Journal of Feline Medicine and Surgery (2009) **11**, 556–564
doi:10.1016/j.jfms.2009.05.004

CLINICAL REVIEW

FELINE CALICIVIRUS INFECTION
ABCD guidelines on prevention and management

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Overview Feline calicivirus (FCV) is a highly variable virus. More severe, systemic forms of FCV infection have been observed recently.
Infection Sick, acutely infected or carrier cats shed FCV in oronasal and conjunctival secretions. Infection occurs mainly through direct contact.
Disease signs The main clinical signs are oral ulcers, upper respiratory signs and a high fever. Feline calicivirus may be isolated from nearly all cats with chronic stomatitis or gingivitis. Cats with 'virulent systemic FCV disease' variably show pyrexia, cutaneous oedema, ulcerative lesions on the head and limbs, and jaundice. Mortality is high and the disease is more severe in adult cats.
Diagnosis Diagnosis of FCV can be achieved by virus isolation or reverse-transcriptase PCR. Viral RNA can be detected in conjunctival and oral swabs, blood, skin scrapings or lung tissue using PCR. Positive PCR results should be interpreted with caution, as these may be a consequence of low-level shedding by persistently infected carriers. The diagnosis of virulent systemic FCV disease relies on clinical signs and isolation of the same strain from the blood of several diseased cats.
Disease management Supportive therapy (including fluid therapy) and good nursing care are essential. Anorexic cats should be fed highly palatable, blended or warmed food. Mucolytic drugs (eg, bromhexine) or nebulisation with saline may offer relief. Broad-spectrum antibiotics may be administered to prevent secondary bacterial infections. Feline calicivirus can persist in the environment for about 1 month and is resistant to many common disinfectants.

Vaccination recommendations
Two injections, at 9 and 12 weeks of age, are recommended, followed by a first booster 1 year later. In high-risk situations, a third vaccination at 16 weeks is recommended. Boosters should be given every 3 years. However, cats in high-risk situations should be revaccinated annually. Cats that have recovered from caliciviral disease are probably not protected for life, particularly if infected with different strains. Vaccination of these cats is still recommended.

Virus properties

Feline calicivirus (FCV) is a highly contagious pathogen with a widespread distribution in the feline population. The virus has a small single-stranded RNA genome of positive (messenger) polarity; this allows FCV to evolve quickly. The genome is enclosed by a single major capsid protein. Its surface contains the most variable region of the virus, which is the principal target for the host's immune response.[1,2] Despite this variability, there is sufficient similarity between isolates to allow their classification into a single serotype.[3] However, antigenic differences exist between most FCV isolates, which creates considerable difficulties when trying to maximise vaccine cross-protection.

Epidemiology

There are no important reservoirs or alternative hosts for FCV, and humans are not susceptible. In addition to there being a specific canine calicivirus, FCV-like viruses have also been isolated from dogs.[4] Their role in the epidemiology of FCV is uncertain, but is probably not important.[5]

The virus is shed predominantly in oral and nasal secretions in acute disease. After recovery, many cats continue shedding – the majority for more than 30 days, and a few for several years.[6] A small proportion of cats is resistant to infection, probably due to host and virus strain factors.[7]

Feline calicivirus infection is widespread in cat populations. The prevalence is roughly proportional to the number of cats in the household, with the highest prevalence in large groups housed together. The prevalence in household cats kept in small groups is generally around 10%,

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 calicivirus infection guidelines presented in this article is available at www.abcd-vets.org

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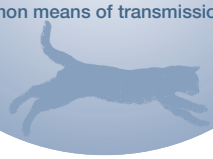
ELSEVIER
jfms Journal of Feline Medicine and Surgery Clinical Practice

1098-612X/09/070556+9 $34.00/0

Feline calicivirus infection is widespread in cat populations. The prevalence is roughly proportional to the number of cats in the household, with the highest prevalence in large groups housed together.

Transmission

Infection occurs through direct contact with secretions from acutely infected and carrier cats. However, the virus can persist in the environment and remain infectious for up to 1 month on dry surfaces at room temperature, and longer in colder conditions.[12] Indirect transmission can therefore occur, especially within the close confines of a cattery where secretions may contaminate cages, feeding and cleaning tools or personnel. Direct contact between susceptible cats and carriers shedding FCV is probably the most common means of transmission.[13]



whereas prevalences of 25–40% have been reported from colonies and shelters.[5,8,9] The prevalence varies between colonies, ranging from low to high (50–90%).[7,10,11]

Pathogenesis

Cats are infected via the nasal, oral or conjunctival routes. The oropharynx is the primary site of replication. Transient viraemia occurs 3–4 days after infection, when the virus can be detected in many other tissues. The virus induces necrosis of epithelial cells. Vesicles, typically on the margin of the tongue, develop into ulcers; in the affected regions, the dermis is infiltrated with neutrophils. Healing takes place over a period of 2–3 weeks.[14]

Less commonly, other tissues are infected, leading to pneumonia (focal alveolitis progresses via areas of acute exudative pneumonia to proliferative interstitial pneumonia) and lameness (acute synovitis with thickening of the synovial membrane and increased synovial fluid).[15] The pathogenesis of the limping syndrome is not clear.

Recently, so-called 'virulent systemic FCV disease' has been described, which differs from the picture described above. The disease manifests as widespread vasculitis, multiorgan involvement and death in up to two-thirds of affected cats.[16,17] The pathogenesis of virulent systemic FCV infection is unknown and may include viral evolution and/or immune-mediated components as well as environmental and management factors.[18]

After recovery from acute disease, most cats clear the infection in about 30 days; a few shed virus for much longer, possibly for life. In these healthy carriers, FCV can localise in the tonsillar epithelium; however, tonsillectomy does not terminate the carrier state, suggesting persistence also at other sites. Amino acid changes in the capsid protein probably allow FCV variants to escape the host immune response and to persist.[19,20]

After recovery, many cats continue shedding – the majority for more than 30 days, and a few for several years.

Immunity

Passive immunity acquired via colostrum

Maternally derived antibodies (MDA) protect kittens during the first weeks of life and may interfere with vaccination. In general, levels are higher and persist longer than for feline herpesvirus (FHV). In an experimental study, the average half-life of MDA was 15 days and titres persisted for 10–14 weeks.[21] In a field study, however, 20% of kittens had no detectable antibodies against a widely used vaccine strain as early as 6 weeks of age.[22]

Active immune response

Virus neutralising antibodies (VNA) appear by about 7 days after infection.[23] In general, their titres are higher than for FHV, and their levels correlate well with protection against homologous challenge.[3] There is wide antigenic variability among FCV strains, but it was concluded from studies of in vitro cross-reactivity that FCVs belong to a single serotype.[24] Prior infection with one strain can significantly reduce the acute clinical signs upon exposure to a heterologous strain and oral shedding may be reduced.[3] In general, the level of heterologous protection will depend on the virus strains involved.

Cats may be protected also in the absence of detectable VNA; indeed, cellular responses have been demonstrated in vaccinated cats.[25,26]

Clinical signs

Feline calicivirus infection can cause acute oral and upper respiratory signs but has also been associated with chronic stomatitis, which may be immune-mediated. As mentioned, the newly described virulent systemic FCV disease presents rather differently (see below).

Acute oral and upper respiratory tract disease

Clinical findings after FCV infection differ depending on the virulence of the infecting strain, the age of the affected cat and husbandry factors. While subclinical infections

FIG 1 Tongue ulcer in a cat with feline calicivirus infection. *Courtesy of Albert Lloret*

FIG 2 Sloughing oral ulcer and rhinitis in a cat infected with feline calicivirus. *Courtesy of Merial*

occur, most clinical courses show a typical syndrome of lingual ulceration and mild acute respiratory disease (Figs 1 and 2). More severe signs can resemble the respiratory disease caused by FHV.

Acute oral and upper respiratory disease is seen mainly in kittens. After an incubation period of 2–10 days, oral ulceration, sneezing and serous nasal discharge are the main signs.[14] Fever is also observed. Anorexia is sometimes accompanied by hypersalivation due to the erosions, which are located mainly on the tongue and are usually more prominent than rhinitis. The erosions usually resolve after several days. In some severe cases, pneumonia, manifesting as dyspnoea, coughing, fever and depression, can occur, particularly in young kittens.

Chronic stomatitis

Feline calicivirus can be isolated from nearly all cats presenting with the chronic lymphoplasmacytic gingivitis/stomatitis complex. It is characterised by a proliferative/ulcerative faucitis (Fig 3), which is possibly an immune-mediated reaction to FCV (and to other oral antigens). However, the disease has not been reproduced experimentally, and the exact role of FCV remains unclear.

