FELINE PANLEUKOPENIA
ABCd guidelines on prevention and management

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Overview Feline panleukopenia virus (FPV) infects all felines as well as raccoons, mink and foxes. This pathogen may survive in the environment for several months and is highly resistant to some disinfectants.

Infection Transmission occurs via the faecal-oral route. Indirect contact is the most common route of infection, and FPV may be carried by fomites (shoes, clothing), which means indoor cats are also at risk. Intrauterine virus transmission and infection of neonates can occur.

Disease signs Cats of all ages may be affected by FPV, but kittens are most susceptible. Mortality rates are high – over 90% in kittens. Signs of disease include diarrhoea, lymphopenia and neutropenia, followed by thrombocytopenia and anaemia, immunosuppression (transient in adult cats), cerebellar ataxia (in kittens only) and abortion.

Diagnosis Feline panleukopenia virus antigen is detected in faeces using commercially available test kits. Specialised laboratories carry out PCR testing on whole blood or faeces. Serological tests are not recommended, as they do not distinguish between infection and vaccination.

Disease management Supportive therapy and good nursing significantly decrease mortality rates. In cases of enteritis, parenteral administration of a broad-spectrum antibiotic is recommended.

Disinfectants containing sodium hypochlorite (bleach), peracetic acid, formaldehyde or sodium hydroxide are effective.

Vaccination recommendations All cats – including indoor cats – should be vaccinated. Two injections, at 8–9 weeks of age and 3–4 weeks later, are recommended, and a first booster 1 year later. A third vaccination at 16–20 weeks of age is recommended for kittens from environments with a high infection pressure (cat shelters) or from queens with high vaccine-induced antibody levels (breeding catteries). Subsequent booster vaccinations should be administered at intervals of 3 years or more. Modified-live virus vaccines should not be used in pregnant queens or in kittens less than 4 weeks of age.

Feline panleukopenia virus (FPV) is the prototype parvovirus of carnivores.1 Currently, FPV and the canine parvovirus (CPV) are regarded as a single taxonomic entity, but for the purposes of these guidelines FPV refers to parvovirus in cats. Feline panleukopenia virus is known to infect other members of the Felidae, as well as raccoons, mink and foxes.2,3 In dogs, FPV replication was seen only in some lymphoid tissues such as the thymus, but not in the gut, and the virus was not shed.4

A new parvovirus, very closely related to FPV, was discovered in dogs in 1978.5 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. Canine parvovirus type 2 probably evolved from FPV by the acquisition of five or six amino acid changes in the capsid protein gene such that the mutated virus lost its capacity to infect cats.6 However, it subsequently adapted further to the canine host, with amino acid changes that enabled it to bind better to the canine cellular receptor, with the consequence that the virus regained the ability to infect cats.7 The parvoviruses now circulating in dogs worldwide can be genetically and antigenically defined as types CPV-2a, -2b and -2c; all are able to infect cats and may even cause disease.8-10 However, feline CPV infections are rare in Europe, and the canine virus is found only sporadically in feline diagnostic material.9 During the evolution from FPV to CPV-2, with its various antigenic types, neutralising epitopes have been affected such that cross-neutralisation by FPV antisera is markedly lower against the canine viruses.11

Epidemiology

Feline panleukopenia virus is a non-enveloped virus that is highly resistant to physical factors and chemical substances. In contaminated environments it may remain infectious for months.12 Diseased carnivores shed virus at high titres (up to 10⁹ TCID₅₀ per gram faeces), and it rapidly

European Advisory Board on Cat Diseases
The European Advisory Board on Cat Diseases (ABCD) is a body of experts in immunology, vaccinology and clinical feline medicine that issues guidelines on prevention and management of feline infectious diseases in Europe, for the benefit of the health and welfare of cats. The guidelines are based on current scientific knowledge of the diseases and available vaccines concerned.

An extended version of the feline panleukopenia guidelines presented in this article is available at www.abcd-vets.org

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Clinical Practice
accumulates in affected shelters and catteries. As it is also highly contagious, susceptible animals may still become infected even after thorough disinfection of the premises. It is, therefore, recommended that only successfully vaccinated kittens and cats should enter an environment that is potentially contaminated with parvovirus.

Although few data on FPV prevalence are available, breeding catteries and rescue shelters are particularly at risk.13,14

**Pathogenesis**

Feline panleukopenia virus 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 a cell-free viraemia to virtually all tissues. The genome of FPV is a single-stranded DNA molecule, which requires cells in the S-phase of division for its replication, and virus growth is therefore restricted to mitotically active tissues. All ‘autonomous’ parvoviruses require cellular DNA polymerases that synthesise the complementary DNA strand – this is the first step in viral DNA replication and a prerequisite for transcription.

The virus infects lymphoid tissues, and through cellular depletion can cause a functional immunosuppression. Lymphopenia may arise directly as a result of lymphocytolysis, but also indirectly, following lymphocyte migration into tissues. The bone marrow is affected as well, and virus replication has been described in early progenitor cells, explaining the dramatic effect on virtually all myeloid cell populations.15 This is also reflected by the defining panleukopenia that is observed in FPV-infected cats.16

**Clinical signs**

The hallmark of FPV infection is diarrhoea, caused by the shortening of the intestinal villi due to a loss – sometimes complete – of epithelial cells.17 The virus replicates in the rapidly dividing cells of the crypts of Lieberkühn, impairs regeneration of the intestinal epithelium and the lesions described above are the result (Figs 1 and 2). Their severity correlates with the turnover rate of these cells, and co-infection with enteric viruses such as feline coronavirus may aggravate the disease.

Intrauterine or perinatal infection may affect the central nervous system of the fetus, leading to cerebellar ataxia and intention tremor in affected kittens. The FPV feline ataxia syndrome results from an impaired development of the cerebellum due to lytic virus replication in the Purkinje cells (Table 1).18,19

Although FPV affects cats of all ages, kittens are most susceptible. Mortality rates are high – over 90% in kittens (Fig 3).
Immunity

Passive immunity acquired via colostrum
The biological half-life of maternally derived antibodies (MDA) is about 10 days.\(^\text{20,22}\) Having waned below a haemagglutination inhibition titre of about 40, MDA do not protect reliably against infection, but may still interfere with active immunisation. In most cats, MDA remain at protective titres until 6–8 weeks of age. However, later vaccinations have proven to offer advantages,\(^\text{23}\) supporting the ABCD’s recommendation of vaccinations at 16–20 weeks of age (as explained later) [EBM grade I]. It should be taken into account that queens living in high-risk environments – particularly those that have survived panleukopenia – possess very high MDA titres, and their kittens must therefore receive a last vaccination at 16 weeks of age or older.

Since the endotheliocorial placentation of the cat restricts materno-fetal passage of solutes, immunoglobulins of the IgG isotype can reach the fetus only during the last third of gestation and contribute to less than 10% of the kitten’s maternal immunity. Therefore, sufficient colostrum must be ingested to acquire protective levels of neutralising antibodies from the queen. Maximum absorption occurs around the eighth hour of life. Later, the kitten’s intestinal cells are replaced by epithelium that can no longer absorb and transport antibodies. Kitten serum antibody titres generally approach 50% of those of the dam, but vary depending on individual colostrum intake – which explains the large variations between littermates.\(^\text{24}\) Titres decrease in the first weeks of life by decay and dilution in the growing kitten. By analogy with CPV, an immunity gap around 8–12 weeks of age is postulated, when antibody levels are too low to protect against natural infection, but still high enough to interfere with vaccination (Fig 4).\(^\text{22,23,25}\)

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**FIG 3** High mortality (up to 90%) accompanied by dehydration is a feature of feline panleukopenia in kittens. Courtesy of Tadeusz Frymus

**FIG 4** The immunity gap is defined as being the period during which maternal immunity no longer protects the kitten from infection by feline panleukopenia virus, but does still interfere with the development of a vaccinal immunity. Adapted from Thiry E. Clinical virology of the dog and cat. Maisons-Alfort: Editions du Point Vétérinaire, 2006

Queens living in high-risk environments – particularly those that have survived panleukopenia – possess very high MDA titres, and their kittens must therefore receive a last vaccination at 16 weeks of age or older.
**Active immune response**

Antibodies play an important role in the immune response to FPV, and MDA efficiently protect kittens from fatal infection. Passively acquired immunity is later replaced by an active response, either by vaccination or as a consequence of natural infection.

Active immunity is solid and long lasting, and can be achieved by both inactivated and modified-live virus (MLV) vaccines. Feline panleukopenia virus antiserum has been used to protect cats before a vaccine-induced, active response is obtained. In kittens, this postpones the time at which active immunisation would be successful.

The cellular immune response against one parovirus capsid protein (VP2) 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 CPV-2.

**Diagnosis**

Feline panleukopenia can be diagnosed by virus isolation from blood or faeces in cultures of CrFK or MYA-1 cells and by the demonstration of haemagglutination of porcine erythrocytes. However, these methods are now rarely used for routine diagnosis.

In practice, FPV antigen is detected in faeces using commercially available latex agglutination or immunochromatographic tests. These tests have an acceptable sensitivity and specificity when compared with reference methods. Tests marketed for the detection of both FPV antigen and CPV-2 antigen may be used to diagnose FPV in faeces [EBM grade I].

Diagnosis by electron microscopy has lost its importance due to more specific, rapid and automated alternatives. Specialised laboratories offer PCR-based testing of whole blood or faeces. Whole blood is recommended in cats without diarrhoea or when no faecal samples are available. The analytical sensitivity of the antigen tests can be compromised by the presence of antibodies, which may bind to viral epitopes and render them inaccessible to the monoclonal antibodies in the test kit. This may lead to false negative results in samples from cats recently infected with FPV.

Antibodies to FPV can be demonstrated by ELISA or indirect immunofluorescence, but these tests are of limited diagnostic value as they do not differentiate between infection- and vaccination-induced antibodies. The presence of antibodies is taken as proof of protection against panleukopenia under field conditions.

**Evidence-based medicine (EBM) ranking used in this article**

Evidence-based medicine (EBM) is a process of clinical decision-making that allows clinicians to find, appraise and integrate the current best evidence with individual clinical expertise, client wishes and patient needs (see Editorial on page 529 of this special issue, doi:10.1016/j.jfms.2009.05.001).

This article uses EBM ranking to grade the level of evidence of statements in relevant sections on immunity, diagnosis, disease management and control, as well as vaccination. Statements are graded on a scale of I to IV as follows:

- **EBM grade I** This is the best evidence, comprising data obtained from properly designed, randomised controlled clinical trials in the target species (in this context cats);
- **EBM grade II** Data obtained from properly designed, randomised controlled studies in the target species with spontaneous disease in an experimental setting;
- **EBM grade III** Data based on non-randomised clinical trials, multiple case series, other experimental studies, and dramatic results from uncontrolled studies;
- **EBM grade IV** Expert opinion, case reports, studies in other species, pathophysiological justification. If no grade is specified, the EBM level is grade IV.

**Further reading**


**Disease management**

A cat diagnosed with feline panleukopenia, based on clinical signs and confirmed by laboratory evidence, should be kept in isolation.

**Supportive therapy**

Supportive therapy and good nursing significantly decrease mortality. Restoration of fluid, electrolytes and acid-base balance, preferably by intravenous drip, is most important in symptomatic treatment (Fig 5).

As the gut barrier is often destroyed in FPV-infected cats, intestinal bacteria may invade the...
blood stream. Bacteraemia in combination with the existing neutropenia may lead to sepsis in these immunocompromised patients. Prevention of sepsis is essential, and a broad-spectrum antibiotic with 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. However, the potential side effects of these drugs should be taken into consideration. Antibiotics should be administered parenterally (preferably intravenously).

Oral intake of water and food should be restricted only if vomiting persists; feeding should be continued as for as long as possible, and restarted as soon as possible. Beneficial effects of early enteral nutrition have been reported in canine parvovirusosis [EBM grade IV]. 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 B vitamin complex, can be given to prevent thiamine deficiency (which occurs only infrequently).

Hypoproteinaemic cats may require plasma or whole blood transfusions to restore oncotic pressure. Plasma transfusion in combination with heparin may control disseminated intravascular coagulation, as it supplements anti-thrombin III and other important plasma proteins. In anorexic, seriously vomiting and/or diarrhoeic cats, or in patients with persistent hypoproteinaemia, parenteral nutrition is required, preferably via a central venous catheter in the jugular vein.40

**Antiviral therapy**

Immune serum containing FPV antibodies can be used to prevent infection of susceptible animals. The prophylactic efficacy of this measure has been demonstrated in dogs and may be expected to operate also in cats [EBM grade IV].

Feline recombinant interferon-omega is effective in the treatment of parvoviral enteritis in dogs and also inhibits replication of FPV in cell culture. So far, no data are available on the efficacy of this cytokine in FPV-infected cats, but it is expected to perform well – if not better – in the homologous host [EBM grade IV].

**Passive immunisation**

Susceptible kittens and unvaccinated older animals should not be in contact with other cats until they are properly immunised. In a disease outbreak, passive immunisation can be used to protect young kittens with an incomplete vaccination history, colostrum-deprived kittens or unvaccinated adult cats. Anti-FPV serum can be given subcutaneously or intraperitoneally and may protect for 2-4 weeks. If a product of equine origin is used, repeated administration is not recommended as this may lead to anaphylactic reactions. These animals should not be vaccinated within 3 weeks of passive immunisation.

**Vaccination**

Because of the serious consequences of an infection and the ubiquity of the virus, vaccination is recommended for every cat; FPV vaccines belong to the ‘core’ category (see box on page 543). Even cats kept strictly indoors cannot avoid encountering the virus, since it is so stable in the environment that it can be transmitted on fomites.50,51

**Disease control in specific situations**

**Shelters**

Random source populations with unknown vaccination histories, continuous resident turnover and high risk for infectious disease are characteristics of most shelters. Budget constraints become a crucial management aspect, and only vaccines that demonstrate a clear benefit against common and serious shelter diseases will be employed.

Feline panleukopenia virus has re-emerged as a major cause of mortality in cats in shelters and rescue homes. With rare exceptions, all kittens and cats over 4-6 weeks of age should therefore 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, using MLV vaccines. Cats of unknown status should not be housed together. Vaccination should be repeated every 3-4 weeks in kittens until 16 weeks of age. In the face of an outbreak, the more rapid onset of immunity induced by MLV preparations makes them preferable to killed preparations.

Passive immunisation can be used in shelters; it is useful at admission if the disease is present, as it provides immediate protection. The efficacy of immunoglobulins in preventing panleukopenia was proven experimentally and in the field some 50 years ago. It depends on

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Vaccination recommendations

General considerations
Both MLV and inactivated FPV vaccines are available for administration by injection, and both provide solid immunity against disease. In healthy cats, protection by MLV vaccines is more rapid [EBM grade II].47,48 However, a single dose of an inactivated FPV vaccine may quickly induce good antibody responses in naïve cats.49,50 In the field, inactivated vaccines are not popular and have all but disappeared from the market (eg, in Germany, they are only used in exotic felids). There are no data to suggest that particular vaccine brands are more efficacious than others.

