Feline panleukopenia

Virus

Feline panleukopenia virus (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. Current taxonomy defines canine parvovirus and feline panleukopenia virus as a single entity (Tattersall, 2006), but in the present guidelines, FPV refers to the parvovirus in cats.

FPV infects cats and other members of the *Felidae*, as well as raccoons, mink, and foxes (Steinel et al., 2001). It also infects dogs, where FPV replication was seen in lymphoid tissues (thymus, spleen, bone marrow) and not in the gut, but the virus is not shed (Truyen and Parrish, 1992).

In 1978 a new parvovirus, closely related to FPV, was first described in dogs (Carmichael, 2005). It was named canine parvovirus type 2 (CPV-2), to distinguish it from another parvovirus isolated from dogs in 1970, which is now called “canine minute virus”. CPV-2 has evolved from FPV by acquiring 5 or 6 amino acid changes in the capsid protein gene (Parrish, 1990; Truyen, 1999) and is no longer able to infect cats. However, during further adaptation to the canine host, which most likely occurred in the raccoon, the raccoon virus acquired the amino acid changes that had enabled the new virus to better bind to the canine cellular receptor but also retained its ability to infect cats (Hueffer and Parrish, 2003; Allison et al., 2012). This led to the generation of the new type CPV-2a that acquired further mutations including those at amino acid 426 of the VP2, which determine the different antigenic types 2a, 2b, and 2c. The parvoviruses now circulating in the dog populations worldwide - genetically and antigenically defined as types CPV-2a, -2b, and -2c - can infect cats and may even cause disease (Truyen et al., 1995, 1996; Mochizuki et al., 1996). However, CPV infections of cats are rare in Europe and the USA, and the virus has only sporadically been found in diagnostic material from cats (Truyen et al., 1996). CPV was isolated from feline peripheral blood lymphocytes after numerous blind passages, and viral DNA was demonstrated by PCR (Ikeda et al., 2000). Recently, however, a case of CPV-2c infection in a cat with severe clinical disease was described in Portugal (Miranda et al., 2014).

During the evolution from FPV to CPV-2 with its various antigenic types, neutralizing epitopes have been affected such that cross-neutralization by FPV antisera is markedly lower against the new viruses (Truyen and Parrish, 2013).

Epidemiology

FPV is a non-enveloped, single-stranded DNA virus which is 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 10^9 $TCID_{50}$ 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 replicates in tissues of the oropharynx and is then distributed via cell-free viraemia to virtually all tissues. Replication of the parvoviral single-stranded DNA requires cells in the S-phase of division and is therefore restricted to mitotically active tissues. Parvoviruses require cellular DNA polymerases to synthesize the complementary DNA strand, which is the first step in replication and a prerequisite for transcription.

The virus infects lymphoid tissues where it may cause cellular depletion and a functional immunosuppression. Lymphopenia may 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 the intestinal villi due to a sometimes 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 above. Their severity correlates with the epithelial turnover rate, and co-infection with enteric viruses - like feline coronavirus - may enhance the severity of disease.

Intrauterine transmission or perinatal infection may affect central nervous system development. “Feline ataxia syndrome” results from an impaired development of the cerebellum due to lytic infection of the Purkinje cells in the kitten (Csiza et al., 1971; Kilham et al., 1971). An FPV-like virus has been described as the cause of reproductive disorders in pregnant foxes (Veijalainen and Smeds, 1988).

Foetal infection may 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).

Table 1. Pathological consequences and clinical manifestations of FPV infection

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	Cerebellar hypoplasia	Cerebellar ataxia

Adapted from: Chandler, Feline Medicine and Therapeutics, 3rd Ed, 2004.

Immunity

Passive immunity acquired via colostrum

In the kitten, 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 may interfere with active immunisation. Most cats have maternal antibodies at protective titres until weeks 6 to 8. Later immunisations are effective (Dawson et al., 2001), which makes ABCD recommend vaccinations at 15 to 16 weeks of age, as explained in the present Guidelines.

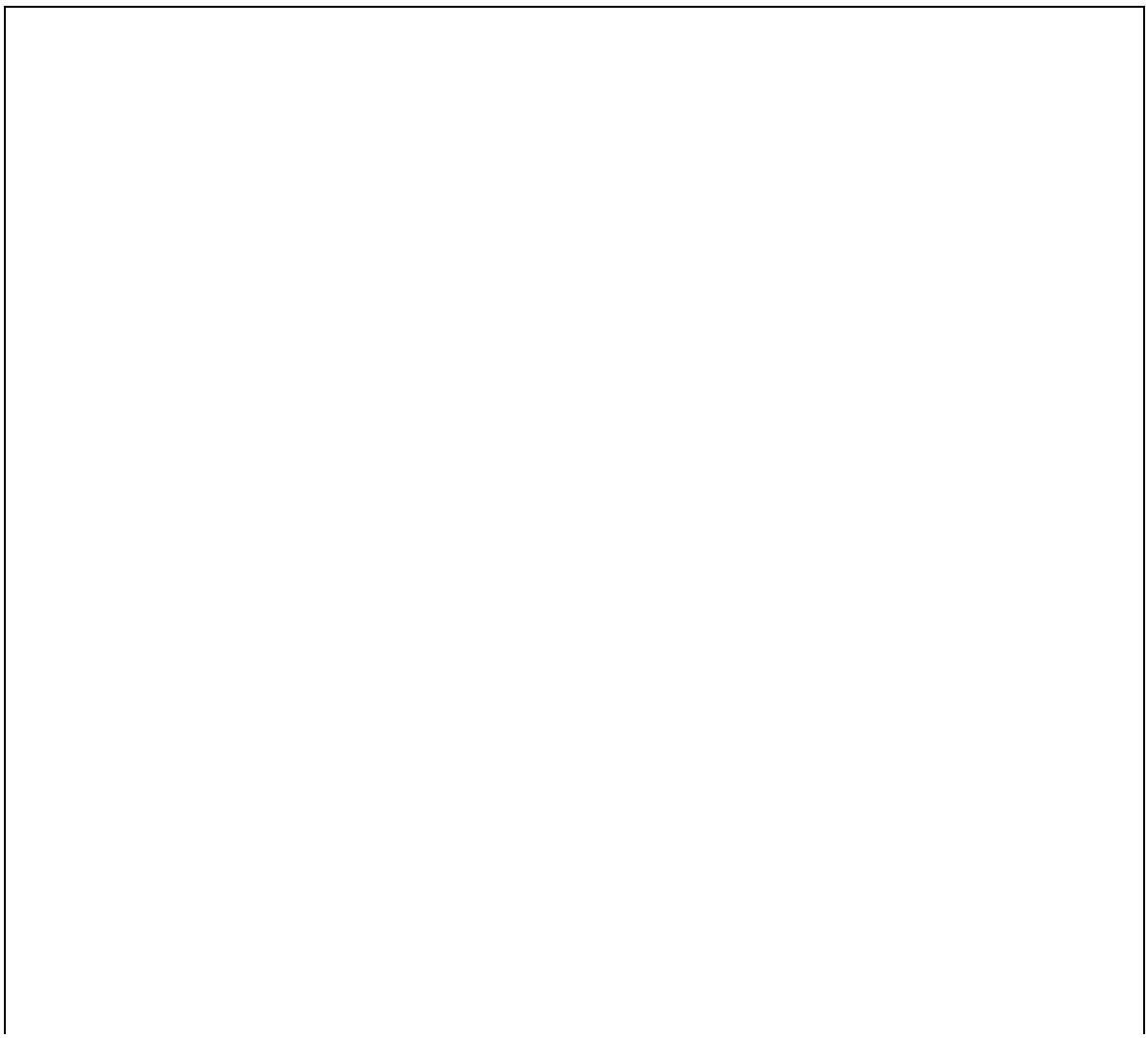

Figure 1: Graph illustrating the immunity gap (Thiry, 2002c). In this example, the critical period is between week 8 and 12 post natum.

The endotheliochorial placentation of the cat restricts maternofetal 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 around the 8th hour of life. Later, the kitten's intestinal cells are replaced by new epithelium that no longer absorbs and transports antibodies.

Kitten serum antibody titres are generally about half of those of the dam. Their levels depend on the individual colostrum intake, which explains the large variations between littermates (Casseleux and Fontaine, 2006). The titres decrease in the first weeks of life, by decay and by dilution in the growing organism. In analogy with

canine parvovirus, an immunity gap around 6 to 10 weeks of age is expected to exist, when antibody levels are too low to protect against natural infection, but still high enough to interfere with vaccination (Scott et al., 1970; Dawson et al., 2001; Thiry, 2002b).

Active immune response against FPV

Antibodies play an important role in the immune response to FPV. Maternally-derived antibodies (MDA) efficiently protect kittens from fatal infection. This passively acquired immunity is later replaced by an active immune response obtained by vaccination or as a consequence of a natural infection.

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 unvaccinated animals 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 T-helper CD4+ lymphocytes and CD8+ cytotoxic T lymphocytes. Parvovirus uptake occurs by phagocytosis but also by other non-phagocytic mechanisms such as fluid pinocytosis or receptor-mediated endocytosis (Sedlik et al., 2000).

Diagnosis of feline parvovirus infection

Feline panleukopenia has been diagnosed by virus isolation from blood or faeces in cultures of CRFK or Mya 1 cells (Miyazawa et al., 1999), and by the demonstration of haemagglutination of porcine erythrocytes (Goto, 1975). However, these methods are now rarely used.

In practice, FPV antigen detection in faeces is usually carried out using commercially available latex agglutination or immunochromatographic tests (Veijalainen et al., 1986; Addie et al., 1998). These tests have a good specificity and acceptable sensitivity when compared to reference methods (Neuerer et al., 2008; Schmitz et al., 2009). Tests marketed for the detection of FPV antigen as well as those for detecting canine parvovirus antigen may be used to diagnose FPV in faeces.

Diagnosis by electron microscopy has lost its importance due to more rapid and automated alternatives. Specialised laboratories offer PCR-based test on whole blood or faeces. Whole blood is recommended from cats without diarrhoea or when no faecal samples are available (Schunck et al., 1995; Ryser-Degiorgis et al., 2005). By PCR, healthy cats have tested positive in faeces over weeks, but the epidemiological significance of this finding is unknown. Clinicians need to bear this in mind when interpreting diagnostic data.

The analytical sensitivity of the antigen tests can be compromised by antibodies bound to viral epitopes, which render them inaccessible to the monoclonal antibodies in the test kit (Lutz et al., 1995).

Antibodies to FPV can be detected by haemagglutination inhibition (HI), ELISA (Fiscus et al., 1985) or indirect immunofluorescence tests (Hofmann-Lehmann et al., 1996). However, their use is of limited value, because neither differentiates between infection- and vaccination-induced antibodies (Fiscus et al., 1985). However, the mere presence of antibodies is taken as proof of protection against panleukopenia under field conditions, whether these have been obtained through active immunization or after infection (Lappin et al., 2002). Passively acquired antibodies (maternal or from hyperimmune serum) are considered protective at HI titres of 80 or higher, in analogy to CPV infections in dogs.

Feline panleukopenia disease management

A cat showing clinical signs of feline panleukopenia, substantiated by laboratory evidence should be kept in isolation. Supportive therapy and good nursing care significantly decrease mortality. Restoration of fluid and electrolyte, and of the acid-base balance preferably by intravenous drip is most important in symptomatic treatment.

As the gut barrier often is destroyed in FPV-infected cats, intestinal bacteria may invade the blood stream. Bacteriaemia may ensue, facilitated by the existing neutropenia, and lead to sepsis in these immunocompromised patients. Prevention of sepsis is essential, and a broad-spectrum antibiotic with a proven efficacy against gram-negative and anaerobic bacteria is recommended. Examples are amoxicillin/clavulanic acid or piperacillin in combination with aminoglycosides,

fluoroquinolones, cephalosporins or piperacillin/tazobactam. The potential side effects of these drugs should be taken into consideration. Antibiotics should be administered parenterally (preferentially intravenously).

Oral intake of water and food should only be restricted if vomiting persists, and feeding should be continued as long as possible, and restarted as soon as possible. Beneficial effects of early enteral nutrition have been reported in canine parvovirosis (Mohr et al., 2003). A highly digestible diet is preferred, but if the cat does not accept it, any diet is better than no food intake at all. If vomiting persists, anti-emetics should be considered. Vitamin supplements, particularly of the B vitamin complex can be given to prevent development of thiamine deficiency, an infrequent sequel.

Cats that develop hypoproteinaemia may require plasma or whole blood transfusions to restore oncotic pressure. Plasma transfusion in combination with heparin may control disseminated intravascular coagulation (DIC), as it supplements anti-thrombin III and other important plasma proteins. In cats that are anorexic or show severe vomiting and/or diarrhoea, or in patients with persisting hypoproteinaemia, full or partial parenteral nutrition is required, preferably via a central venous catheter in the jugular vein (Hartmann and Hein, 2002).

Table 2. Overview of treatment in cats with FPV (all measures are EBM level 4)

Drug	**Comment**	**ABCD recommendation**
Antiviral Therapy		
anti-FPV serum	anti-CPV serum effective in dogs	beneficial effects in cats expected
feline recombinant Interferon-omega	effective in dogs	beneficial effects in cats expected
Symptomatic Therapy		
fluid therapy	to control dehydration and restore electrolyte and acid base balance	necessary in every cat with vomiting and diarrhea
antibiotics (amoxicillin/clavulanic acid	prevention of sepsis	broad-spectrum antibiotic with proven efficacy against gram-

in combination with - aminoglycosides or - fluoroquinolones* or - cephalosporins, third generation)		negative and anaerobic bacteria recommended
highly digestible diet	feeding should be continued as long as possible and restarted as soon as possible	any diet is better than no food
Antiemetics	to control vomiting	recommended for vomiting animals
B vitamin complex	prevention of thiamine deficiency	recommended
plasma or whole blood transfusion	to restore oncotic pressure	recommended in cats with hypoproteinaemia
full or partial parenteral nutrition	to restore oncotic pressure and meet energy requirements	recommended in cats with anorexia, severe vomiting/diarrhea or persisting hypoproteinaemia
low-molecular heparin (fragmin)	to control DIC	recommended in cats with DIC

* not to be used in kittens

Anti-FPV serum can be used to prevent infection of susceptible animals after exposure. The therapeutic efficacy of immune serum has been demonstrated in dogs (Meunier et al., 1985; Macintire et al., 1999), and similar beneficial effects are expected in cats.

Feline recombinant Interferon-omega is effective in the treatment of parvoviral enteritis in dogs (Minagawa et al., 1999; Martin et al., 2002; De Mari et al., 2003) and inhibits replication of FPV in cell culture (Mochizuki et al., 1994). So far no data are

available on the efficacy of this cytokine in FPV-infected cats, but it is expected to work in the homologous host.

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 (Köhler et al., 2009). Commercially available chemical disinfectants proven effective against non-enveloped viruses or a disinfectant (solution or dry fog) based on formaldehyde or peracetic acid can be used for room disinfection.

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 can be used to protect susceptible cats (young kittens with an incomplete vaccination history, colostrum-deprived kittens or unvaccinated cats). Anti-FPV serum can be given subcutaneously or intraperitoneally and may protect for 2-4 weeks (Greene and Addie, 2005). If a commercial product of equine origin is used, repeated administration is not recommended as this may lead to anaphylactic reactions (Hartmann and Hein, 2002). Since the administered immunoglobulins will bind to parvoviral epitopes, these animals should not be vaccinated within the first three weeks after passive immunisation.

General recommendations on vaccine type and vaccination protocol

Both MLV and adjuvanted inactivated FPV vaccines are available for administration by injection, and both provide solid immunity against disease. In immune-competent cats, MLV vaccines generally result in a more rapid protection (Greene and Addie, 2005; Levy et al., 2006a). However, even a single dose of an inactivated FPV vaccine may rapidly induce good antibody responses in naïve cats (Levy et al., 2006a, 2006b). 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 the other in an individual cat; MLV products are being used generally, because of the more rapid

onset of protection and a better resistance to MDA. There may be considerations affecting this decision:

MLV FPV vaccines should not be used in **pregnant queens** because of the risk of placental virus passage to the foetus and damage, especially to the developing cerebellum (Pollock and Postorino, 1994). In some countries, inactivated FPV vaccines are licensed for use in pregnant queens, but their vaccination should always 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: the FPV vaccine is defined as a core vaccine. Even cats with a strictly indoor 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 serological testing, the level of protection and the point at which a kitten will become susceptible to infection and/or can respond immunologically to vaccination is unknown.

In general, MDA will have waned by 8 to 12 weeks of kitten age to a level that allows an immunological response, 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 may be vulnerable (and capable of responding to vaccination) at an earlier age, while others may possess MDA at such high titres that they are incapable of responding to vaccination until some time after 12 weeks of age.

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

- All kittens should receive FPV vaccines

- A minimum of two doses – one at 8 to 9 weeks of age and a second 3 to 4 weeks later (at a minimum of 12 weeks of age) should be administered to cats living in low risk situations.
- In higher risk situations, a third vaccination at 16 weeks is recommended. Maternal antibodies may persist beyond week 12 in some cats, as field data suggest (Dawson et al., 2001; Jakel et al., 2011), such that vaccination at 12 weeks may fail to induce protection (Kruse et al., 2010). Therefore, a third kitten vaccination at 16 weeks of life should be given to kittens in e.g. breeding catteries or cat shelters. A 16-week-vaccination should also be considered for kittens born to queens with high antibody titres, as these are likely to transmit high levels of MDA that may persist for more than 12 weeks in their kittens (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).
- If prophylactic administration of immunoglobulins is not possible, additional earlier vaccinations should be considered, especially if MDA is known or suspected to be poor and/or if the kitten is in a high risk situation. If a kitten is vaccinated at or before 4 weeks of age, this should only be done using an inactivated product.
- Adult cats of unknown vaccination status should receive a single initial FPV vaccine injection (MLV) followed by a booster vaccination one year later.

Booster vaccinations

Cats that respond to FPV vaccination maintain a solid immunity for at least seven years – the latest point in time tested - in the absence of any repeat vaccination or natural challenge (Scott and Geissinger, 1999; Lappin et al., 2002). Nevertheless, the ABCD recommends the following revaccination protocol:

- All cats receive a first booster 12 months after completion of the primary vaccination course (this will ensure adequate vaccine-induced immunity for cats that may not have adequately responded to the primary course)
- Following this first booster, subsequent revaccinations are recommended at intervals of three years or longer, unless special conditions apply.

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

Feline panleukopenia control in specific situations

Shelters

Random source populations with unknown vaccination histories, continuous resident turnover, and high risk for infectious disease characterize most shelters. The cost of a vaccine is a significant management aspect - when multiplied by the many required doses. Therefore, only 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 an important cause of cat mortality in shelters and rescue homes throughout Europe and the United States. With rare exceptions, all kittens and cats over 4 to 6 weeks of age should therefore be vaccinated, regardless of their housing sstatus. 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 never receive a live FPV vaccine. Alternatively passive immunisation with FPV antiserum may be considered (or anti-CPV-2 canine globulin). Kittens should be vaccinated beginning at 4 weeks of age in the face of an outbreak, and otherwise at 6 weeks of age. MLV vaccines are recommended because of their faster onset of action, greater efficacy at overcoming maternal antibody, and greater likelihood of conferring sufficient immunity (Greene and Addie, 2005; Greene and Schultz, 2005). Reversion to virulence has never been documented (Greene and Schulz, 2005). Cats of unknown status should not be housed together. Vaccination should be repeated every 3 to 4 weeks in kittens, until 16 weeks of age. If adult cats are ill 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).

Passive immunisation can be used in shelters. 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 against the specific agent, the volume administered, the relative importance of serum antibodies in controlling the infection involved, and the timing of administration in relationship to exposure.

Multivalent hyperimmune globulin preparations are commercially available in some European countries for cats (heterologous preparation produced in horses, containing antibodies against FPV, FHV-1, and FCV). They are marketed for prophylactic (usually 1 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. During this period, active immunization (vaccination) must be avoided, because the immunoglobulins will bind to the vaccinal antigens, tying them up in immune complexes. Allergic reactions and side effects are rare if a cat is treated for the first time. Repeated treatment (with an interval of more than 1 week) is discouraged because cats can display anaphylactic reactions to equine protein (Hartmann and Hein, 2002).

Besides commercial products, customised homologous (hyper)immune serum may be prepared and administered. Immune serum is derived from healthy individuals or groups of animals that have recovered from a specific disease, whereas hyperimmune serum comes from animals that had been repeatedly vaccinated against specified infectious agents. The antibody content and hence the duration of protection of such sera are unknown.

If feline immune sera are prepared in veterinary practice, the blood donors must be screened for insidious infections (e.g. FIV, FeLV, *Bartonella* infection). Ideally, the blood type of donor and recipient should match; if cross-matching cannot be performed, only type A cats should be used as donors. The minimum amount required for protection is unknown, but the dose recommended for cats is 2 to 4 ml serum per kilogram body weight. Attention must be paid to sterility during collection, storage and administration. For the preferred jugular vein puncture, the area over the vein should be shaved and disinfected. Blood should be collected (at least twice the amount of required serum) into sterile tubes without additives and allowed to clot. Serum can be stored at -20° C in single dose aliquots, as the IgG is stable and can be kept for up to a year if frozen promptly after collection (Levy and Crawford, 2000). Usually, sera are given subcutaneously; intraperitoneal injection is more feasible in

kittens. If for an instant effect intravenous administration is required, plasma (instead of serum) should be used (Greene and Schultz, 2005). For details see the ABCD Guidelines “Blood transfusion in cats. ABCD guidelines for minimizing risks of infectious iatrogenic complications” (www.abcdcatsvets.org) and Pennisi et al. (2015).

As FPV and CPV are closely related viruses with a high degree of cross-neutralization, it may be expected that hyperimmune sera raised against CPV are also effective against FPV. This is of particular importance in countries where commercial anti-FPV serum is not available. The remarks above about heterologous preparations apply.

Breeding catteries

Vaccination schedules recommended for privately owned cats are appropriate for most breeding catteries. Queens not up-to-date on vaccinations may receive booster injections before breeding, to maximize delivery of MDA to kittens (Lawler and Evans, 1997). As a consequence, their kittens may need an extra vaccination at 16 to 20 weeks, because of a longer persistence of MDAs. As stated before, pregnant cats should not be vaccinated.

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

Vaccination of immunocompromised cats

Vaccines cannot generate optimum protection in animals with conditions that compromise their immune function. Such conditions include genetic immunodeficiencies, but also deficient nutrition, systemic disease, concurrent administration of immunosuppressive drugs, and environmental stress. Efforts should be made to correct the latter conditions before vaccination, and to protect cats from exposure to infectious agents; if this cannot be assured, vaccination should be performed nevertheless.

In **immunocompromised individuals**, inactivated FPV vaccines are recommended.

In **cats receiving corticosteroids**, vaccination should be considered carefully. Depending on dosage and duration of treatment, corticosteroids may cause functional suppression of particularly cell-mediated immune responses, but pertinent studies are lacking. In dogs, corticosteroids do not hamper effective immunization if given for short periods of time at low to moderate doses (Nara et al., 1979). However, the use of corticosteroids at the time of vaccination should generally be avoided.

In **cats with chronic illness** vaccination may sometimes be necessary. Manufacturers evaluate vaccine safety and efficacy in healthy animals and accordingly label their vaccines for use in healthy animals only. Nonetheless, cats with stable chronic conditions such as chronic renal disease, diabetes mellitus or hyperthyroidism should receive vaccines at the same frequency as healthy cats. In contrast, cats with acute illness, debilitation, or high fever should not be vaccinated, unless there are compelling reasons to do so. In these cases, inactivated preparations should be used.

Retrovirus-infected cats should be kept indoors and isolated, to diminish the likelihood of infecting other cats and to reduce exposure to other infectious agents. FeLV-infected cats should be vaccinated against FPV. Although there is no evidence that they are at an increased risk of vaccine-induced disease from MLV vaccines, inactivated (“killed”) products are recommended. FeLV-infected cats may not be able to mount adequate immune responses to rabies vaccines, perhaps also not to other vaccines. Therefore, more frequent vaccination should be considered in these cats.

FIV-infected cats mount immune responses to administered antigens except during the terminal phase of infection; also primary immune responses may be delayed or diminished (Dawson et al., 1991; Reubel et al., 1994; Foley et al., 2003). In one study, cats experimentally infected with FIV developed vaccine-induced panleukopenia when given MLV FPV vaccines (Buonavoglia et al., 1993). Immune stimulation of FIV-infected lymphocytes *in vitro* promotes virus production, and *in vivo*, vaccination of chronically infected cats with a synthetic peptide was associated with a decrease in the CD4+/CD8+ ratios (Lehmann et al., 1992; Reubel et al., 1994). Therefore, a potential trade-off to protection from secondary disease is the progression of FIV infection due to increased virus production. Thus only FIV cats at high risk of exposure to infectious agents should be vaccinated, and only with killed products.

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