Limping syndrome

An acute transient lameness with fever can follow FCV infection and vaccination. In natural infection, it occurs a few days or weeks after the acute oral or respiratory signs.[27]

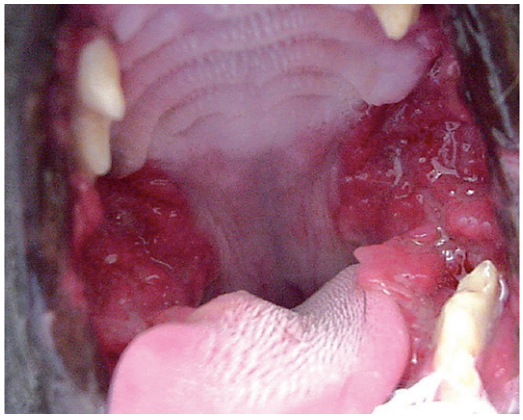


FIG 3 Chronic ulcerative proliferative gingivostomatitis. A chronic feline calicivirus infection is associated with this painful syndrome but the disease has not been reproduced experimentally. *Courtesy of Albert Lloret*

Virulent systemic FCV disease

Outbreaks of highly virulent, and often lethal, FCV infection have recently been described in the United States and in Europe.[16,17] The disease has been named 'highly virulent feline calicivirus disease' and previously 'hemorrhagic-like fever'. The causative strains are most commonly referred to as 'virulent systemic feline calicivirus'.

The incubation period in cases of virulent systemic FCV infection in hospitals is 1–5 days, but in the home environment it may extend up to 12 days.[28] The disease is more severe in adults than in kittens. In studies, vaccination did not protect against field infections, although, experimentally, some protection has been achieved.[16,28,29] It is unknown whether this is due to inherent characteristics of these hypervirulent strains or because common strains are unlikely to cause outbreaks since vaccination is so widely practised.[16,18]

Virulent systemic FCV disease is characterised by a systemic inflammatory response syndrome, disseminated intravascular coagulation, multiorgan failure and death, with mortality rates of up to 67%.[30]

While subclinical infections occur, most clinical courses show a typical syndrome of lingual ulceration and mild acute respiratory disease.

The clinical signs vary, and initially often appear as a severe acute upper respiratory tract disease. Characteristic signs are cutaneous oedema, mainly involving the head and limbs, and ulcerative lesions on the skin and paws.[28] Crusted lesions, ulcers and alopecia can be seen on the nose, lips and ears, around the eyes and on the footpads. Some cats are jaundiced (eg, due to hepatic necrosis, pancreatitis), and some may show severe respiratory distress (eg, due to pulmonary oedema). Thromboembolism and coagulopathy caused by disseminated intravascular coagulation may be observed, manifesting as petechiae, ecchymoses, epistaxis or bloody faeces.[17,28]

Diagnosis

Because of the asymptomatic carrier state, any FCV-positive result should be interpreted with suspicion: the presence of virus and the clinical signs are poorly correlated [EBM grade III].[31]

Virulent systemic FCV is diagnosed on the basis of clinical signs, high contagiousness, high mortality and isolation of the same calicivirus strain from the blood of several diseased cats (assessed, by genome sequencing, of hypervariable regions in the capsid gene).

Virus and antigen detection

- **Detection of nucelic acid** Conventional, nested and real-time reverse-transcriptase PCR (RT-PCR) assays have been developed to detect FCV RNA in conjunctival and oral swabs, blood, skin scrapings and lung tissue, depending on the clinical form and the outcome of the disease. Diagnostic sensitivity depends on both the primers and the strain, because of the high variability of the viral genome.[31–33] Therefore, molecular assays should be validated using a large panel of strains to minimise false-negative results. Reverse transcriptase PCR has the advantage of identifying unique virus strains and has proven useful in molecular epidemiology and outbreak investigations. However, consistent genetic markers associated with virulence, specifically in virulent systemic FCV strains, are as yet unavailable.[34]
- **Virus isolation** Virus isolation demonstrates the presence of replicating virus and is less sensitive to strain variation than RT-PCR. Feline calicivirus replicates in cell lines of feline origin; its rapid growth in tissue culture may compromise identification of concurrent FHV, which takes longer to produce cytopathic effects.[35] Virus can be isolated from nasal, conjunctival and oropharyngeal swabs, but virus isolation may fail due to small numbers of infectious virions in the sample, virus inactivation during transit, or the presence of antibodies in the sample that neutralise the virus in vitro.[36] The likelihood of successful virus isolation can be maximised if swabs are collected from both the conjunctiva and oropharynx.[32]

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Antibody detection

Feline calicivirus antibodies can be detected by virus neutralisation or ELISA. The seroprevalence is generally high in cat populations due to natural infection and vaccination. Consequently, serology is not useful for diagnosis [EBM grade I].[36]

However, VNA titres can be useful to predict whether or not a cat is protected. False-negative results may be obtained if the antibody does not neutralise the laboratory strains used in the test. Also, titres may appear higher when homologous (rather than heterologous) virus–antibody pairs are used. When the strain used in VNA is not defined, interpretation is difficult.[22,37]

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 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

Roudebush P, Allen TA, Dodd CE, Novotny BJ. Application of evidence-based medicine to veterinary clinical nutrition. *J Am Vet Med Assoc* 2004; **224:** 1765–71.

