Guidelines on Feline Infectious Diseases

FELINE HERPESVIRUS-1

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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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ABCD GUIDELINES ON:

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2. Feline herpesvirus-1

2.1 Biology of the virus

2.1.1 Virus properties

Feline herpesvirus 1 (FHV-1) is the agent of feline viral rhinotracheitis and is distributed worldwide. The virus belongs to the family *Herpesviridae*, subfamily *Alphaherpesvirinae*, genus *Varicellovirus*. Although only one serotype is described, the virulence can differ between viral strains (Gaskell et al. 2007). Some differences can also be observed by restriction endonuclease analysis of viral DNA (Hamano et al. 2005; Thiry 2006).

FHV-1 is a typical herpesvirus: the genomic double-stranded DNA is packaged into an icosahedral capsid surrounded by a proteinaceous tegument and a phospholipid envelope. At least ten different glycoproteins are present on the envelope. FHV-1 grows in both epithelial cells of the conjunctiva and the upper respiratory tract, and in neurones. The neuronal infection enables the virus to establish lifelong latency after primary infection. FHV-1 is related antigenically to canine herpesvirus and phocid herpesviruses 1 and 2, although there is no known cross species transfer (Gaskell et al., 2006).

The virus is inactivated within 3 hours at 37°C and is susceptible to most commercially available disinfectants, antiseptics and detergents. At low temperatures, the virus has shown to remain infective for five months (154 days at 4°C), although its survival is shorter at higher temperatures (33 days at 25°C, 4-5 minutes at 56°C) (Pedersen, 1987).

2.1.2 Epidemiology

The domestic cat is the main host of FHV-1 but the virus has been isolated also from other felids, including cheetahs and lions, and antibodies have been detected in pumas. There is no evidence of human infection.

Latent chronic infection is the typical outcome for FHV-1 acute infection and intermittent reactivation gives rise to viral shedding in oronasal and conjunctival secretions. Apart from in catteries, contamination of the environment is not a primary source for transmission. Virus shedding from acutely infected cats and from latently infected cats experiencing reactivation are the two main sources of infection (Gaskell and Povey, 1982).

Transplacental infection has not been demonstrated in the field. Latently infected queens may transmit FHV-1 to their offspring because parturition and lactation are typical stress-inducing factors leading to viral reactivation and shedding. Kittens may therefore acquire FHV-1 infection at a very early age before vaccination. The outcome depends on the level of maternally derived antibodies (MDA). When high levels are present, kittens are protected against disease and develop subclinical infection leading to latency whereas in the absence of sufficient MDA, clinical disease may follow (Gaskell and Povey, 1992).

In healthy small populations, the prevalence of viral shedding may be less than 1% whereas in large populations, especially with clinical disease present, prevalence may be up to 10 20% (Coutts et al., 1994; Binns et al., 2000; Helps et al., 2005). In shelters, risk of contagion is higher: with only 4% of shedding cats entering the shelter, 50% of cats present may excrete the virus one week later (Pedersen et al., 2004). This low prevalence is likely to reflect the intermittent nature of viral shedding during latency.

2.2 Pathogenesis

The virus enters via the nasal, oral or conjunctival routes. It causes a lytic infection of the nasal epithelium with spread to the conjunctival sac, pharynx, trachea, bronchi and bronchioles. Lesions are characterised by multifocal necrosis of epithelium, with neutrophilic infiltration and inflammation. A transient viraemia associated with blood mononuclear cells can be observed rarely after natural infection. This may be observed exceptionally in neonates or hypothermic individuals as viral replication is usually restricted to lower temperature tissues (Gaskell et al., 2007).

Viral excretion starts as soon as 24 hours after infection and lasts for 1 to 3 weeks. Acute disease resolves within 10 to 14 days. Some animals may develop chronic lesions in the upper respiratory tract and ocular tissues.

During infection, the virus spreads along the sensory nerves and reaches neurons, particularly in the trigeminal ganglia, which are the main sites of latency. Almost all cats experiencing primary infection become lifelong latent carriers. There are no direct diagnostic methods to identify latency, because the virus persists as genomic DNA in the nucleus of the latently infected neurons without virus replication. Reactivation of virus shedding can be induced experimentally by glucocorticoid treatment in approximately 70% of cats. Other stressors that may cause reactivation include lactation (40 %), and the cat moving into a new environment (18%) (Gaskell and Povey, 1977; Ellis, 1981; Gaskell and Povey, 1982; Pedersen et al., 2004).

Some adult cats may show acute lesions at the time of viral reactivation. Disease at reactivation is referred to as recrudescence.

Conjunctivitis may be associated with corneal ulcers, which may develop into chronic sequestra. Stromal keratitis is a secondary immune-mediated reaction due to the presence of virus in the epithelium or the stroma. In some cases damage to the nasal turbinates in acute disease is thought to predispose some cats to developing chronic rhinitis (Gaskell et al., 2007)

2.3 Immunity

2.3.1 Passive immunity acquired via colostrum

Kittens are protected against disease by maternally derived antibodies (MDA) during the first weeks of their lives but in general levels of MDA for FHV infection are low. It has been demonstrated that MDA may persist for 2-10 weeks (Johnson & Povey, 1985) although in a more recent study levels of MDA were shown to be low, with approximately 25% of kittens appearing negative for MDA as early as 6 weeks of age (Dawson et al., 2001).

2.3.2 Active immune response against FHV-1

Glycoproteins embedded in the membrane of the herpesviruses are important in the induction of immunity; following infection the detection of virus neutralizing antibodies (VNA) correlates with the recognition of FHV glycoproteins (Burgener and Maes, 1988). Furthermore, immunisation of rabbits with FHV-gD led to the production of high titres of VNAs, indicating a role of these proteins in the induction of VNA (Spatz et al., 1994).

Solid immunity is not induced after natural infection; in general the immune response protects against disease but not against infection and mild clinical signs have been observed following reinfection, only 150 days after primary infection (Gaskell and Povey, 1979). The titres of VNA induced by natural infection are often low and rise slowly. Indeed, VNA may still be absent 40 days post infection (Gaskell and Povey, 1979). VNA most likely contribute to the

protection against acute infection. Other antibody-mediated mechanisms e.g. antibody mediated cellular cytotoxicity (ADCC) and antibody-induced complement lysis have been demonstrated (Wardley, 1976). However, (as with other alpha-herpesviruses) cell-mediated cellular immunity plays an important role in protection, since the absence of detectable serum antibody levels in vaccinated cats does not necessarily indicate that cats are susceptible to disease (Lappin et al., 2002). On the other hand, seroconversion did correlate with protection against virulent FHV challenge (Lappin et al., 2002). It is important to take into consideration that presence of antibodies against any infectious agent may provide an indirect indication of cellular immune responses, since T-lymphocytes are required for maintenance of B-lymphocyte function.

Although a general correlation between presence of antibodies to FHV-1 and protection against clinical signs has been demonstrated for FHV-1 infection, there is currently no reliable test available that predicts the degree of protection in individual cats.

Since FHV is a pathogen of the respiratory tract, mucosal cellular and humoral responses are important. Several studies with intranasal vaccines have shown clinical benefits as early as 2-6 days after vaccination (Lappin et al., 2006; Weigler et al., 1997, Slater & York, 1976).

2.4 Clinical signs

Table 2.1. FHV-1 Disease forms, lesions and clinical signs [Note: concurrent infection with other agents is required to determine the aetiology of chronic rhinitis]

Disease type	Consequences	Main clinical manifestations
Classical acute disease (cytolytic disease)	Rhinitis, conjunctivitis, superficial and deep corneal ulcers, in particular dendritic ulcers	Sneezing, nasal discharge, conjunctival hyperaemia and serous discharge
Atypical acute disease	Skin disease	Nasal and facial ulcerated and crusting lesions
	Viraemia, pneumonia	Severe systemic signs, coughing, death (acute death in kittens, “fading kittens”)
Chronic disease (immune-mediated disease)	Stromal keratitis	Corneal oedema, vascularisation, blindness
	Chronic rhinosinusitis	Chronic sneezing and nasal discharge
FHV-1 related diseases with no definitive causal association	Corneal sequestra Eosinophilic keratitis Neurological disease? Uveitis	

Source: ABCD

FHV-1 infection typically causes acute upper respiratory and ocular disease, which can be particularly severe in young kittens. Viral replication causes the erosion and ulceration of mucosal surfaces, producing rhinitis, conjunctivitis and, occasionally, corneal ulcerative disease, mainly dendritic ulcers which are considered a pathognomonic clinical manifestation (Maggs, 2005).

Typical clinical signs are pyrexia, depression and anorexia, serous or serosanguineous ocular and/or nasal discharge, conjunctival hyperaemia, sneezing and, less frequently, salivation and coughing (Gaskell et al., 2006). Secondary bacterial infection is common in which case secretions tend to become purulent. In certain susceptible kittens, the disease may be more severe and FHV-1 infection has been associated with primary pneumonia and a viraemic state that can produce severe generalized signs and eventually death (Gaskell et al., 2006).

Less frequent clinical signs associated with FHV-1 are oral ulceration or dermatitis and skin ulcers (Hargis et al, 1999) and neurological signs (Gaskell et al., 2006). Abortion may occur as a rare secondary clinical sign, although, in contrast to other herpesviruses, it is not a direct consequence of viral replication.

After reactivation and recrudescent disease, some cats may show acute cytolytic disease as described above. Others may show chronic ocular immune-mediated disease in response to the presence of FHV-1 virus. Strong experimental evidence suggests that stromal keratitis, associated with corneal oedema, inflammatory cell infiltrates and vascularisation and eventually blindness, is an example of this disease mechanism (Nasisse et al., 1989; Maggs, 2005).

Corneal sequestra and eosinophilic keratitis in cats have been linked to the presence of FHV-1 in the cornea and/or blood in some of the affected cats. However, a definite causal association cannot be made since some affected cats are negative to FHV-1 (Cullen et al., 2005, Nasisse et al., 1998). FHV-1 DNA has been also detected in aqueous humor of a larger proportion of cats suffering from uveitis compared to healthy cats, suggesting that FHV-1 may cause uveal inflammation (Maggs et al., 1999).

Chronic rhinosinusitis, a frequent cause of chronic sneezing and nasal discharge in cats, has been associated with FHV-1 infection. Viral DNA can be detected in some affected cats, but is also found in controls without clinical signs (Henderson et al., 2004). Recent investigations show that the virus is not actively replicating in such cats, suggesting that chronic rhinosinusitis might be initiated by FHV-1 infection, but perpetuated by immune-mediated mechanisms producing inflammatory and remodelling phenomena, leading to permanent destruction of nasal turbinates and bone complicated by secondary bacterial infection (Johnson et al., 2005).

Very often, FHV-1 infection occurs combined with feline calicivirus and/or *Chlamydophila felis, Bordetella bronchiseptica*, *Mycoplasma spp*. and other micro-organisms, including *Staphylococcus spp.*, *Escherichia coli*, may lead to secondary infection of the respiratory tract, causing a multi-agent respiratory syndrome (Gaskell et al., 2006).

2.5 Diagnosis of feline herpesvirus infection

2.5.1 Methods detecting FHV-1

PCR is now the preferred method to detect FHV-1 in biological samples. Viral isolation lost interest but is a valid method still used in several laboratories. The sensitivity and the specificity of the tests, and especially PCR, are good but may differ depending on the laboratory because there is no harmonisation. These tests, and immunofluorescence are described in this chapter.

2.5.1.1 Detection of nucleic acid

PCR is currently used to detect FHV-1 DNA in conjunctival, corneal or oropharyngeal swabs, corneal scrapings, aqueous humor, corneal sequestra, blood or biopsies. Conventional PCR,

nested-PCR and real-time PCR are used routinely to detect FHV-1 DNA in diagnostic laboratories (Hara et al., 1996; Helps et al., 2003; Marsilio et al, 2004; Maggs et al., 1999a; Nasisse et al., 1997; Stiles et al., 1997a, 1997b; Sykes et al 2001, Vögtlin et al., 2002; Weigler et al., 1997). Most PCR primers are based on the highly conserved thymidine kinase gene.

Molecular diagnostic methods appear to be more sensitive than virus isolation or indirect immunofluorescence (Burgesser et al., 1999; Reubel et al., 1993; Stiles et al., 1997; Weigler et al., 1997).

Because the very low amounts of viral nucleic acids detectable by PCR may not be associated with disease, PCR positive results should be interpreted with caution. The sensitivity of PCR depends on the test (Maggs and Clarke, 2005) and it is advisable to use a system that includes a control that detects feline DNA to give an indication of how much material was on the swab, and to check for substances that might inhibit PCR. Due to its high sensitivity, PCR may also detect viral DNA in scrapings of the cornea and/or tonsils suggesting non-productive infection (Maggs et al., 1999b; Reubel et al., 1993; Stiles et al., 1997a). Consequently its predictive value for clinical infection may be poor, depending on the test sensitivity, the samples analysed (corneal scrapings and biopsies more frequently yield positive results than conjunctival ones) and the population tested (e.g. shelter cats are more likely to test positive than owned pet cats).

Additionally, many if not all PCR tests are able to detect FHV-1 DNA in modified-live vaccines (Maggs and Clarke, 2005) and it is not presently known if vaccinal strains may be detected in recently vaccinated animals and if so, for how long after vaccination.

A positive PCR result may represent low level shedding or viral latency and does not mean that the virus is responsible for clinical signs, although it indicates the possibility of recurring signs in the future. However, when quantitative real-time PCR is used (Vögtlin et al., 2002), the viral load present in the material tested may provide additional information on the etiological importance of the agent. When high loads are present in the nasal secretion or tears, this suggests active replication and therefore involvement of the virus in the clinical signs. If low copy numbers are detected in corneal scrapings, this would indicate a latent infection.

Molecular diagnosis may be more convenient for clinicians, because the use of fluorescein does not interfere with specificity of the test and samples can be mailed over several days at ambient temperature (Maggs 2005). It also allows the simultaneous detection in the same samples of other feline pathogens frequently implicated in respiratory and ocular diseases, especially *Chlamydophila felis* and, less reliably, feline calicivirus (Helps et al., 2003; Marsilio et al., 2004).

2.5.1.2 Virus isolation

If PCR is not available, virus isolation (VI) is an alternative method of diagnosing FHV-1 infection. Virus isolation is less sensitive than PCR but does indicate that replication-competent virus, not just DNA is present. VI also allows the simultaneous detection of feline calicivirus.

In cats undergoing primary FHV-1 infection, the virus can be easily detected by isolation from conjunctival, nasal or pharyngeal swabs or scrapings, or from post-mortem lung samples But during chronic infections when the aetiological origin of disease has to be confirmed, VI may be more difficult.

Asymptomatic carriers may also be detected by VI and both positive and negative predictive values of VI appear to be low in some studies (Gaskell and Povey, 1977; Maggs et al., 1999b). Samples must be collected before application of fluorescein or Rose Bengal stain

which can inhibit viral replication in cell culture (Brooks et al., 1994; Storey et al., 2002) and clinical specimens should be sent quickly to the laboratory and is ideally refrigerated during shipping. For logistic reasons and despite its good sensitivity in acute disease, VI is not routinely used for FHV-1 infection diagnosis.

2.5.1.3 Immunofluorescent assay (IFA)

FHV-1-specific proteins can be detected by immunofluorescent assay (IFA) on conjunctival or corneal smears or biopsy. As for VI, fluorescein instillation should be avoided before sampling. For IFA, this may give false positive results and interfere with the interpretation of the test. IFA has been reported to be less sensitive than VI or PCR, especially in chronic infections (Nasisse et al., 1993; Burgesser et al., 1999). Although no correlation between VI and IFA testing has been observed, combination of VI and IFA may predict the presence of virus better than either test alone (Nasisse et al., 1993; Maggs et al., 1999b). Because of lack of sensitivity and the interference with fluorescein, often used in ophthalmology practice, IFA is not the most suitable diagnostic test in chronic ocular diseases (Nasisse et al., 1993).

2.5.2 Detection of infection by serology

FHV antibodies can be detected by serum neutralization or ELISA in serum, aqueous humour and cerebrospinal fluid (Dawson et al., 1998; Maggs et al., 1999b). The seroprevalence is very high in cats due to natural infection and vaccination. Consequently, the presence of specific antibodies does not correlate with disease and active infection (Maggs et al., 1999b).

Moreover, antibody detection does not allow differentiation between infected and vaccinated animals, neutralizing antibodies are undetectable until 20 to 30 days after a primary infection and antibody titres may be low in animals with either acute or chronic disease. Consequently serology has a very limited value in the diagnosis of feline herpesvirus infection (Nasisse and Weigler, 1997; Maggs et al., 1999b; Maggs, 2005).

2.6 Feline herpesvirus disease management

2.6.1 Supportive Treatment

The restoration of fluids, electrolytes and the acid-base balance (e.g. replacement of losses of potassium and bicarbonate due to salivation and reduced food intake), preferably by intravenous administration, is required in cats with severe clinical signs. Food intake is extremely important. Many cats with FHV infection do not eat because of their loss of smell due to nasal congestion or because of ulcers in the oral cavity. Food may be blended to cause less pain when eating, should be highly palatable, and may be warmed up to increase the smell. Appetite stimulants (e.g. cyproheptadine) may be used. If the cat is not eating for more than three days, placement of a nasal or an oesophageal feeding tube is indicated.

Antibiotics should be given to treat all acute cases of feline upper respiratory tract disease to prevent secondary bacterial infections. Broad-spectrum antibiotics with good penetration in the respiratory tract should be given.

Cats severely affected by FHV-1 need intensive nursing care and appropriate supportive therapy is very important. If there is nasal discharge, this should be cleaned away several times a day with physiologic saline solution, and be treated afterwards with local ointment. Drugs with mucolytic effects (e.g. bromhexine) may be helpful. Eye drops or ointment can be

administered several times a day. Nebulisation with saline can be used to combat dehydration of the airways.

Vitamins are sometimes used although their value is unclear.

2.6.2 Antiviral therapy

Table 2.2. Antiviral drugs recommended for the treatment of acute FHV-1 ocular disease. The drugs are listed in decreasing order of preference.

Drug	**Type of drug**	**Route of administration**	**Efficacy *in vitro***	**Efficacy *in vivo***	**Controlled study *in vivo*?**	**Comments**
Trifluridine	Nucleoside analogue	Topical Use every hour for 1st day and every 4 hours thereafter (Maggs, 2001)	Excellent	n.d.	no	Topical treatment of choice in ocular FHV manifestations. Some cats averse to application topically. Toxic if given systemically. (Maggs, 2001)
Feline IFN-ω	Interferon	Systemic 1 MU/kg SC sid or eod Oral 50,000 – 100,000 Units daily Topical dilute 10MU vial in 19ml 0.9% NaCl and use as eye drops: 2 drops in each eye 5 times a day for 10 days (*Jongh, 2004*).	yes	n.d.	no	Safe and licensed for use in cats. No published controlled in vivo studies for use of this product in FHV infection at time of writing. Used along with l-lysine in chronic infections.
Human IFN-α	Interferon	SC high dose PO low dose 5-35 Units daily	yes yes	yes yes	yes yes	Less bioactive than feline interferon. 5-35 Units daily reduces clinical disease but not FHV shedding. Used along with l-lysine in chronic infections.
L-lysine	Amino-acid	Oral 250 mg bid or 400 mg sid	yes	yes	yes	Safe, reduces spontaneous ocular viral shedding rate in latently infected cats (Maggs, et al, 2000; Maggs, et al, 2001; Stiles et al. 2002; Maggs et al, 2003)
Idoxuridine	Nucleoside analogue	Topical use initially ever 2-4 hours (*Maggs, 2001*)	excellent	n.d.	no	Topical treatment for ocular FHV. Difficult to source, pharmacists can formulate a 0.1% ophthalmic solution. Toxic if given systemically.
Ganciclovir	Nucleoside analogue	Topical	excellent	n.d.	n.d.	Topical treatment for ocular FHV. Good in vitro activity against FHV (van der Meulen et al, 2006; Maggs et al, 2004)
Acyclovir	Nucleoside analogue	Topical and oral	Poor *(high doses may be needed to overcome*	some	yes	Minimal in vitro effect of all the anti-herpesvirals (van der Meulen et al, 2006, Williams et al., 2004), moderate in

			viral resistance)			vivo effect (Williams et al., 2005). Marked synergy in combination with human IFN–α (Weiss, 1989). Toxic systematically. (Maggs, 2001)

n.d. = not determined; eod = every other day; sid = once daily; bid = twice daily; tid = three times daily.

It should be noted that the above drugs may not be readily available or licensed for cats.

Other drugs have been proposed for the treatment of FHV-1 ocular infections, including bromovinyldeoyuridine, cidofovir, HPMA, pencyclovir, ribavirin, valacyclovir, vidarabine, foscarnet and lactoferrin. However, the efficacy of these drugs is not supported by appropriate data.

2.7 General recommendations on vaccine type and vaccination protocol

FHV-1 infection is common and may induce severe disease. ABCD therefore recommends that all cats should be vaccinated against FHV-1. FHV-1-vaccines provide protection by inducing both humoral immunity, associated with a serological response, and cellular immunity. Vaccination provides good protection against clinical disease, but in common with many localised respiratory tract infections, it does not provide 100% protection (approx. 90+% reduction in clinical scores has been achieved following experimental challenge soon after vaccination)(Gaskell et al., 2007). Less effective protection can be expected in some vaccinated individuals in particular circumstances following exposure to virus, e.g. extreme challenge, immunosuppression. There is no evidence that any variation in isolates of FHV-1 creates problems in protection provided by vaccination.

Vaccination protects from the development of clinical signs, but not necessarily from infection. However, there is some evidence that it can reduce subsequent excretion of virus. (Gaskell et al., 2007).

Currently, FHV-1 vaccines are usually combined with FCV, either in divalent vaccines (only in some countries) or, more commonly with other antigens. Both modified live and inactivated parenteral vaccines are available. Subunit FHV-vaccines and modified intranasal vaccines have been available previously or are available outside Europe, however they are not currently available in Europe.

Both inactivated and modified live FHV-1 vaccines have relative advantages and disadvantages. There is generally little reason to prefer any specific FHV vaccine for routine vaccination, particularly since these are all based on a single serotype. Modified live vaccines retain some pathogenic potential and may rarely induce disease if administered incorrectly, i.e. accidentally aerosolised or intake of vaccine virus spilt on the skin.

The value of serological tests in predicting protection is controversial. Methodological issues can complicate comparison of titres and some suggest that titres are not good predictors of protection. In other studies, cats without any evidence of seroconversion appear to show protection (Lappin et al., 2002; Mouzin 2004). Cats that have been vaccinated usually develop an anamnaestic response following exposure.

2.7.1 Primary vaccination course

ABCD recommends that all kittens should be vaccinated against FHV-1. Maternally derived immunity can interfere with the response to vaccination and the primary course of vaccination is usually started at around nine weeks of age, although some vaccines are licensed for use at an earlier age. Kittens should receive a second vaccination two to four weeks later, with the second given around twelve weeks of age. This protocol has been developed to ensure optimal protection. For longer intervals, no information is available and a new primary vaccination course should be considered.

In contrast to vaccines against certain other infectious agents, where single vaccination is acceptable for cats of unknown or uncertain vaccination status, in the case of FHV-1, they should also receive two vaccinations at an interval of two to four weeks, irrespective of the vaccination type.

2.7.2 Booster vaccinations

Vaccination against FHV-1 prevents disease, reduces virus shedding and recrudescence. Although the issue of recommended intervals between boosters is controversial, in view of currently available scientific evidence, ABCD recommends that boosters should be given at annual intervals to protect individual cats against FHV-1 field infections, with the exception of cats in low-risk situations (e.g. indoor-only cats without contact to other cats). In these cases, three-yearly intervals would be recommended. An informed decision should be made on the basis of a risk-benefit analysis, but annual boosters are particularly important to cats that may be exposed to high risk situations e.g. entry to boarding catteries, breeding cats.

Experimental studies and serological studies in field situations clearly indicate that immunity against FHV lasts longer than one year in most vaccinated cats (Lappin et al., 2002, Mouzin et al., 2004). However, there is a significant proportion of cats for which this is not true. Field studies have shown that almost 100% of cats either have serological titres against FCV and FPV, or show an anamnestic response following administration of a booster vaccine, but around 30% of the cat population appear to have no detectable titres against FHV and around 20% fail to show an anamnestic response following booster vaccinations (Lappin et al., 2002, Mouzin et al., 2004). Assessment of the duration of protection is complicated by failure of vaccination to provide 100% clinical protection shortly after vaccination has been administered, but in experimental vaccine efficacy studies, the efficacy of protection afforded by vaccination clearly decreases with time.

If booster vaccinations have lapsed, a single injection is considered adequate if the interval since the last vaccination is less than three years, but if it is more than three years, two vaccinations should be considered to ensure that optimal protection is provided.

Boosters using FHV vaccines produced by another manufacturer are acceptable.

Cats that have recovered from disease associated with FHV may not have lifelong protection against further episodes of disease. Furthermore, in most cases, definitive identification of the infectious agent involved in diagnostic testing will not usually have been undertaken and the cat may be susceptible to infection with other respiratory tract pathogens. Therefore, vaccination of recovered cats is generally recommended.

2.8 Feline herpesvirus disease control in specific situations

2.8.1 Shelters

FHV-1 can represent a particular problem in cat shelters. Management to prevent and limit the potential for transfer of infection is as important as vaccination in control. In shelters where the incoming cats are mixed, very high infection rates for FHV-1 are frequently encountered. New cats should be quarantined for the first two weeks and cats should be kept individually – unless known to originate from the same household. The design of the shelter and management used should be aimed at avoiding cross infection of cats. New cats should be vaccinated as soon as possible once they have been assessed as healthy and no contraindications to vaccination have been identified. If there is a particular high risk, i.e. past or recent infection with FHV-1 in the shelter, a modified live vaccine may be preferable as it may provide earlier protection. If acute respiratory infection occurs in a shelter, definitive diagnosis of the agent involved with differentiation of FHV-1 and FCV can be useful in deciding on the appropriate preventative measures that should be adopted.

2.8.2 Breeding catteries

FHV-1 can be a major problem in breeding catteries. Infection most often appears as an infection in young kittens prior to weaning. It typically occurs at around 4-8 weeks as maternally derived immunity (MDI) wanes. The source of infection is frequently the mother who is a carrier and has shown reactivation of latent infection following the stress of kittening and lactation.

Infection in such young kittens can be severe and frequently involves all the kittens in the litter. Mortality can be a consequence and some kittens that recover from acute disease are left with chronic complications, most notably chronic rhinitis. Vaccination of the queen will not prevent this problem since it will not prevent the queen from becoming a carrier. However, if the queen has a good antibody titre, this should ensure that the kittens benefit from good levels of MDI through the colostrum, providing protection for the first month or so of life.

Booster vaccinations of the queen may therefore be indicated to ensure transfer of strong levels of MDI; this should ideally take place prior to mating. Vaccination during pregnancy may be considered if this has been overlooked previously. However, vaccines are not licensed for use in pregnant cats and in this situation, an inactivated vaccine may be preferable. Breeding management plays a crucial role in control of FHV in breeding catteries.

Queens should kitten in isolation and the litter should not mix with other cats until they have been fully vaccinated to avoid the risk of exposure to potential carrier cats. Early vaccination should be considered for litters from queens that have had infected litters previously or for which there is concern of infection. The earliest age for which FHV-1 vaccines are licensed for use is 6 weeks but kittens may become susceptible to infection earlier than this as MDI wanes and vaccination from around 4 weeks of age may be considered. This is usually repeated every 2 weeks until the primary vaccination course is given in the normal way.

Early weaning into isolation from around 4 weeks of age is an alternative approach to protecting kittens from potential exposure of infection from their mother. There are no reliable tests that will identify which queens are carriers and predict which may potentially infect their own kittens.

2.8.3 Vaccination of immunocompromised cats

Vaccines may not efficiently stimulate immunity in animals with a substantially compromised immune function. Such situations include the presence of systemic diseases, viral-induced immunodeficiency, nutritional deficiencies, genetic immunodeficiencies, concurrent administration of immunosuppressive drugs and severe, prolonged stress. Such patients should be protected from potential exposure to infectious agents where possible but it may be necessary to consider vaccination to ensure protection. It is generally suggested that an inactivated vaccine is preferable in this situation, based on safety considerations, although there is no evidence to support this recommendation.

2.8.3.1 FIV positive cats

It is important that FIV-positive cats that are **clinically healthy** are protected against FHV-1. An effective approach is to confine cats indoors and limit potential for exposure. If this is not possible, vaccination should be considered. Concerns have been raised that vaccination may contribute to progression of disease, but this may be outweighed by the benefit of protection in a potentially immunocompromised cat. It is possible that other infections may contribute to FIV progression.

In FIV-positive cats with **a history of clinical problems** that are well controlled and in a stable medical condition, vaccination should be considered to ensure protection is maintained. In cats that are sick with FIV-related problems, vaccination is generally contra-indicated as in any systemically ill cat.

2.8.3.2 FeLV-positive cats

The same considerations apply to FeLV-positive cats as to FIV-positive cats. Vaccination is contra-indicated if there are clinical signs related to the FeLV infection but, if the cat appears to be clinically healthy, vaccination should be considered to maintain protection if prevention of potential exposure to FHV-1 cannot be ensured.

2.8.3.3 Chronic disease

Booster vaccination should be continued in cats with stable chronic medical conditions, such as hyperthyroidism and renal disease. Such cats are often elderly and the consequences of infection can be particularly severe.

2.8.3.4 Cats receiving corticosteroids or other immunosuppressive drugs

In cats receiving corticosteroids, vaccination should be considered carefully. Depending on dosage and duration of treatment, corticosteroids may cause suppression of immune responses. The effect of corticosteroids on vaccine efficacy in cats is not known. However, concurrent use of corticosteroids at the time of vaccination should be avoided if possible.

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