

# Common virus infections in cats, before and after being placed in shelters, with emphasis on feline enteric coronavirus

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Accepted 15 August 2003

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**Summary** The purpose of this study was to determine the origin and subsequent spread of feline calicivirus (FCV), feline herpesvirus (FHV), and feline enteric coronavirus (FECV) in cats relinquished to shelters. FCV was isolated from the oral faeces of 11% of healthy cats upon entry, and isolation rates were highest for kittens (33%). FHV shedding was very low (4%) at the time of entry and occurred mainly in juveniles. FECV shedding was also common among newly relinquished cats (33%), especially older kittens and juveniles (90%). The subsequent spread of all three viruses was rapid and efficient in the shelter environment. Fifteen percent of cats were shedding FCV, 52% FHV, and 60% FECV after 1 week. More detailed studies were done with FECV shedding, which could be accurately quantitated. The amounts of FECV shed by infected cats ranged from  $10^2$  to  $10^{16}$  particles/swab of feces. FECV shedding was several logs higher in young kittens with primary infection than adult cats with primary infections. The mean levels of FECV shedding among adults were the same for primary and chronic infections. Although shelters were not the primary source of these viruses for many relinquished cats, factors intrinsic to the shelter environment were critical in amplifying shedding and spread to susceptible individuals. Extrinsic factors were especially important for the spread of FHV and FECV. FHV shedding rates increased from 4% to 50% in 1 week's time. The speed and magnitude of the increase in FHV shedding suggested that there was reactivation of latent infections as well as acquisition of new infections. FECV shedding increased 10 to 1,000,000 fold in 1 week among cats that were already infected at entry, and more than one-half of initially negative cats were shedding FECV a week later. Feline calicivirus infection was the least likely to spread in the shelter. The infection rate only increased from 11 to 15% in 1 week.

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The biannual APPMA national pet owners' surveys show the proportion of cats obtained from shelters increasing from 12 to 20% in the United States between 1996 and 2000.<sup>1</sup> Unfortunately, the shel-

ter environment can be stressful, and husbandry, feeding practices, and housing procedures favor contagion. Infectious diseases are particularly troublesome in large multiple cat environments such as shelters (Pedersen, 1991). Acute infections are a major cause for triage and euthanasia of cats in traditional shelters and an economic hardship in no-kill shelters. Chronic sequelae of certain infections can also be a major problem for

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adopted cats. Acute feline calicivirus infection is usually not a serious problem in shelters in its own right (Pedersen, 1988a), but may enhance mortality to feline panleukopenia in dual infections (Bittle et al., 1961). Shelter environments have occasionally served as sources for highly virulent FCV mutants (Pedersen et al., 2000). A proportion of FCV recovered cats will continue to shed virus from their oral fauces and a fraction of these carriers will ultimately develop a chronic, largely untreatable, ulceroproliferative faucitis (Reubel et al., 1992). Similarly, acute FHV infection may require two or more weeks of supportive treatment and is therefore a manageable, albeit troublesome, disease (Pedersen, 1988b). A large proportion of acutely FHV infected cats will go on to become latent carriers (Hickman et al., 1994). