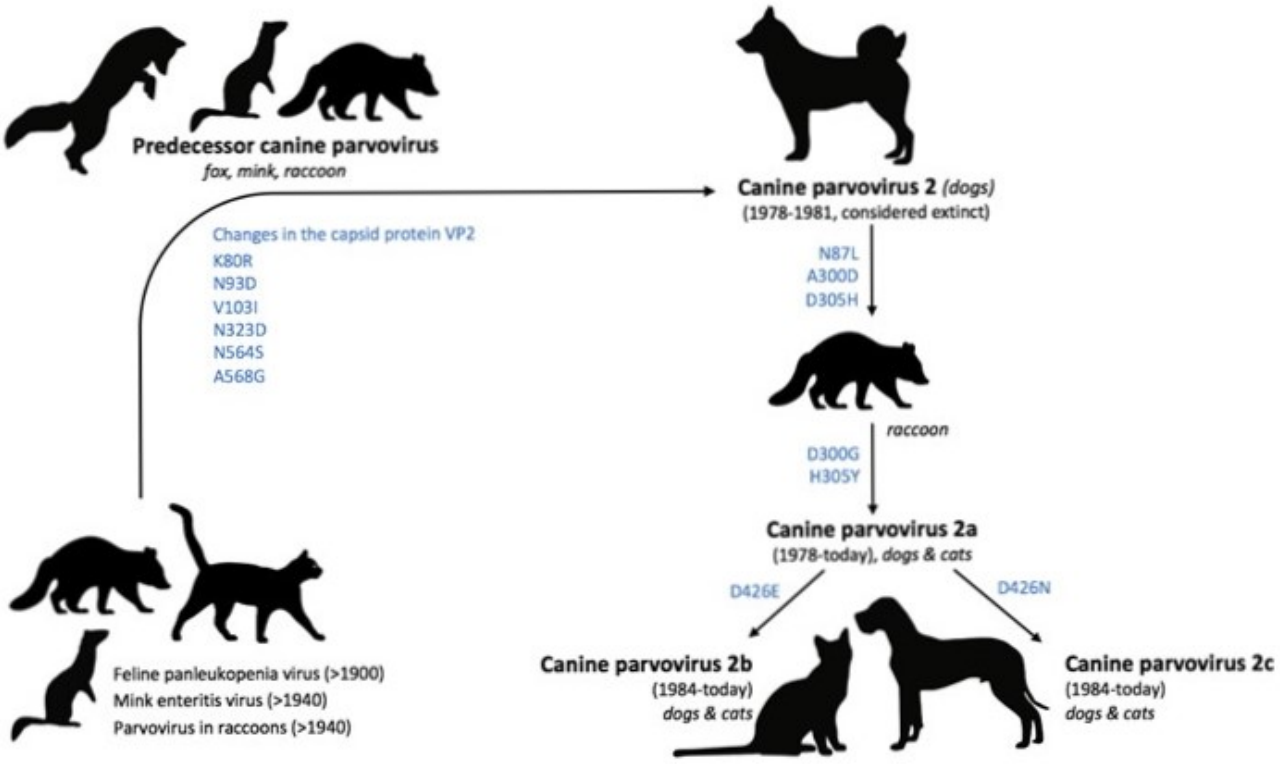


Fig. 3. Cartoon of the evolution of CPV and its so-called antigenic types from the long known FPV through passages through various carnivores. ©ABCD, Karin de Lange

Parvoviruses are now circulating in dog populations worldwide, genetically and antigenically defined as types CPV-2a, CPV-2b, and CPV-2c; these can all infect cats and can even cause the disease panleukopenia in cats (Truyen et al., 1995, 1996; Mochizuki et al., 1996). These CPV types can be isolated from feline peripheral blood lymphocytes after numerous blind passages, and viral DNA can be demonstrated by PCR (Ikeda et al., 2000). A case of CPV-2c infection in a cat with severe clinical signs was described in Portugal (Miranda et al., 2014). However, CPV infections of cats were considered rare in Europe and the USA, and the virus has only sporadically been found in diagnostic material (Truyen et al., 1996). However, a recent study reported the presence of CPV in shelter cats in the UK; CPV was demonstrated in 32.5% (13/50) of faecal samples in a cross-sectional study of 50 cats from a feline-only shelter, and 33.9% (61/180) of faecal samples in a longitudinal study of 74 cats at a mixed canine and feline shelter, while in Australia no CPV shedding was found in shelter cats (Clegg et al., 2012; Byrne et al., 2018).

During the evolution from FPV to CPV-2, and its various antigenic types, neutralizing epitopes have been affected such that cross-

neutralization by FPV antisera is markedly lower against the newer CPV viruses (Truyen and Parrish, 2013).

A comparable evolution of FPV has not been observed. The virus appears highly adapted to its feline host and shows only marginal sequence evolution without obvious selection of specific mutations, although regional outbreaks can be traced to different viruses, with sequences specific for that outbreak (Barrs, 2019; van Brussel et al., 2019; Jenkins et al., 2020).

Epidemiology

FPV is non-enveloped and highly resistant to physical factors and chemical substances. In contaminated environments, it may remain infectious for weeks or even months (Uttenthal et al., 1999). Diseased carnivores shed virus at high titres (up to 109 TCID50 per gram of faeces), and virus quickly accumulates in affected shelters and catteries. As it is highly contagious, susceptible animals may still become infected, even after a seemingly thorough disinfection of the premises. It is therefore recommended that only successfully vaccinated kittens and cats should enter such an environment.