Disease management

Treatment of acute upper respiratory tract disease

Severely affected cats require intensive nursing care and supportive therapy. The resolution of dehydration and restoration of electrolyte and acid–base disturbances by intravenous fluid administration is required. Food intake is extremely important. Many ill cats do not eat, mainly because of pyrexia and/or ulcers in the oral cavity but sometimes also because of loss of sense of smell due to nasal congestion. Non-steroidal anti-inflammatory drugs can be used to treat fever and oral pain. Food may be blended, should be highly palatable, and may be warmed to increase the smell. If the cat does not eat for more than 3 days, placement of a feeding tube and enteral nutrition is indicated. At the clinician's discretion, broad-spectrum antibiotics should be administered to cats with severe disease and suspected bacterial infection. It is crucial to use antibiotics that achieve good penetration into the respiratory tract and/or oral mucosa.

Nasal discharge should be cleaned away several times a day with physiological saline solution, and ointment should be applied locally. If there is a mucous nasal discharge, drugs with mucolytic effects (eg, bromhexine) may be helpful, and nebulisation with saline can be used to combat dehydration of the airways.

Antiviral therapy

Most antivirals used in veterinary medicine only inhibit replication of DNA viruses or retroviruses, and antiviral treatments for FCV infections have not entered clinical practice. Ribavirin is one of the few antiviral agents able to inhibit FCV replication in vitro. However, it appears to be toxic to cats, and side effects have precluded its systemic use [EBM grade III].[38] Feline interferon-omega (licensed for the treatment of canine parvovirus and feline leukaemia virus (FeLV) infections in some European countries) inhibits FCV replication in vitro; controlled field studies, however, are not available [EBM grade IV].[39,40]

Treatment of virulent systemic FCV disease

Cats severely affected by virulent systemic FCV have been treated with intensive supportive therapy (fluid therapy, antibiotics) plus steroids and interferon, and clinical improvement has been reported anecdotally [EBM grade III].[18] However, controlled clinical studies have not been published.

Treatment of chronic stomatitis

Controlled studies to determine the best means of treating chronic ulceroproliferative stomatitis are lacking. Recommended options include antibiotics plus rigorous dental cleaning, corticosteroids and/or other immunosuppressant or immunomodulatory drugs (gold salts, clorambucil, thalidomide and ciclosporin) [EBM grade IV] and total teeth extractions [EBM grade III].[41,42] Anecdotal and case reports have suggested the use of both feline interferon-omega and human interferons for treating cats with chronic stomatitis associated with FCV shedding, by intralesional or combined systemic plus intralesional application [EBM grade IV].[42]

Vaccination

Because FCV infection is ubiquitous and may cause severe disease, the ABCD considers calicivirus to be a core vaccine component and recommends that all healthy cats are vaccinated against FCV (see box on page 561). Although vaccination provides good protection against acute oral and upper respiratory tract disease in most cases, it does not prevent infection or shedding.[43] In addition, no vaccine protects against all FCV field strains.

Disease control in specific situations

Shelters

Disease caused by FCV is often a shelter problem. Measures to limit virus transmission are as important as vaccination, and shelter design and management should keep this objective in mind. Cats should be housed individually, unless they come from the same household.

If acute respiratory disease occurs in a shelter, identification of the agent (with differentiation of FCV from FHV, *Chlamydophila felis*, *Bordetella bronchiseptica* and *Mycoplasma* species) may be useful in deciding on the appropriate preventive measures. Feline calicivirus can persist in the environment for about 1 month; effective disinfectants include

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Vaccination recommendations

General considerations

Currently, FCV is either combined with FHV alone in divalent vaccines (in some countries) or, more commonly, with additional antigens as well. Both modified-live and inactivated parenteral vaccines exist; modified-live intranasal vaccines are no longer available in Europe, but are still available in the USA.

Feline calicivirus vaccines provide protection mainly by inducing VNA. A major mechanism by which viruses like FCV evolve is through mutation and selection of mutants that escape herd immunity (ie, neutralisation by pre-existing antibody in a population). In FCV, this creates the potential for field strains to evolve that are resistant to vaccine-induced immune responses, and this potential would be predicted to be greater where a particular strain (or strain combination) has been used for a long time. Although there are some studies that lend support to this hypothesis,[45–47] the evidence for FCV escaping vaccine-induced immunity at a population level is not yet convincing. Such studies are conducted to obtain more information about strains circulating in Europe, and to identify more broadly protective FCV variants.[25] The most commonly used strains in vaccine products are the F9 (the oldest, isolated in the 1950s) and FCV 255, and, more recently, strains G1 and 431.[25,48] Some companies do not disclose the virus strain(s) present in their vaccines.

Core vaccine

The ABCD considers vaccines that protect against FCV infections as being core.

In the absence of compelling published data, it is difficult to make general recommendations about which vaccine and combination of strains to use. However, if virologically confirmed FCV disease occurs in a fully vaccinated community, then changing to different vaccine antigens may offer advantages.

The impact of vaccination on the shedding of field viruses is controversial, with one study showing a moderate reduction while others show that vaccination might actually extend the period of virus shedding after infection.[10,20,25,50,51] Live parenteral FCV vaccine strains can be shed, although this is rare.[50–52]

Live vaccines retain some virulence and may induce disease if administered incorrectly – for example, accidentally aerosolised or spilled on the skin and ingested.[50–52] However, this too is rare.

Cats that have recovered from caliciviral disease are probably not protected for life, particularly not against infections caused by other, distinct strains. Therefore, vaccination of recovered cats is generally recommended, even in situations where FCV is endemic.

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The value of serological data in predicting protection is limited, because antibodies to the calicivirus strain used in a laboratory test may not necessarily protect against the strains that the cat will subsequently be exposed to in the field.

Primary course

The primary course is usually started at around 9 weeks of age, although some vaccines are licensed for earlier use. Kittens should receive a second vaccination 2–4 weeks later, but not earlier than at 12 weeks. However, due to a longer persistence of MDA, some kittens may fail to respond to this protocol [EBM grade I].[22] In high-risk situations, particularly where FCV has previously caused disease in vaccinated kittens, a third injection at 16 weeks should be considered. The ABCD recommends using the same brand for the entire primary vaccination course.

Older cats of uncertain FCV vaccination status should also receive two injections at an interval of 2–4 weeks, using vaccines containing the same virus strains. This applies even to modified-live virus vaccines.

Booster vaccinations

Based on results published by several independent groups, the ABCD recommends that boosters should be given at 3-yearly intervals to individual cats in low-risk situations, such as indoor-only cats with little contact with other cats [EBM grade II]. However, owners should be made aware of the observation that with increasing time since the last vaccination, protection will decrease. Cats in crowded, high-risk situations (eg, boarding catteries) should be revaccinated at yearly intervals. For other cats, an informed decision should be made on the basis of a risk–benefit analysis.

The ABCD recommends a single injection if the interval since the last vaccination is less than 3 years. If the interval is longer, two vaccinations would ensure optimal protection. Boosters using FCV vaccines from different manufacturers are acceptable.

Because single-component vaccines are unavailable, annual boosters intended to protect against other diseases may entail more frequent FCV boosters.

sodium hypochlorite (5% bleach diluted at 1:32), potassium peroxymonosulfate, chlorine dioxide and commercial products approved for calicivirus inactivation.

Healthy newcomers should be vaccinated as soon as possible. Modified-live virus vaccines are preferred in shelters as they induce an earlier onset of protection.

Breeding catteries

Feline calicivirus infection is a frequent problem for cat breeders. Infections present as upper respiratory disease in young kittens, typically at around 4–8 weeks as MDA wane. Severe disease signs frequently are seen in all kittens of a litter, some of which may die. Vaccination of the queen will not prevent

virus shedding, but may ensure that the kittens benefit from higher MDA levels, with protection for the first month or so of life.

Queens should be given a booster vaccination prior to mating. Vaccination during pregnancy is discouraged. Modified-live virus vaccines are not licensed for use in pregnant queens and, if considered at all, an inactivated vaccine must be used.

