

## ABCD GUIDELINES ON:

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The attached recommendations have been formulated by the European Advisory Board on Cat Diseases.



The European Advisory Board on Cat Diseases is an independent panel of 17 veterinarians from ten European countries, with an expertise in immunology, vaccinology and/or feline medicine. The ABCD was set up to compile guidelines for the prevention and management of major feline infectious disease in Europe based on current scientific knowledge and available vaccines.

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# 1. Feline panleukopenia

## 1.1 Virus

Feline panleukopenia virus (FPV) is an autonomous parvovirus. It is the prototype of a number of closely related parvoviruses which were isolated from various carnivores such as dogs, mink, raccoons, raccoon dogs, foxes and other canids (Parrish, 1990). The viruses were initially named after the hosts from which they had been isolated. Current taxonomy defines canine parvovirus and feline panleukopenia virus as one single taxonomic entity (Tattersall, 2006), but in the present guidelines, FPV refers to parvovirus in cats.

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

In 1978 a new parvovirus, very 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 (CaMV). CPV-2 is believed to have evolved from FPV by acquiring 5 or 6 amino acid changes in the capsid protein gene (Truyen, 1999). Interestingly, CPV-2 was no longer able to infect cats. However, during subsequent further adaptation to the canine host, the amino acid changes that had enabled the new virus to better bind to the canine cellular receptor also resulted in its ability to infect cats (Hueffer and Parrish, 2003). The parvoviruses now circulating in the dog populations worldwide and which can be genetically and antigenically defined as the types CPV-2a, -2b, and “-2c”, are able to infect cats and may even cause disease (Truyen et al., 1995, 1996; Mochizuki et al., 1996). However, feline CPV infections are rare in Europe and the USA, and CPV is found only sporadically in diagnostic material (Truyen et al., 1996). CPV was isolated from feline peripheral blood lymphocytes after numerous blind passages, and viral DNA was demonstrated by polymerase chain-reaction (PCR), as reported in a study from Taiwan (Ikeda et al., 2000).

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, 1997).

### 1.1.1 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<sub>50</sub> 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).

## 1.2 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 parvovirus with its single-stranded DNA genome requires cells in the S-phase of division and is therefore restricted to mitotically active tissues. The reason for this is that parvoviruses require cellular DNA polymerases that synthesize the complementary DNA strand, which is the first step in viral DNA replication and a prerequisite for transcription.

The virus readily infects lymphoid tissues and can cause cellular depletion and a functional immunosuppression. Lymphopenia may arise as a result of lymphocytolysis but may also result from indirect effects, such as lymphocyte migration into tissues. The bone marrow is also affected, and virus replication has been described in early progenitor cells, which may explain the dramatic effect on virtually all myeloid cell populations (Parrish, 1995). This is also reflected by the defining panleukopenia observed in FPV infected cats (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 of the epithelium, the crypts of Lieberkühn. This impairs the regeneration of the epithelium and results in the lesions described above. The severity of these lesions appears to correlate with the turnover rate of these cells, and co-infection with enteric viruses like feline coronavirus may enhance the severity of disease.

Intrauterine transmission or perinatal infection may affect the central nervous system. A feline ataxia syndrome has been described that results from an impaired development of the cerebellum due to lytic virus replication in the Purkinje cells in the infected 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).

### 1.2.1 Immunopathogenesis of FPV infection

Foetal infection may induce a form of immunological tolerance so that kittens continue to shed virus for extended periods of time after birth (Pedersen, 1987).

Foetuses infected between the 35<sup>th</sup> and 45<sup>th</sup> days of gestation have depressed T-lymphocyte mediated immunity. Infection of adult cats leads to a transient decrease in the immune response. Neutrophils decrease severely and lymphocytes disappear from the circulation, lymph nodes, bone marrow and thymus (Ikeda et al., 1998; Pedersen, 1987).

Table 1.1. 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)
All cells in foetus	Foetal death	Loss of pregnancy
Developing cerebellum	Cerebellar hypoplasia	Cerebellar ataxia

*Adapted from: Chandler, Feline Medicine and Therapeutics, 3<sup>rd</sup> Ed, 2004.*

## 1.2.2 Passive immunity acquired via colostrum

Maternal antibodies have a biological half-life of about ten days (Scott et al., 1970; Pedersen 1987). Waning antibodies below a titre of about 40 (haemagglutination inhibition) do not reliably protect against infection but may interfere with active immunization. Most cats have maternal antibodies at protective titres until weeks 6 to 8. However, the effectiveness of later vaccinations was demonstrated (Dawson et al., 2001), which supports the recommendation by ABCD of vaccinations at 15 to 16 weeks of age, as explained in the present Guidelines.

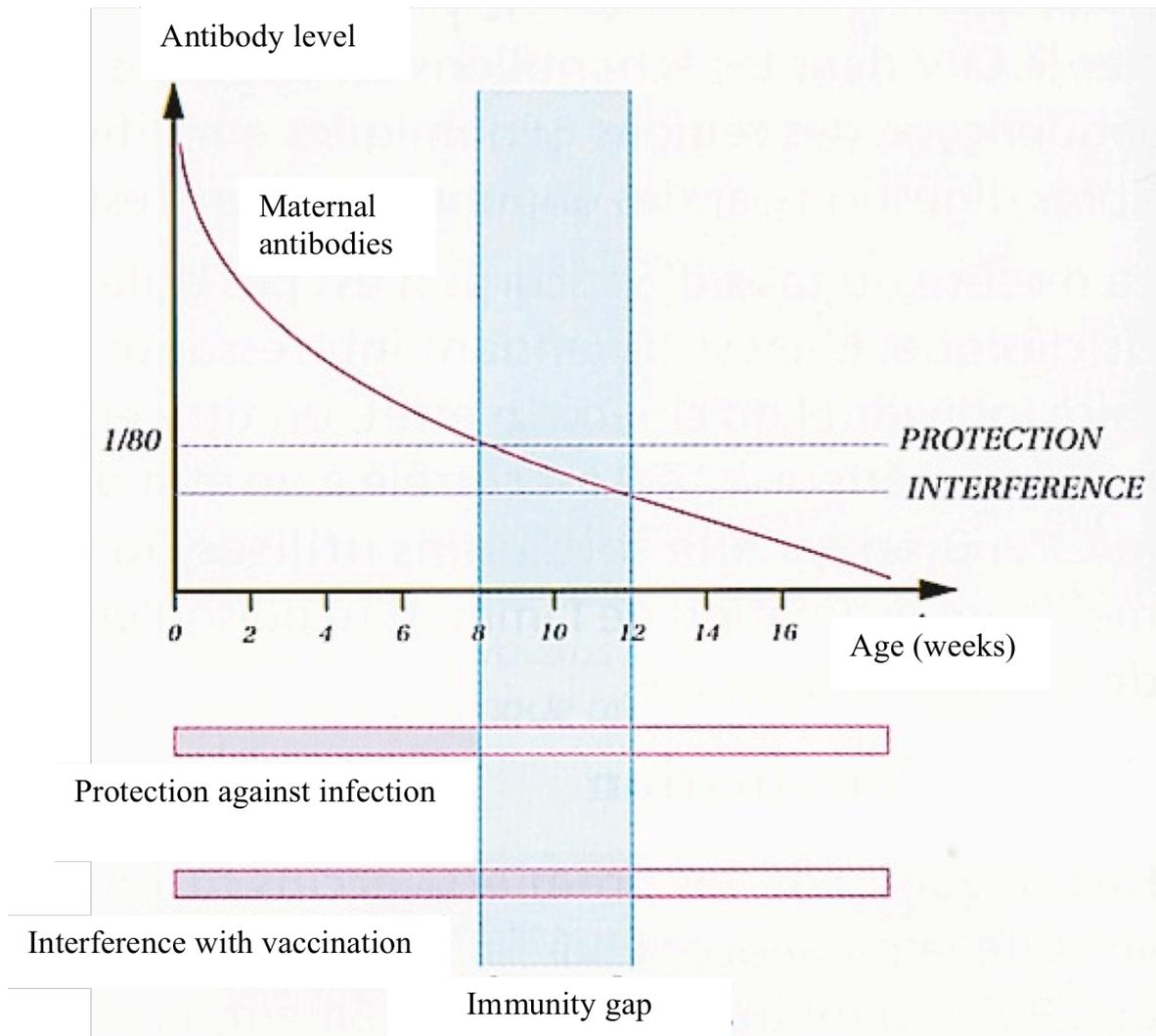


Figure 1.1. The immunity gap (Thiry, 2002c)

Since the endotheliochorial placentation of the cat restricts maternofetal passage of solutes, IgG can only cross the placenta barrier in the last trimester of gestation. This passive immunity affords <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 8<sup>th</sup> hour of life. Later, the kitten's intestinal cells are replaced by new cells that can no longer absorb and transport antibodies.

Kitten serum antibody titres are generally equivalent to 50 % of those of the dam. However, the antibody level is also dependent on the individual colostrum intake. This explains the large variations between littermates (Casseleux and Fontaine, 2006). The antibody titres decrease in the first weeks of life, by decay and by dilution in the growing organism. By

analogy with canine parvovirus, an immunity gap around 6 to 8 weeks of age is assumed 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).

### **1.2.3 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 natural infections.

Acquired immunity is solid and long lasting (Thiry, 2002a). Both inactivated and modified live virus (MLV) vaccines induce durable immunity. FPV antiserum can be used for passive immunisation when unvaccinated animal 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. The cellular response against the VP2 parvovirus capsid protein is mediated by CD4+ and CD8+ T lymphocytes in the context of the Major Histocompatibility Complex type II, as evidenced by the production of interleukin 2 by T lymphocytes stimulated with CPV2 (Rimmelzwaan et al., 1990). Parvovirus can be captured by phagocytosis but also by other non-phagocytic uptake mechanisms such as fluid pinocytosis or receptor-mediated endocytosis (Sedlik et al., 2000).

## **1.3 Diagnosis of feline parvovirus infection**

Feline panleukopenia can be diagnosed directly by isolation of the virus 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 for routine diagnosis.

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 an acceptable sensitivity and specificity when compared to reference methods (Neuerer et al., 2006, in press). 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 in cats without diarrhoea or when no faecal samples are available (Schunck et al., 1995; Ryser-Degiorgis et al., 2005). The analytical sensitivity of the antigen tests can be compromised by the presence of antibodies which may bind the viral epitopes and therefore render them inaccessible to the monoclonal antibodies in the test kit (Lutz et al., 1995).

Antibodies to FPV can also be detected by ELISA (Fiscus et al., 1985) or indirect immunofluorescence (Hofmann-Lehmann et al., 1996). However, the use of an antibody test is of limited value, because serological tests do not differentiate between infection- and vaccination-induced antibodies (Fiscus et al., 1985). The mere presence of antibodies is taken as proof of protection against panleukopenia under field conditions (Lappin et al., 2002).

## **1.4 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 decreases mortality caused by FPV. 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, leading 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 restart as soon as possible. Beneficial effects of early enteral nutrition have been reported in canine parvovirus (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, which occurs infrequently.

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).

Anti-FPV serum can be used to prevent infection of susceptible animals following exposure. The therapeutic efficacy of immune serum has been demonstrated in dogs (Meunier et al., 1985; Macintire et al., 1994), and similar beneficial effects may be 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 also 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 perform well 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, and 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 2006). Sodium hypochlorite (household bleach, 1:30 dilution) can be used on smooth hard surfaces like litter trays that tolerate this disinfectant, while formaldehyde gas 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.

## **1.5 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 general, in a cat capable of mounting an appropriate response, MLV vaccines result in a more rapid protection. However, also a single dose of an inactivated FPV vaccine may induce good antibody responses in naïve cats within a short time span. 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 more generally, because of the more rapid onset of protection and a better resistance to MDA. Sometimes 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. In some countries, inactivated FPV vaccines are licensed for use in pregnant queens, but vaccination of pregnant queens should be avoided in general.
- 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.

Because of the serious consequences of an infection and because of the ubiquity of the virus, vaccination is recommended for every cat: a FPV vaccine is regarded 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.

### **1.5.1 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 cannot be determined; also, there is considerable variation between individuals. In general, MDA will have waned by 8 to 12 weeks of kitten age to a level that allows an active 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. Many vaccines carry data sheet 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 sometime after 12 weeks of age.

No single primary vaccination policy will therefore cover all potential 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
- 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, and repeat vaccinations can be done at 3 to 4 week intervals until  $\geq 12$  weeks of age.

- In circumstances where MDA may have persisted beyond 12 weeks, vaccination at 16-20 weeks of age should be considered. This may apply to kittens in breeding catteries or cat shelters and to kittens from cats that had previously lived in a low-exposure environment and moved into a high risk situation. (Dawson et al., 2001)
- Adult cats of unknown vaccination status should receive a single initial FPV vaccine injection (MLV) followed by a booster vaccination one year later.

### **1.5.2 Booster vaccinations**

Cats that respond to FPV vaccination maintain a solid immunity for several years (seven or more), in the absence of any repeat vaccination or natural challenge (Scott and Geissinger, 1999). 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 given 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 afford protection against these new CPV variants, although additional studies are needed to verify this.

## **1.6 Feline Panleukopenia control in specific situations**

### **1.6.1 Shelters**

Random source populations with largely unknown vaccination histories, continuous resident turnover, and high risk for infectious disease characterize most shelters. Vaccine costs become a significant management aspect when multiplied by thousands of doses. Therefore, only those antigens that demonstrate a clear benefit against common and significant shelter diseases should be utilized.

FPV has re-emerged as a significant cause of mortality in cats 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 be vaccinated regardless of physical condition, pregnancy, or housing status. Kittens should be vaccinated beginning at 4 weeks of age in the face of an outbreak, and at 6 weeks of age otherwise. MLV vaccines are advantageous for their faster onset of action, greater efficacy at overcoming maternal antibody, and greater likelihood of conferring sufficient immunity. (Greene and Addie, 2005; Greene and Schulz, 2005). Although concerns have been raised regarding their reversion to virulence, this 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 or otherwise compromised at the time of initial vaccination, another injection when the cat is in good health (at least two weeks after the initial vaccine) should be considered.

When vaccination is being used to control disease in the face of an outbreak, the more rapid induction of immunity induced by a MLV preparations is of clinical advantage over killed vaccines.

**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. Efficacy of immunoglobulins to prevent infection, including FPV, has been proven in experimental studies and in the field some 50 years ago. Efficacy of immunoglobulins depends on many factors, including the antibody titre against the specific agent and volume administered, the relative importance of serum antibodies in controlling the particular infection involved, and the timing of administration of the antibodies compared to exposure.

Commercial products containing highly concentrated immunoglobulins (multivalent hyperimmune immunoglobulin preparations) are available in some European countries for cats (heterologous preparation produced in horses, containing a combination of 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) is not recommended because the immunoglobulins will bind to the vaccinal antigens, tying them up in immune complexes. Although large amounts of foreign protein are administered, allergic reactions are rare if a cat is treated for the first time, and treatment is usually not associated with side effects. Repeated treatment (with an interval of more than 1 week), however, is not recommended because cats can display anaphylactic reactions to the product produced in horses (Hartmann and Hein, 2002).

Besides commercial products, customised (hyper)immune serum may be administered. Immune serum is derived from healthy individuals or from 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. If such sera are used, their antibody content and consequently the duration of protection are unknown. Like all exogenous proteins, administered antibodies are quickly eliminated from the body.

Feline immune sera can be prepared in veterinary practice, but blood donors must be carefully 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. Careful 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 prepared for aseptic venipuncture. Blood should be collected (at least twice the amount of required serum) into sterile tubes without additives. Serum can be stored at -20° C in single dose aliquots as IgG is a very stable molecule 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).

## 1.6.2 Breeding catteries

Vaccination schedules used for privately owned cats are appropriate in most breeding catteries. Queens not up-to-date on vaccinations may receive booster vaccines prior to breeding to maximize delivery of MDA to kittens (Lawler and Evans 1997). As a

consequence, kittens from such queens may need an extra primary vaccination at 16 to 20 weeks in case of persisting MDAs. As stated before, routine vaccination of pregnant cats should be avoided.

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.

### 1.6.3 Vaccination of immunocompromised cats

Vaccines cannot generate optimum protection in animals with conditions that compromise immune function. Such conditions include deficient nutrition, genetic immunodeficiencies, systemic disease, concurrent administration of immunosuppressive drugs, and environmental stress. Efforts should be made to protect cats from exposure to infectious agents and to correct these conditions if possible prior to vaccination; if this cannot be assured, vaccination should be performed nevertheless and repeated after the animal is fully recovered.

Modified live FPV vaccines should be used with caution in severely immunocompromised individuals, as the failure to control viral replication could potentially lead to clinical signs.

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 FeLV-infected cats are at an increased risk of vaccine-induced disease from residual virulence of MLV vaccines, non-infectious vaccines are preferred if available. FeLV-infected cats may not be able to mount adequate immune responses to rabies vaccination and perhaps also to other vaccines. Therefore, more frequent vaccination should be considered in these cats.

FIV-infected cats are capable of mounting 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+ ratio (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 vaccines.

## 1.7 References

- Addie, D.D., S. Toth, H. Thompson, N. Greenwood & J.O. Jarret (1998). Detection of feline parvovirus in dying pedigree kittens. *Vet Rec* 142:353-356
- Barlough, J.E., M. Barr, F.W. Scott & J.R. Richards (1997). Viral Diseases, In *The Cornell Book of Cats*, 2<sup>nd</sup> ed., Ed. M. Siegal
- Buonavoglia C.F., F. Marsilio, M. Tempesta, D. Buonavoglia, P.G. Tiscar, A. Cavalli & M. Compagnucci (1993). Use of a Feline Panleukopenia modified-live virus vaccine in cats in the primary stage of Feline immunodeficiency virus-infection. *J Vet Med B-Zbl Vet B-Infect* 40:343-346
- Carmichael, L.E. (2005). An annotated historical account of canine parvovirus. *J Vet Med B Infect Dis Vet Public Health* 52, 303-311
- Casseleux, G. & E. Fontaine (2006). Gestion de la parvovirose en élevage canin. *Le Point Vétérinaire* 37:42-46
- Cave T.A., H. Thompson, S.W. Reid & D.R. Hodgson (2002). Kitten mortality in the United Kingdom: a retrospective analysis of 274 histopathological examinations (1986 to 2000). *Vet Rec* 151(17):497-501
- Chandler E.A. (2004). In *Feline Medicine and Therapeutics* 3rd ed. Blackwell Science (UK)
- Csiza, C.K., A. De Lahunta, F.W. Scott & J.H. Gillespie (1971). Pathogenesis of Feline Panleukopenia Virus in Susceptible Newborn Kittens II. Pathology and Immunofluorescence. *Infect Immun* 3:838-846
- Dawson S., N.R. Smyth, M. Bennett, R.M. Gaskell, C.M. McCracken, A. Brown & C.J. Gaskell (1991). Effect of primary-stage feline immunodeficiency virus infection on subsequent feline calicivirus vaccination and challenge in cats. *J Acq Immun Defic Syndrome* 5:747-750
- Dawson, S., K. Willoughby, R. M. Gaskell, G. Wood & W.S.K. Chalmers (2001). A field trial to assess the effect of vaccination against feline herpesvirus, feline calicivirus and feline panleukopenia virus in 6-week-old kittens. *J Fel Med Surg* 3:17-22
- De Mari K, L. Maynard, H.M. Eun & B. Lebreux (2003). Treatment of canine parvoviral enteritis with interferon-omega in a placebo-controlled field trial. *Vet Rec* 152:105-8
- Fiscus, S. A., M. M. Mildbrand, J. C. Gordon, Y. A. Teramoto & S. Winston (1985). Rapid enzyme-linked immunosorbent assay for detecting antibodies to canine parvovirus. *Am J Vet Res* 46:859-863
- Foley J.E., C.M. Leutenegger, J.S. Dumler, N.C. Pedersen & J.E. Madigan (2003). Evidence for modulated immune response to *Anaplasma phagocytophila sensu lato* in cats with FIV-induced immunosuppression. *Comp Immunol Microbiol Infect* 26:103-113
- Goto, H. (1975). Feline panleukopenia in Japan. II. Hemagglutinability of the isolated virus. *Nippon Juigaku Zasshi* 37:239-245
- Greene, C.E. & D.D. Addie (2005). Feline panleukopenia. In *Infectious diseases of the dog and cat*, Ed. C.E. Greene, W.B. Saunders Company, Philadelphia. pp 78-88
- Greene C.E. & R.D. Schulz (2005). Immunoprophylaxis and immunotherapy. In *Infectious diseases of the dog and cat*, Ed. C.E. Greene, W.B. Saunders Company, Philadelphia pp 1069-1119.
- Hartmann K, & J. Hein (2002). Feline Panleukopenie. Praxisrelevante Fragen anhand eines Fallbeispiels. *Tierärztl Prax* 30: 393-9
- Hofmann-Lehmann, R., D. Fehr, M. Grob, M. Elgizoli, C. Packer, J. S. Martenson, S. J. O'Brien & H. Lutz (1996). Prevalence of antibodies to feline parvovirus, calicivirus, herpesvirus, coronavirus and immunodeficiency virus and of feline leukemia virus antigen

- and the interrelationship of these viral infections in free-ranging lions in east Africa. *Clin Diagn Lab Immunol* 3:554-562
- Hueffer, K. & C.R. Parrish (2003). Parvovirus host range, cell tropism and evolution. *Curr Opin Microbiol* 6:392-398
  - Ikeda Y., M. Mochizuki, R. Naito, K. Nakamura, T. Miyazawa, T. Mikami & E. Takahashi (2000). Predominance of canine parvovirus (CPV) in unvaccinated cat populations and emergence of new antigenic types of CPVs in cats. *Virology* 278:13-19
  - Ikeda Y., J. Shinozuka, T. Miyazawa, K. Kurosawa, Y. Izumiya, Y. Nishimura, K. Nakamura, J. Cai, K. Fujita, K. Doi & T. Mikami (1998). Apoptosis in feline panleukopenia virus-infected lymphocytes. *J Virol* 72:6932-6
  - Kilham, L., G. Margolis & E.D. Colby (1971). Cerebellar ataxia and its congenital transmission in cats by feline panleukopenia virus. *J Am Vet Med Assoc.* 158:888-901
  - Köhler, C. (2006). Untersuchungen zur Änderung der DVG-Desinfektionsmittelrichtlinien (Viruzidie) (in German). Thesis Dr. med. vet. Veterinary Faculty, University of Leipzig
  - Lappin, M. R., J. Andrews, D. Simpson & W. A. Jensen (2002). Use of serologic tests to predict resistance to feline herpesvirus 1, feline calicivirus and feline parvovirus infection in cats. *J Am Vet Med Assoc* 220:38-42
  - Lawler D.H. & R.H. Evans (1997). Strategies for controlling viral infections in feline populations. In Consultations in Feline Internal Medicine 3., J.R. August (Ed.). W.B. Saunders Company, Philadelphia. pp 603-610
  - Lehman R., B. von Beust, E. Niederer, M.A. Condrau, W. Fierz, A. Aubert, C.D. Ackley, M.D. Cooper, M.B. Tompkins & H Lutz (1992). Immunization-induced decrease of the CDA+:CD8+ ratio in cats experimentally infected with feline immunodeficiency virus. *Vet Immunol Immunopathol* 35:199-214
  - Levy J.K. & P.C. Crawford (2000). Failure of passive transfer in neonatal kittens: correction by administration of adult cat serum. *J Vet Intern Med* 14:362
  - Lutz, H., I. Castelli, F. Ehrensperger, A. Pospischil, M. Roskopf, G. Siegl, M. Grob & S. Martinod (1995). Panleukopenia-like syndrome of FeLV caused by co-infection with FeLV and feline panleukopenia virus. *Vet Immunol Immunopathol* 46:21-33
  - Macintire D.K., S. Smith-Carr, R. Jones & L. Swango (1999). Treatment of dogs naturally infected with canine parvovirus with lyophilized canine IgG. *Proceedings 17th Annual Conference of the American College of Veterinary Internal Medicine.* June 10-13, 1999, abstract 118, p 721
  - Martin V., W. Najbar, S. Gueguen, D. Grousson, H.M. Eun, B. Lebreux & A. Aubert (2002). Treatment of canine parvoviral enteritis with interferon-omega in a placebo-controlled challenge trial. *Vet Microbiol* 89(2-3):115-27
  - Meunier P.C., B.J. Cooper, M.J. Appel, M.F. Lanieu & D.O. Slauson (1985). Pathogenesis of canine parvovirus enteritis: sequential virus distribution and passive immunization studies. *Vet Pathol* 198 :22:617-24
  - Minagawa T., K. Ishiwata & T. Kajimoto (1999). Feline interferon-omega treatment of canine parvovirus infection. *Vet Microbiol* 69:51-3
  - Miyazawa, T., Y. Ikeda, K. Nakamura, R. Naito, M. Mochizuki, Y. Tohya, D. Vu, T. Mikami & E. Takahashi (1999). Isolation of feline parvovirus from peripheral blood mononuclear cells of cats in northern Vietnam. *Microbiol Immunol* 43:609-612
  - Mochizuki, M., M. Horiuchi, H. Hiragi, M.C. San Gabriel, N. Yasuda & T. Uno (1996). Isolation of canine parvovirus from a cat manifesting clinical signs of feline panleukopenia. *J Clin. Microbiol* 34:2101-2105
  - Mochizuki M., H. Nakatani & M. Yoshida (1994). Inhibitory effects of recombinant feline interferon on the replication of feline enteropathogenic viruses in vitro. *Vet Microbiol* 39:145-52

- Mohr A.J., Leisewitz A.L., Jacobson L.S., Steiner J.M., Ruaux C.G. & Williams D.A. (2003). Effect of early enteral nutrition on intestinal permeability, intestinal protein loss and outcome in dogs with severe parvoviral enteritis. *J Vet Intern Med* 17(6):791-8
- Nara P.L., S. Krakowka & T.E. Powers (1979). Effects of prednisolone on the development of immune response to canine distemper virus in beagle pups. *Am J Vet Res* 40(12):1742-7
- Neuerer F., K. Horlacher, U. Truyen & K. Hartmann (2006). Comparison of different in-house test systems to detect parvovirus in feces of cats. *Journal of Feline Medicine and Surgery*, in press
- Parrish, C.R. (1990). Emergence, natural history and variation of canine, mink and feline parvoviruses. *Adv Virus Res* 38:403-450
- Parrish, C.R. (1995). Pathogenesis of feline panleukopenia virus and canine parvovirus. *Baillière's Clin Haematol* 8:57-71
- Parrish, C.R. (2006). Pathogenesis of feline panleukopenia virus and canine parvovirus. In Parvoviruses, Eds. J. Kerr, S.F. Cotmore, M.E. Bloom, R.M. Linden & C.R. Parrish, Oxford University Press, New York, USA, pp 429-434
- Pedersen, N.C. (1987). Feline Panleukopenia Virus, In Virus Infections of Carnivores, Ed. M. J. Appel, Elsevier, Amsterdam. pp 247-254
- Reubel G.H., G.A. Dean, J.W. George, J.E. Barlough & N.C. Pedersen (1994). Effects of incidental infections and immune activation on disease progression in experimentally feline immunodeficiency virus-infected cats. *J Acq Immun Defic Syndrome* 7:1003-1015
- Rimmelzwaan, G.F., R.W. van der Heijden, E. Tijhaar, M.C. Poelen, J. Carlson, A.D. Osterhaus & F.G. UytdeHaag (1990). Establishment and characterization of canine parvovirus-specific murine CD4<sup>+</sup> T cell clones and their use for the delineation of T cell epitopes. *J Gen Virol* 71 (5):1095-102
- Ryser-Degiorgis, M. P, R. Hofmann-Lehmann, C. M. Leutenegger, C. H. Af Segerstad, T. Morner, R. Mattsson & H. Lutz (2005). Epizootiologic investigations of selected infectious disease agents in free-ranging Eurasian lynx from Sweden. *J Wildl Dis* 41:58-66
- Schunck, B., W. Kraft & U. Truyen (1995). A simple touch-down polymerase chain reaction for the detection of canine parvovirus and feline panleukopenia virus in feces. *J Virol Methods* 55:427-433
- Scott, F., C.K. Csiza & J. H. Gillespie (1970). Maternally derived immunity to feline panleukopenia. *J Am Vet Med Assoc* 156:439-453
- Scott, F.W. & C.M. Geissinger (1999). Long-term immunity in cats vaccinated with an inactivated trivalent vaccine. *Am J Vet Res* 60(5):652-8
- Sedlik, C., G. Dadaglio, M.F. Saron, E. Deriaud, M. Rojas, S.I. Casal & C. Leclerc (2000). In vivo induction of a high-avidity, high-frequency cytotoxic T-lymphocyte response is associated with antiviral protective immunity. *J Virol* 74:5769-75
- Steinel, A., C.R. Parrish, M.E. Bloom & U. Truyen (2001). Parvovirus infections in wild carnivores. *J. Wildlife Dis* 37:594-607
- Tattersall, P (2006). The evolution of parvovirus taxonomy. In Parvoviruses, Eds. J. Kerr, S.F. Cotmore, M.E. Bloom, R.M. Linden, C.R. Parrish, Oxford University Press, New York. pp 5-14
- Thiry, E. (2002a). Panleucopénie féline, In Virologie clinique du chien et du chat, Editions du Point Vétérinaire, Maisons-Alfort, France, pp 137-142
- Thiry, E. (2002b). Parvovirose canine. In Virologie clinique du chien et du chat, Editions du Point Vétérinaire, Maisons-Alfort, France, pp 29-40
- Thiry, E. (2002c). Virologie clinique du chien et du chat, Editions du Point Vétérinaire, Maisons-Alfort, France, p 38
- Truyen, U. (1997). Canine Parvoviren in Deutschland: Ein Update (in German). Proceedings of the 22<sup>nd</sup> Congress of the German Veterinary Society (DVG), 204-208