Although few data on FPV prevalence are available, particularly breeding catteries and rescue shelters are at risk (Addie et al., 1998; Cave et al., 2002).

Persistent infections and persistent viral shedding are rare; using PCR, healthy cats have been found positive in faeces over weeks; it is unknown whether this is of epidemiological significance (Jakel et al., 2012). Interestingly, CPV-2 viruses could be isolated from feces of healthy cats in the UK in two shelters. It is unclear if this is of epidemiological importance (Clegg et al., 2012).

After intrauterine infection, FPV antigen is present in the cerebellum of kittens for weeks (Csiza et al., 1971).

The analysis of parvovirus sequences recovered from wild carnivores (pumas, coyotes, raccoons, and others) revealed a broad range of virus types. This implicates the infection of predators by their prey, if the latter was infected with parvoviruses, and thus a new route of infection (Allison et al., 2013).

Pathogenesis

FPV causes a systemic infection. The virus is transmitted via the faecal-oral route, initially replicating in the tissues of the oropharynx and is then distributed via cell-free viraemia to virtually all tissues in the body. Replication of the parvoviral single-stranded DNA requires cells in the S-phase of division and is therefore restricted to mitotically active tissues; in the gut, this results in enteritis (Figs. 4, 5). Parvoviruses require cellular DNA polymerases to synthesize the complementary DNA strand of their ssDNA, which is the first step in replication and a prerequisite for transcription.

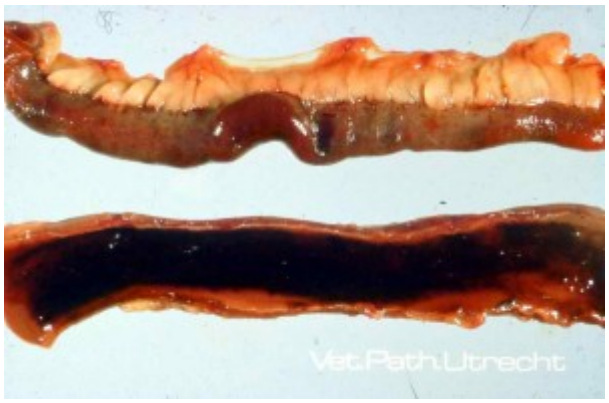


Fig. 4. Hemorrhagic enteritis as a consequence of feline panleukopenia virus infection ©Vet.Pathol. Utrecht

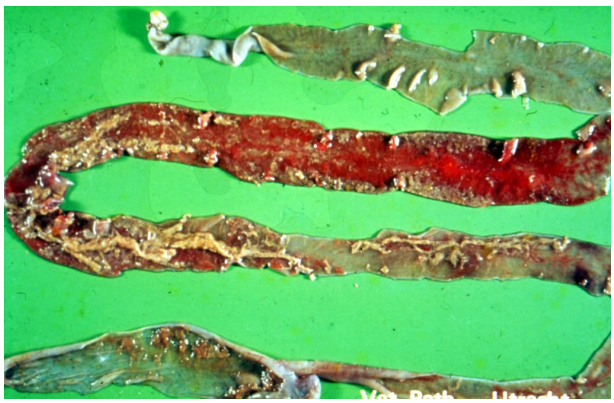


Fig. 5. Intestinal damage as a consequence of feline panleukopenia virus infection; sloughing of gut epithelium and fibrinous "casts" are prominent ©Vet.Pathol. Utrecht

The virus infects lymphoid tissues where it can cause cellular depletion and a functional immunosuppression. Lymphopenia can arise as a result of lymphocytolysis but also indirectly, from lymphocyte emigration into tissues. The bone marrow is affected, and virus replication has been described in early progenitor cells, with dramatic effects on virtually all myeloid cell populations (Parrish, 1995). "Panleukopenia", i.e., the deficiency of all white cell populations, is the result (Truyen and Parrish, 2000).

The hallmark of FPV replication is the shortening of intestinal villi due to, sometimes, a complete loss of epithelial cells in the gut (Parrish, 2006). The virus replicates in the rapidly dividing cells in the crypts of Lieberkühn, which impairs regeneration of the epithelium and results in the lesions described below (Fig. 6). The severity of the lesions correlates with the epithelial turnover rate, and co-

infection with enteric viruses – like feline coronavirus – can enhance the severity of disease.

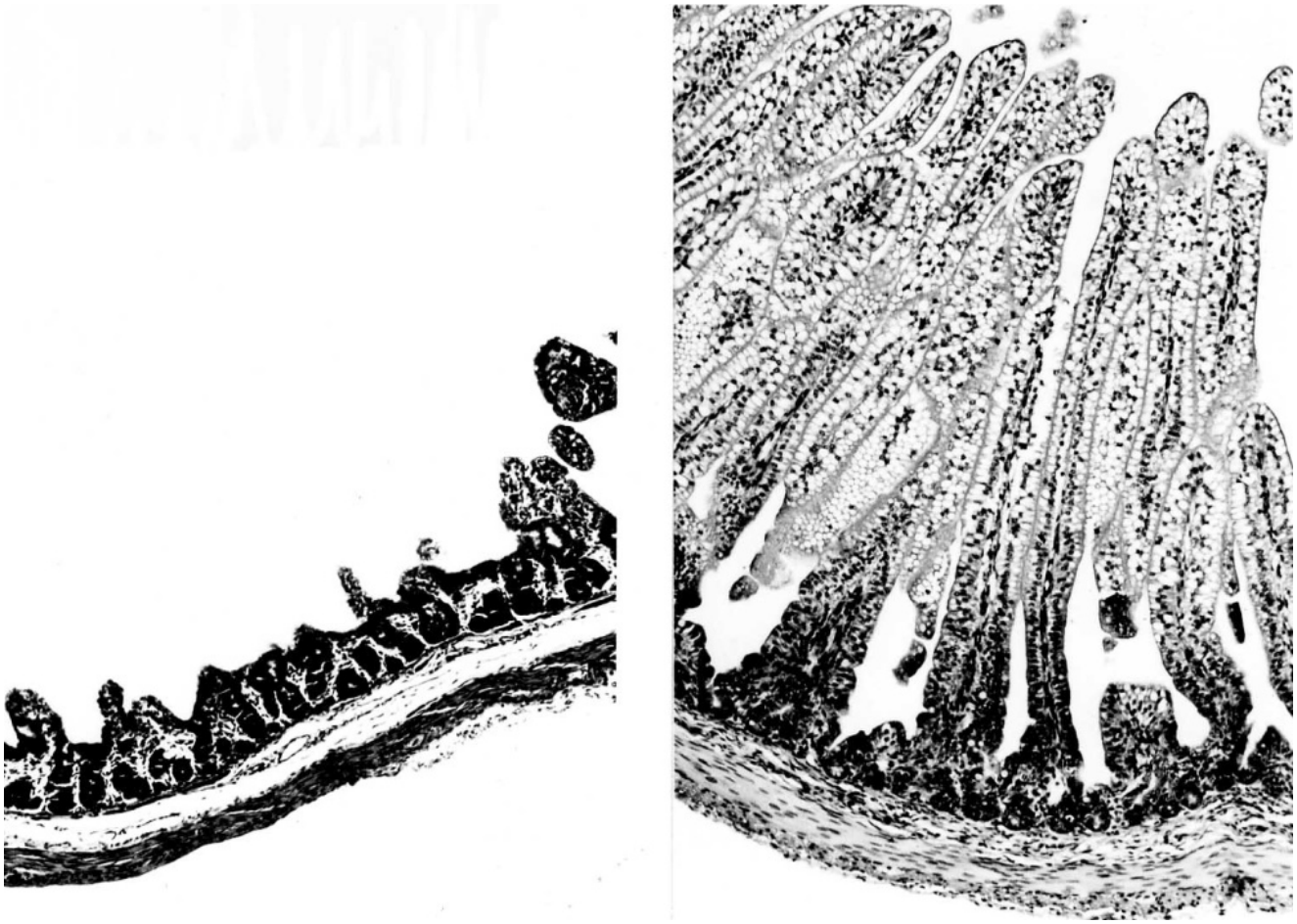


Fig. 6. Damage to the gut epithelium after an FPLV infection (left); the villi have virtually disappeared. A normal gut is shown for comparison (right). ©Leland E. Carmichael

Intrauterine transmission or perinatal FPV infection can affect central nervous system development. So-called “Feline ataxia syndrome” results from an impaired development of the cerebellum due to lytic infection of the Purkinje cells in the kitten (Figs. 7, 8; Csiza et al., 1971; Kilham et al., 1971). Parvovirus DNA has also been reported in maternal tissues, but not in foetal material, of queens with reproductive failure, but as only PCR and no virus isolation or antigen detection in tissues was conducted, the relevance of these findings is not clear (Pristo de Medeiros Oliveira et al., 2018). Interestingly, a FPV-like virus has been described as the cause of reproductive disorders in pregnant foxes (Veijalainen and Smeds, 1988).

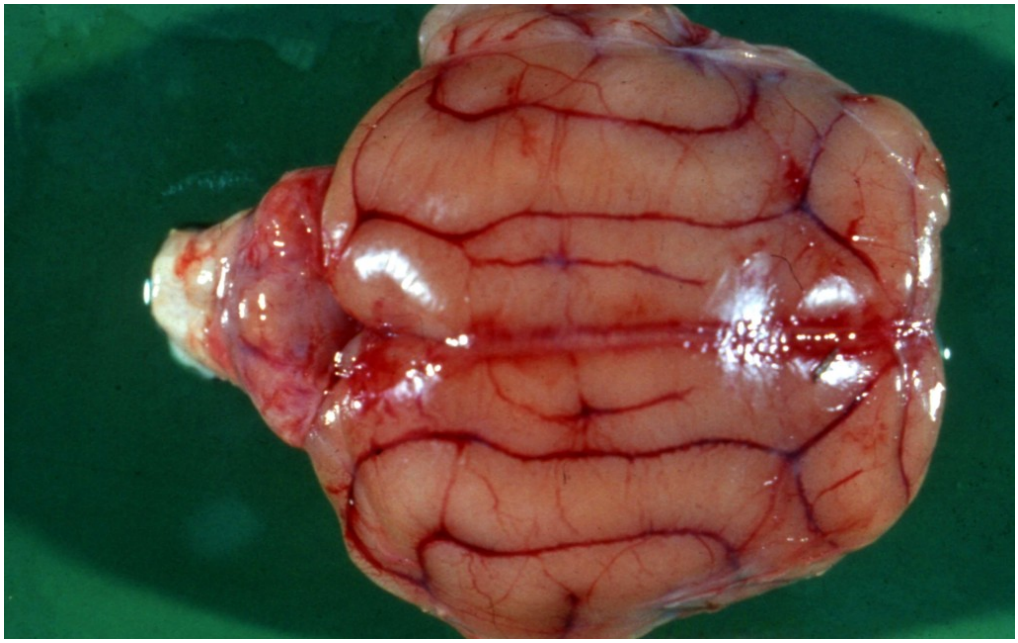


Fig. 7. Cerebellar hypoplasia in a kitten infected in utero with feline panleukopenia virus ©Marian C. Horzinek

Fig. 8. Cerebellar hypoplasia (below) in a kitten infected in utero with feline panleukopenia virus; a normal brain is shown for comparison (above) ©Diane Addie

Foetal infection can induce immunological tolerance, so that kittens continue shedding virus for extended periods of time (Pedersen, 1987).

Foetuses infected between the 35th and 45th days of gestation have depressed T-lymphocyte mediated immunity.

In adult cats, infection leads to a transient decrease in the immune response: neutrophil counts decrease severely, and lymphocytes disappear from the circulation, lymph nodes, bone marrow and thymus (Pedersen, 1987; Ikeda et al., 1998).

Immunity

Passive immunity

Antibodies play an important role in the immune response to FPV. Maternally derived antibodies (MDA) efficiently protect kittens from fatal infection.

The endotheliochorial placentation of the cat restricts maternofoetal passage of solutes, and IgG can only cross the placenta barrier in the last trimester of gestation. This immunoglobulin transfer accounts for <10 % of the kitten's maternal immunity. Therefore, ingesting sufficient colostrum is essential for acquiring protective levels of neutralising antibodies from the queen. Maximum absorption is at around the 8th hour of life. Later, the kitten's intestinal cells are replaced by new epithelium that no longer absorbs and transports colostral antibodies.

Kitten serum antibody titres are generally about half of those of the queen. Their levels depend on the individual colostrum intake, which explains the large variations between litter mates. The titres decrease in the first few weeks of life, by decay and by dilution in the growing kitten.

In kittens, maternal antibodies have a biological half-life of about ten days (Scott et al., 1970; Pedersen, 1987). When antibodies have waned below a titre of 40 to 80 (as measured by haemagglutination inhibition) they do not reliably protect against infection but can interfere with active immunisation (Fig. 9). Most cats have maternal antibodies at protective titres until at least 8-12 weeks of age. ABCD recommends FPV vaccinations at 15 to 16 weeks of age, as explained below, to avoid interference with vaccine efficacy by MDA (Dawson et al., 2001; Jakel et al., 2012).

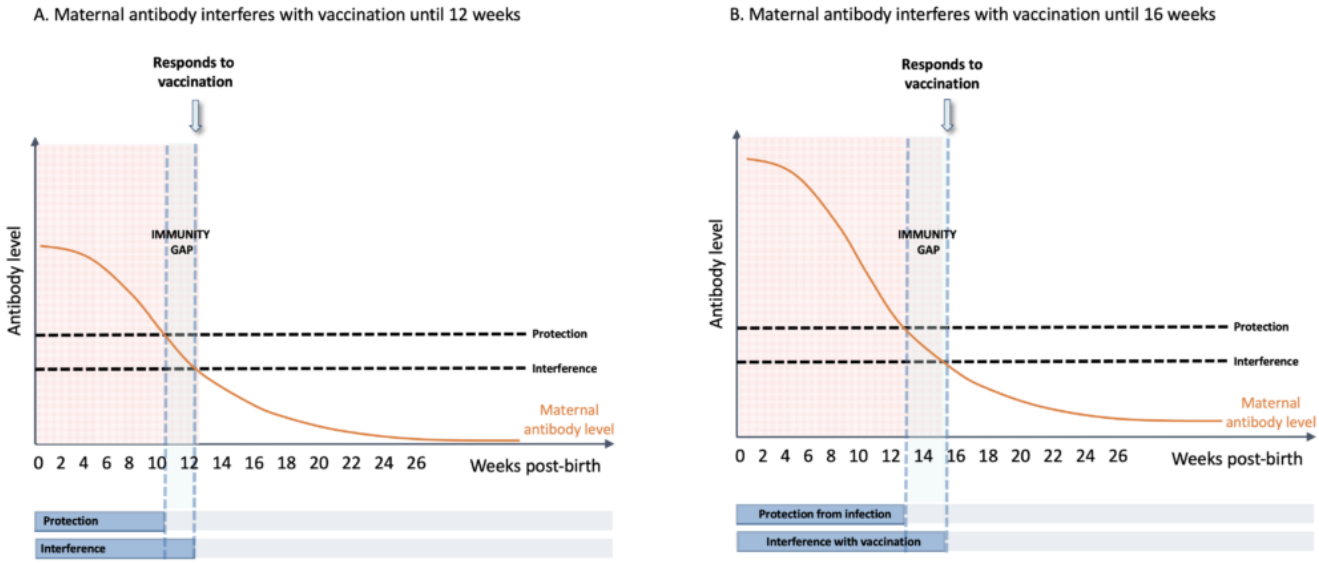


Fig. 9.Graph illustrating the immunity gap, or zone of interference. In this example, for kittens that acquire moderate levels of maternal antibodies (A), the critical period, or immunity gap, is between weeks 10 and 12 of age whereas for kittens that acquire higher levels of maternal antibodies (B), the immunity gap occurs later, between weeks 13 and 15. In both examples, before 7 weeks of age the maternal antibody titres are sufficient for protection and would neutralize the vaccine virus so it does not induce an immune response. Maternal antibodies can still interfere with the vaccine virus and prevent or impair the immune response of the vaccinated kitten until the end of the immunity gap, which is earlier or later, depending on the titre of maternal antibodies acquired.

Active immunity

Passively acquired immunity is later replaced by an active immune response present as a result of vaccination or as a consequence of natural infection (Proksch et al., 2018).

Acquired immunity is solid and long lasting (Thiry, 2002a) and can be induced by both, inactivated and modified live virus (MLV) vaccines. FPV antiserum can be used for passive immunisation when unprotected cats are likely to be exposed to virus before the initiation of a vaccine-induced, active response (Barlough et al., 1997).

Parvoviruses induce a range of immune responses including reactions of T-helper CD4+ lymphocytes and possibly CD8+ cytotoxic T lymphocytes.

Clinical signs

The clinical manifestations according to the cell types affected are summarized in table 1.

Table 1 – FPV infection: pathological consequences and clinical manifestations (adapted from Chandler, 2004).

AFFECTED CELLS	CONSEQUENCES	CLINICAL MANIFESTATION
Intestinal crypt epithelium	Villous collapse, enteritis	Diarrhoea
Lymph node, thymus	Germinal centre depletion, apoptosis of lymphocytes, thymic atrophy	Lymphopenia
Bone marrow	Stem cell depletion	Neutropenia (later also thrombocytopenia and anaemia)
Most cells in the foetus	Foetal death	Abortion
Developing cerebellum in the foetus	Cerebellar hypoplasia	Walking with an exaggerated “goose-stepping” gait

ADAPTED FROM: CHANDLER, 2004.

Diagnosis

Post-mortem examination should be performed on any cat suspected to have succumbed to FPV infection as histopathology of the intestinal tract (especially the jejunum and ileum) can show characteristic intestinal crypt necrosis and dilated crypts with mucus and sloughed necrotic cell debris. Neonatally infected cats can have cerebellar hypoplasia.

Laboratory changes

Cats with severe FPV infection, especially kittens with severe gastrointestinal signs, can have markedly reduced white blood cell counts as low as 0.05-3 x 10^9/l (Barrs, 2019). Examination of an in-house stained blood smear microscopically may reveal a profound neutropenia and lymphopenia. Thrombocytopenia is sometimes reported. Serum biochemistry shows non-specific changes but a hypoalbuminaemia, hypochloraemia and hyponatraemia can result from the gastrointestinal signs.

Diagnostic Imaging

Ultrasonography findings in FPV infected cats have recently been described (Isaya et al., 2021) as non-specific, but include diffuse small intestine mucosal layer thinning, muscular layer thickening and mucosal hyperechogenicity.

Detection of the infectious agent

In practice, FPV antigen detection in faeces is usually carried out using commercially available point-of-care (POC) tests based on an ELISA or immunomigration principle (Veijalainen et al., 1986; Addie et al., 1998). These POC tests are marketed for the detection of FPV and/or CPV, but all of them are able to detect FPV antigen. In clinical cases, a positive result with a POC test confirms the diagnosis. However, a negative test does not rule out infection since FPV faecal shedding can be intermittent and POC tests can be negative if the viral load is not high (Neuerer et al., 2008; Schmitz et al., 2009; Bergmann et al., 2019). Thus, if such a test is negative in a cat that is suspected to suffer from panleukopenia, PCR should be performed, which is more sensitive.

PCR-based tests for FPV can be performed on faeces, whole blood, bone marrow or tissues samples, although faecal samples are most frequently used. Healthy cats can also test positive by PCR in faeces (Bergmann et al., 2019). Virus isolation confirms infection in healthy cats showing that they too can shed replicating virus.

Vaccine virus shedding also occurs after vaccination with FPV MLV vaccines, and this can lead to positive results on both faecal antigen

and faecal PCR testing for at least 4 weeks after vaccination (Bergmann et al., 2019).

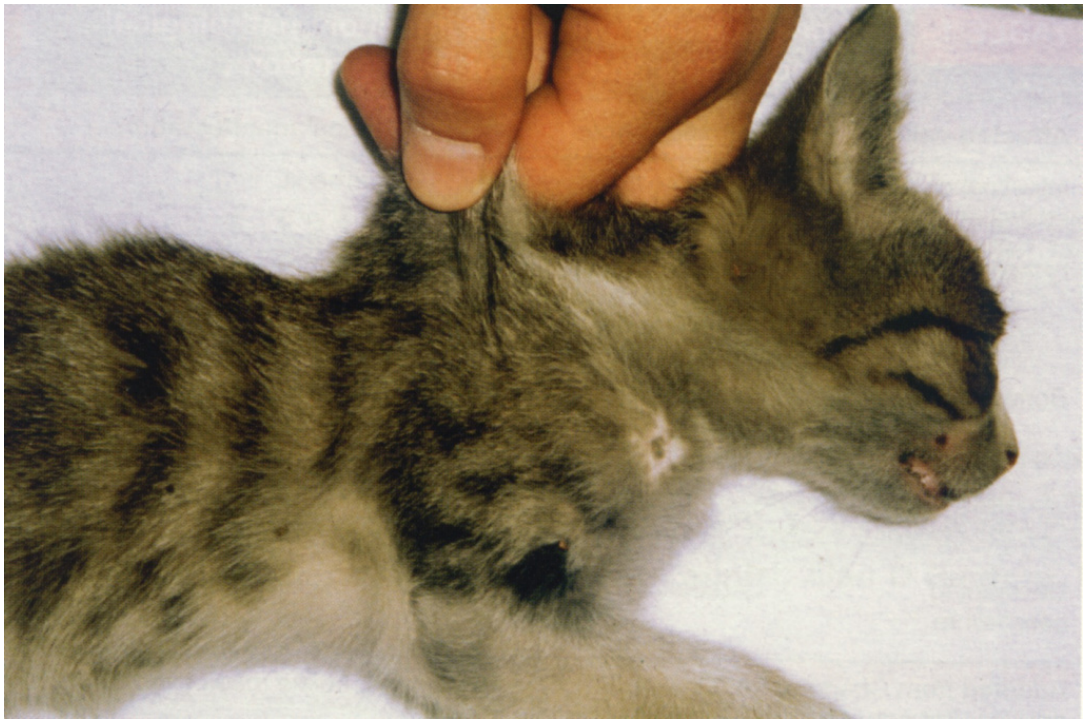
Virus isolation can demonstrate replicating virus. Electron microscopy can show FPV particles. Haemagglutination assays for FPV also exist. However, all of these methods have now largely been superseded by more readily available FPV antigen tests and PCR.

Disease management and treatment

A cat showing clinical signs of FPV, substantiated by laboratory evidence, should be kept in isolation with strict barrier nursing to prevent fomite transmission. Aggressive supportive care and good nursing care are extremely important.

Severe dehydration accelerates disease progression (Figs. 10, 11a and b).

Fig. 10. A kitten with severe signs of dehydration, a result of electrolyte loss as a consequence of feline panleukopenia ©Diane Addie



Figs. 11a and b. Dehydration in the course of FPV is a typical feature ©Tadeusz Frymus

Restoration of fluid and electrolytes, preferably intravenously or intraoesseously (in small kittens), such as with lactated Ringer's solution, is most important as symptomatic treatment (Fig. 12). Blood glucose should also be monitored in kittens and supplemented if required.

Fig. 12. Intensive care is often required for survival from FPV ©Albert Lloret

As the gut barrier often is destroyed in FPV-infected cats, intestinal bacteria can invade the blood stream via translocation. Bacteraemia can result, facilitated by the existing neutropenia, and leading to sepsis in these immunocompromised patients (Marenzoni et al., 2018). Prevention of sepsis is essential, and a broad-spectrum antibiotic with a proven efficacy against gram-negative and anaerobic bacteria is recommended. Examples are ampicillin (10-20 mg/kg IV or SC q8h) or amoxicillin/clavulanic acid, fluoroquinolones or cephalosporins. Antibiotics should be administered parenterally (preferentially intravenously if indicated).

If vomiting is present, anti-emetics should be given such as maropitant (1 mg/kg SC q24h) or metoclopramide (0.2-0.4 mg/kg SC q 6-8 hrs or 1-2 mg/kg IV over 24 hrs as a constant rate infusion). Ondansetron is an option for severe intractable vomiting.

Oral intake of water and food should only be restricted if vomiting persists, but feeding should be continued as long as possible, and restarted as soon as possible. Beneficial effects of early enteral nutrition have been reported in CPV-infected dogs (Mohr et al., 2003), and more data on supportive care are available for dogs (Gerlach et al., 2020) that can also be adapted for use in cats. A highly digestible diet is preferred, but if the cat does not accept it, any diet is better than no food intake at all.

Vitamin supplements, particularly of the B vitamin complex, can be given to prevent development of thiamine deficiency, which occurs occasionally in cats with FPV. Feline recombinant interferon-omega (rFeIFN) is effective in the treatment of CPV-induced enteritis in dogs (Minagawa et al., 1999; Martin et al., 2002; De Mari et al., 2003) and also inhibits replication of FPV in cell culture. In one retrospective study the administration of rFeIFN at 1 MU/kg SC q24 h for 3 days did not lead to increased survival rates (Porporato et al., 2018), although mortality in that study was very high at 80%. More research is needed to confirm the efficacy of IFN-ω in the treatment of cats with FPV disease, although some ABCD members do use it in the treatment of severely ill cats with FPV and find it useful. Prophylactic use of IFN-ω only showed limited efficacy in FPV-infected cats in a non-randomized study (Paltrinieri et al., 2007), and so ABCD currently does not recommend the use of IFN- ω for prophylaxis of FPV disease.

Short oligonucleotides (CpGs) have been shown to reduce parvovirus replication *in vitro*. However, *in vivo*, treated cats did not have significantly better survival, clinical scores, leukocyte or erythrocyte counts, viraemic loads nor faecal shedding at any time-point compared to control cats (Ferri et al., 2020).

It is important to realize, that many cats with panleukopenia also have parasite infestation, especially those originating from shelter environments and therefore, faecal examinations and appropriate anthelmintic treatment (e.g., fenbendazole, milbemycin-praziquantel, imidacloprid-moxidectin) is an important consideration as intestinal parasitism is a common comorbidity (Barrs, 2019).

Susceptible kittens and unvaccinated older animals should not be in contact with other cats until they are properly immunized. Once a disease outbreak occurs, passive immunization using anti-FPV serum, either from a cat recently recovered from FPV-infection or in form of a commercial product (in some countries immune-serum produced in horses containing FPV antibodies is commercially available as

subcutaneous injection for treatment and prevention of infection in susceptible animals) can be used to protect susceptible cats (young kittens with an incomplete vaccination history, colostrum-deprived kittens or unvaccinated cats). Self-produced anti-FPV serum (Levy et al., 2001) can be given subcutaneously or intraperitoneally (150 ml/kg or 2 ml/kitten) and protects for 2-4 weeks. If a commercial product of equine origin is used, repeated administration is not recommended as this can lead to anaphylactic reactions. Since the administered immunoglobulins will bind to parvoviral epitopes, animals that have received passive immunization should not be vaccinated within the first three weeks after passive immunization (Gerlach et al., 2017).

Due to the extreme physicochemical stability of FPV, contaminated cages, litter trays, food dishes, water bowls, shoes and clothing can play an important role in transmission. Therefore, attention to hygiene is of utmost importance. The virus is resistant to many common disinfectants but can be inactivated by products that contain peracetic acid, formaldehyde, sodium hypochlorite, or sodium hydroxide. Commercially available chemical disinfectants with proven efficacy against non-enveloped viruses or a disinfectant (solution or dry fog) for example, based on formaldehyde or peracetic acid can be used for room disinfection.

Prognosis

FPV can cause a severe and potentially fatal disease in cats. Although many subclinical infections probably occur, once disease occurs, it has a poor prognosis. Despite intensive treatment, 30-50 % of diseased cats will die (Kruse et al., 2010; Petini et al., 2020).

Antibodies against FPV on admission were associated with longer survival in cats (Ferri et al., 2020). Cats without signs of lethargy, with a higher body weight, or with a higher rectal temperature at hospital admission were more likely to survive than other cats. Moreover, leukopenia on or after the third day of hospitalization, but not on the day of admission, was associated with a poor outcome (Porporato et al., 2018).

Vaccination

Both MLV and adjuvanted inactivated FPV vaccines are available for administration by injection, and both provide solid immunity against disease. In an immune-competent cat capable of mounting an appropriate response, MLV vaccines generally result in more rapid protection (Levy et al., 2006). However, even a single dose of an inactivated FPV vaccine can rapidly induce good antibody responses in naïve cats within a short time span (Fischer et al., 2007). There are no data to suggest that particular vaccine brands are more efficacious than others.

In most situations, there is no reason to prefer one vaccine type to another in an individual cat; MLV products are used more commonly, because of the more rapid onset of protection and a better resistance to MDA. It has been recommended that immunosuppressed cats should not receive MLV products (see also the ABCD guidelines “Vaccination of immunocompromised cats”), but one study demonstrated no adverse effects when using a FPV MLV vaccine in cats with retrovirus infection (Bergmann et al., 2019).

There are other considerations that can also affect this decision:

MLV FPV vaccines should not be used in **pregnant queens** because of the risk of placental virus passage to the foetus and subsequent damage, especially to the developing cerebellum (Pollock and Postorino, 1994). In some countries, inactivated FPV vaccines are licensed for use in pregnant queens, but vaccination of pregnant queens should generally be avoided.

MLV FPV vaccines should never be administered to **kittens under 4 weeks of age** for the same reason: to avoid damage to the cerebellum, which is still developing in young neonates (Pollock and Postorino, 1994).

Because of the ubiquity of the virus and the serious consequences of an infection, vaccination is recommended for every cat that does not have adequate immunity. Therefore, FPV vaccine is considered as a core vaccine. Even cats with an indoor only lifestyle cannot always avoid encountering FPV, since the virus is so stable in the environment and can be transmitted on fomites (Pollock and Postorino, 1994).

Primary vaccination course

Most **kittens** are protected by MDA in the first weeks of life. However, without antibody testing, the level of protection and the point at which a kitten will become susceptible to infection and/or can respond immunologically to vaccination are unknown; also, there is considerable variation between individual kittens, even within a litter.

In general, MDA will have waned by 12 weeks of age in a kitten to a level that allows an active immunological response to occur with vaccination, and an initial vaccination at 8 to 9 weeks of age followed by a second vaccination 3 to 4 weeks later is commonly recommended. The data sheets of many vaccines contain recommendations to this effect. However, kittens with poor MDA can be vulnerable (and capable of responding to vaccination) at an earlier age, while others might possess MDA at titres that are high enough

for them to persist beyond week 12, as field data suggest (Dawson et al., 2001; Jakel et al., 2012), such that vaccination at 12 weeks can fail to induce protection (Kruse et al., 2010).

No single primary vaccination policy will therefore cover all potential situations. These are ABCD's recommendations:

All kittens should receive FPV vaccines.

Three doses – one at 8 to 9 weeks of age, a second 3 to 4 weeks later, and a third 3 to 4 weeks later (at a minimum of 16 weeks of age) should be administered. The third vaccination at 16 weeks is of particular importance for kittens in e.g. breeding catteries or cat shelters and for kittens born to queens with high antibody titres, as these are likely to transmit high levels of MDA (e.g. queens that have recovered from disease, that have lived in a high-exposure environment, or have received vaccination close before or during pregnancy) to their kittens which could persist until after 12 weeks of age.

In high-risk situations when prophylactic administration of immunoglobulins is not possible, additional earlier vaccinations of kittens should be considered, especially if MDA is known or suspected to be poor. If such a kitten is vaccinated at, or before, 4 weeks of age, this should only be done using an inactivated product, and repeat vaccinations can be done at 3 to 4 week intervals until ≥12 weeks of age using inactivated vaccines or modified live vaccines.

After the kitten primary vaccination course, all cats should receive an additional vaccine dose at 10 to 16 months of age; this will ensure adequate vaccine-induced immunity for cats that did not adequately respond to the primary course.

Revaccinations

In an experimental setting, cats that respond to FPV vaccination maintain a solid immunity for at least seven years – the latest time point tested – and possible life-long, even in the absence of any repeat vaccination or natural challenge (Scott and Geissinger, 1999; Lappin et al., 2002). The ABCD recommends subsequent revaccinations at intervals of three years or more, unless special conditions apply or alternatively antibody testing is performed (see also the ABCD guidelines "Vaccination and antibody testing"). Antibody testing before vaccination is recommended, as cats with FPV-specific antibodies are protected against infection and thus do not need to be re-vaccinated at that time point. Some commercially available POC tests are available for FPV antibody testing (Mende et al., 2014). Many cats already have antibodies even if not vaccinated (Bergmann et al., 2018). Cats that already possess antibodies do not react on vaccination; thus, antibody testing instead of routine vaccination is recommended. In house tests can be used to measure antibodies (Mende et al., 2014).