The following considerations may influence the decision about the vaccine type:

- Modified-live virus vaccines should not be used in pregnant queens because of the risk of placental virus passage and damage to the fetus, especially to the developing cerebellum.50,51 Though inactivated FPV products are licensed in some countries for use in pregnant queens, in general pregnant queens should not be vaccinated.
- Modified-live virus vaccines should not be administered to kittens under 4 weeks of age for the same reason: the cerebellum is still developing in young neonates.50,51

Primary course
Kittens from immune queens are protected by MDA in the first weeks of life. However, the time at which a kitten will become susceptible to infection and/or can respond to vaccination is unknown; also, there is considerable variation between individuals. In general, MDA will have waned by 8–12 weeks of age to a level that allows an immunological response, and an initial vaccination at 8–9 weeks of age followed by a second injection 3–4 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 some time after 12 weeks of age.

No single primary vaccination policy will therefore cover all potential situations. The ABCD recommends that:

- All kittens should receive FPV vaccines;
- At least two doses of vaccine should be administered – the first at 8–9 weeks of age, and the second 3–4 weeks later (at a minimum of 12 weeks of age);
- 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 the kitten is in a high-risk situation [EBM grade I]. If a kitten is vaccinated at or before 4 weeks of age, only an inactivated product should be used, and repeat vaccinations can be given at 3–4 week intervals until 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 catteries or shelters, and to kittens from cats that had previously lived in a low-exposure environment and moved into a high-risk situation [EBM grade II].
- Adult cats of unknown vaccination status should receive a single MLV vaccine injection followed by a booster 1 year later.

Booster vaccinations
Cats that had responded to FPV vaccination have been shown to maintain a solid immunity for 7 years (probably longer) in the absence of any booster vaccination or natural challenge [EBM grade II].51,38 Nevertheless, the ABCD recommends the following revaccination protocol:

- All cats should receive a first booster 12 months after completion of the kitten vaccination course (this will ensure protection of cats that have not adequately responded to the primary course);
- After this first booster, subsequent revaccinations are given at intervals of 3 years or longer, unless special conditions apply [EBM grade II].

While most cases of panleukopenia are caused by infection with FPV, the canine parvovirus variants CPV-2a, CPV-2b and CPV-2c, discussed earlier, have infected cats and caused disease. Current FPV vaccines probably afford protection against these new variants [EBM grade II].52,53

Feline panleukopenia virus has re-emerged as a major cause of mortality in cats in shelters and rescue homes.

Repeated treatment (at an interval of more than 1 week) should be avoided, as cats may display anaphylactic reactions.40

Immune serum (see box on page 544) may also be prepared in the veterinary practice by bleeding healthy donor cats (preferably groups of recovered animals). Hyperimmune serum would be obtained from animals that had been repeatedly vaccinated. If such sera are used, their antibody content and consequently the duration of protection are obviously unknown.

the specific antibody titre, the volume administered, the relative importance of serum antibodies in controlling the particular infection, and the timing of administration.

Products containing highly concentrated immunoglobulins are available in some European countries for cats (horse antibodies directed against FPV, feline herpesvirus and feline calcivirus). They are marketed for prophylactic and therapeutic use, with protection lasting for about 3 weeks. During this period, the cats cannot be vaccinated with a MLV product, because the immunoglobulins will neutralise the attenuated virus. Although large amounts of foreign (equine) protein are administered, allergic reactions and side effects are rare.
Blood donors must be screened for insidious infections (particularly with feline immunodeficiency virus, feline leukaemia virus and Bartonella species). Careful attention should be paid to sterility during collection, serum preparation, storage and administration. The area over the jugular vein should be shaved and disinfected for aseptic venepuncture. Blood should be collected (at least double the volume of serum required) into sterile tubes without additives. Serum can be stored at −20°C in single dose aliquots, as IgG is stable and can be kept for a year if frozen promptly after collection [EBM grade II].

Usually serum is given subcutaneously; the recommended dose is 2–4 ml serum per kilogram body weight; intraperitoneal injection is more feasible in kittens. If intravenous administration is required for an instant effect, plasma (instead of serum) should be used.