Queens should kitten in isolation, and their litters should not mix with those of other cats until they have been fully vaccinated. Early vaccination should be considered for litters from queens that have previously had infected litters. The earliest age at which FCV vaccines are licensed is 6 weeks, but vaccination from around 4 weeks of age may be considered (kittens are already immunocompetent at that age), with repeated injections every 2 weeks until the normal primary vaccination course is started, concluding at 12 weeks. Where all other control strategies have failed, early weaning and isolation from around 4 weeks has been advocated, but the behavioural consequences of such a measure must be taken into account.

Immunocompromised cats

Vaccines cannot confer optimal protection to animals with compromised immune function, such as those with nutritional deficits, genetic and virally acquired immunodeficiencies, systemic disease, those receiving concurrent immunosuppressive and cytostatic drugs, or experiencing environmental stress. If protection of immunocompromised cats from exposure to infectious agents cannot be assured, vaccination should be performed nevertheless. For safety reasons, the ABCD recommends inactivated vaccines in this situation, because replication of the vaccinal FCV could lead to clinical signs.

- **Feline immunodeficiency virus (FIV) positive cats** Cats infected with FIV can mount immune responses to administered antigens other than during the terminal phase of infection, but primary immune responses may be delayed or diminished [EBM grade III].[49,53] Feline calicivirus vaccination was shown to be less effective in cats shortly after experimental FIV infection, and vaccination might enhance long-term shedding of FCV.[49] Immune stimulation of FIV-infected lymphocytes in vitro promotes replication of the retrovirus. In vivo, vaccination of seropositive cats with a synthetic peptide was associated with a decrease in the CD4+/CD8+ ratio.[53,54] Therefore, a potential trade-off to protection from FCV-related disease is the progression of FIV infection as a result of increased virus production. Only healthy FIV-infected cats at a high risk of exposure should be vaccinated, and only using killed vaccines.

KEY POINTS

- Feline calicivirus (FCV) is a highly contagious pathogen of the upper respiratory tract.
- FCV displays a wide spectrum of virulence, antigenicity and induced immunity.
- FCV is also found in nearly all cats with chronic stomatitis or gingivitis.
- Positive PCR results should be interpreted with caution, as they may be due to low-level shedding by persistently infected carriers.
- The diagnosis of 'virulent systemic FCV disease' relies on clinical signs, high contagiousness and high mortality rates, and isolation of the same strain from the blood of several diseased cats.
- FCV can persist in the environment for about 1 month and is resistant to many common disinfectants. Sodium hypochlorite (5% bleach diluted at 1:32) is effective.
- Early vaccination should be considered for kittens from queens that have had infected litters previously, or for cats at risk of infection.
- All healthy cats should be vaccinated against FCV.
- Two injections, at 9 and 12 weeks of age, are recommended, and a first booster 1 year later.
- In high-risk situations, a third kitten vaccination at 16 weeks is recommended.
- Boosters should be given every 3 years. However, cats in high-risk situations should be revaccinated every year.
- Cats that have recovered from caliciviral disease are probably not protected for life, particularly against disease caused by different strains. Vaccination of these cats is still recommended.

- **Feline leukaemia virus positive cats** Cats infected with FeLV should be kept indoors and isolated, not only to avoid exposure to FCV, but also to avoid retrovirus transmission. Asymptomatic FeLV-infected cats should be vaccinated against FCV, using killed preparations. Feline leukaemia virus infected cats may not mount adequate immune responses to rabies vaccines, and perhaps to other antigens including FCV. Protection may not therefore be comparable to that achieved in uninfected cats, and more frequent vaccination should be considered.
- **Cats with chronic disease** Exceptions to the general rule to vaccinate only healthy animals apply for cats with chronic illness. Those with stable chronic conditions (renal disease, diabetes mellitus, hyperthyroidism) should receive vaccines at the same frequency as healthy cats. In contrast, acutely ill or febrile cats should not be vaccinated. In cats with chronic stomatitis and FCV infection, administration of modified-live FCV vaccine is best avoided [EBM grade IV].[50]
- **Cats receiving corticosteroids or other immunosuppressive drugs** Depending on dosage and length of treatment, corticosteroids cause immune suppression, and their use of at the time of vaccination should be avoided. Their effect on vaccine efficacy in cats is unknown.

Acknowledgements

The European Advisory Board on Cat Diseases (ABCD) is indebted to Dr Karin de Lange for her judicious assistance in organising this special issue, her efforts at coordination, and her friendly deadline-keeping. The tireless editorial assistance of Christina Espert-Sanchez is gratefully acknowledged. The groundwork for this series of guidelines would not have been possible without financial support from Merial. The ABCD particularly appreciates the support of Dr Jean-Christophe Thibault, who respected the team's insistence on scientific independence.

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