- Truyen, U. (1999). Emergence and recent evolution of canine parvovirus. *Vet. Microbiol.* 69:47-50
- Truyen, U. & C. R. Parrish (1992). Canine and feline host ranges of canine parvovirus and feline panleukopenia virus. Distinct host cell tropisms of each virus in vitro and in vivo. *J Virol* 66:5399-5408
- Truyen, U. & C. R. Parrish. (2000). Epidemiology and pathology of autonomous parvoviruses. In *Contributions to Microbiology: Parvoviruses*, Eds. S. Faisst and J. Rommelaere. Karger AG, Basel, vol. 4:149-162
- Truyen, U., A. Gruenberg, S.-F. Chang, P. Veijalainen, B. Obermaier & C. R. Parrish (1995). Evolution of the feline subgroup parvoviruses and the control of canine host range. *J. Virol.* 69:4702-4710
- Truyen, U., J. F. Evermann, E. Vieler & C. R. Parrish (1996). Evolution of canine parvovirus involved loss and gain of the feline host range. *Virology* 215:186-189
- Uttenthal A., E. Lund & M. Hansen (1999). Mink enteritis parvovirus. Stability of virus kept under outdoor conditions. *Acta Pathologica, Microbiologica, et Immunologica Scandinavica* 107:353-853
- Veijalainen, P. & E. Smeds (1988). Pathogenesis of blue fox parvovirus on blue fox kits and pregnant vixens. *Am J Vet Res* 49:1941-1944
- Veijalainen, P M., E. Neuvonen, A. Niskanen & T. Juokslahti. (1986). Latex agglutination test for detecting feline panleukopenia virus, canine parvovirus and parvoviruses of fur animals. *J Clin Microbiol* 23:556-559