Breeding catteries
Vaccination schedules used for privately owned cats are appropriate in most breeding catteries. Queens may receive boosters before breeding to maximise delivery of MDA to kittens. The kittens from such queens may need an extra primary vaccination at 16–20 weeks [EBM grade I].

Pregnant cats should not routinely be vaccinated.

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

Immunocompromised cats
Vaccines cannot generate optimum protection in animals with conditions that compromise immune function. Such conditions include deficient nutrition, genetic and acquired immunodeficiencies, systemic disease, concurrent administration of immunosuppressive or cytostatic drugs, and environmental stress. Efforts should be made to protect cats from exposure to infectious agents before vaccination; if this cannot be achieved, they should be vaccinated nevertheless, with another injection given after the animal has recovered.

Modified-live virus vaccines against panleukopenia should be used with caution in immunocompromised individuals, as the failure to control viral replication could lead to clinical signs.

Cats receiving corticosteroids Vaccination should be considered carefully in cats receiving corticosteroids. Depending on the dosage and duration of treatment, corticosteroids may cause functional suppression of immune responses (cell-mediated in particular). In dogs, corticosteroids do not hamper immunisation if given for short periods at moderate doses [EBM grade IV].

In general, however, the use of corticosteroids at the time of vaccination should be avoided.

Cats with chronic disease 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. Nonetheless, cats with stable chronic conditions such as renal disease, diabetes mellitus or hyperthyroidism should receive vaccines at the same frequency as healthy cats. In contrast, acutely ill, weak or febrile cats should not be vaccinated.

Feline leukaemia virus (FeLV) positive cats Retrovirus-infected cats should be kept indoors and isolated to diminish the likelihood of infecting other cats and to protect them from exposure to other infectious agents. Feline leukaemia virus-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 preparations are preferred. Cats infected with FeLV may not mount satisfactory immune responses to rabies vaccines, and perhaps to other vaccine antigens. Therefore, more frequent vaccinations should be considered.

Feline immunodeficiency virus (FIV) positive cats Healthy FIV-infected cats are capable of mounting immune responses to administered antigens (this is not the case during the terminal phase of infection) but primary immune responses may be delayed or diminished [EBM grade III].

In one study, cats experimentally infected with FIV developed vaccine-induced panleukopenia when given MLV FPV vaccines [EBM grade III]. Immune stimulation of FIV-infected lymphocytes in vitro promotes virus production, and stimulation of chronically FIV-infected cats with a synthetic peptide was associated with a decrease in the CD4+/CD8+ ratio. Therefore, a potential trade-off to protection from, for example, panleukopenia is the progression of the FIV infection due to increased virus production [EBM grade III]. This means that only FIV-seropositive cats at high risk of exposure should be vaccinated, and only using killed vaccines.
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KEY POINTS

- Feline panleukopenia virus (FPV) infects all felids as well as raccoons, mink and foxes.
- FPV may survive in the environment for several months.
- Indirect contact is the most common route of infection.
- FPV affects cats of all ages but kittens are most susceptible.
- FPV antigen is detected in faeces with commercial test kits that detect viral antigens. Specialised laboratories carry out PCR testing on whole blood or faeces.
- Supportive therapy and good nursing significantly decrease mortality rates.
- In cases of enteritis, parenteral administration of a broad-spectrum antibiotic is recommended.
- Disinfectants containing sodium hypochlorite (bleach), peracetic acid, formaldehyde or sodium hydroxide are effective.
- All cats – including indoor cats – should be vaccinated.
- Two injections of kittens, at 8–9 weeks of age and 3–4 weeks later, are recommended, and a first booster 1 year later.
- A third vaccination at 16–20 weeks of age is recommended for kittens from environments with a high infection pressure or from queens with high vaccine-induced antibody levels.
- The next booster vaccinations are given at intervals of 3 years or more.
- Although protection starts rapidly after injection of modified-live virus vaccines, they should not be used in pregnant queens and in kittens less than 4 weeks of age.

References