While most cases of feline panleukopenia are caused by infection with FPV, variants of canine parvovirus (CPV-2a, CPV-2b, CPV-2c) can infect cats and cause disease. Current FPV vaccines appear to afford protection against these CPV variants (Chalmers et al., 1999; Nakamura et al., 2001).

Disease control in specific situations

Shelters

(see also the ABCD guidelines "Infectious diseases in shelter situations and their management")

Random source populations with unknown vaccination histories, continuous turnover, and high risk for infections characterize most shelters. The cost of a vaccine is a significant management aspect; therefore, only those antigens that demonstrate a clear benefit against common and significant shelter diseases should be considered.

Feline panleukopenia is such a disease. FPV has re-emerged as a cause of cat mortality in cats in shelters and rescue homes throughout Europe, the United States and Australia (Barrs, 2019; van Brussel et al., 2019; Jenkins et al., 2020).

With rare exceptions, all kittens and cats over 4 to 6 weeks of age should be vaccinated, regardless of their housing status. For sick or pregnant cats, any decision about vaccination has to be taken for the individual cat, but vaccination is recommended whenever and as soon as justifiable. Pregnant cats should not receive a live FPV vaccine. Kittens should be vaccinated beginning at 4 weeks of age in the face of an outbreak, otherwise at 6 weeks of age. MLV vaccines are recommended because of their faster onset of action, greater efficacy at overcoming MDA, and a greater likelihood of conferring sufficient immunity. Although concerns have been raised regarding strain reversion to virulence in MLV, this has never been documented. Vaccination should be repeated every 3 to 4 weeks until 16 weeks of age. If adult cats are ill or otherwise compromised at the time of initial vaccination, another injection should be considered when the cat is again in good health (at least two weeks after the initial vaccine). Cats of unknown status should not be housed together.

Passive immunisation can be used in shelters when available. It is useful at admission if other diseases are present or in an environment with high infection pressure, as it provides immediate protection. The efficacy of immunoglobulins to prevent infection, including FPV,

has been proven in experimental studies and in the field some 50 years ago. It depends upon the antibody titre present against the specific agent, the volume administered, the importance of antibodies in controlling a particular infection, and the timing of administration.

Multivalent hyperimmune immunoglobulin preparations for cats are commercially available in some European countries – these are antisera raised in horses which contain antibodies against FPV, FHV-1, and FCV. They are marketed for prophylactic (usually one injection of 1 vial/animal subcutaneously) and therapeutic (usually 3 injections of 1 vial/animal subcutaneously every 24 hours) use. Protection lasts for about 3 weeks and, like all exogenous proteins, the administered antibodies are quickly eliminated from the body. During this period, active immunization (vaccination) must be avoided, because the immunoglobulins will bind to the vaccinal antigens, tying them up in immune complexes and rendering the vaccine ineffective. Although large amounts of foreign protein are administered, allergic reactions and side effects are rare if a cat is receiving this treatment for the first time. Repeated treatment (with an interval of more than 1 week) is discouraged because cats can develop anaphylactic reactions to the equine protein (Hartmann and Hein, 2002).

Customised homologous (hyper)immune serum can also be prepared and administered. Immune serum is obtained from healthy cats or from groups of animals that have recovered from a disease, whereas hyperimmune serum comes from animals that had been repeatedly vaccinated. The antibody content, and hence the duration of protection, of such sera are unknown.

Feline immune sera can be prepared in veterinary practice, but the blood donors must be screened for insidious infections (e.g. FIV, FeLV, *Bartonella* infection, haemoplasmas). The blood type of donor and recipient should match. The minimum amount required for protection is unknown, but the dose recommended for recipient cats is 2 to 4 ml of serum per kilogram body weight. Attention must be paid to sterility during collection, storage and administration. Jugular vein puncture is preferred, and the area over the jugular vein should be shaved and disinfected. Blood should be collected (at least twice the volume of serum required) into sterile tubes without additives and allowed to clot. Serum is then removed and can be stored at -20° C in single dose aliquots, as IgG is very stable, and can be kept for up to a year if frozen promptly after collection (Levy and Crawford, 2000). Usually, sera are given subcutaneously, but intraperitoneal injection might be more feasible in kittens. If an immediate effect is needed, intravenous administration of plasma (instead of serum) should be used (Greene and Schultz, 2005). For further details see the "ABCD Guidelines for minimizing risks of infectious iatrogenic complications after blood transfusion in cats" and Pennisi et al. (2015).

Breeding catteries

The vaccination schedules used and recommended for privately owned cats are appropriate for most breeding catteries. Queens not up-to-date with vaccinations can receive booster vaccine injections prior to breeding, to maximize delivery of MDA to kittens (Lawler and Evans, 1997). As a consequence, kittens from such queens might need an extra primary vaccination at 16 to 20 weeks, because of a longer persistence of MDAs. As stated before, vaccination of pregnant queens should be avoided.

Lactation is not known to interfere with the immune response. However, administration of any vaccine can stress the queen and result in a temporary deterioration of mothering ability and milk production. Vaccination of lactating queens should therefore be avoided.

See also an overview in the ABCD Tool "Vaccine recommendations for cats according to their lifestyle"

Zoonotic risk

The host range of these viruses appears to be restricted to carnivores. There are no reports of human infections.

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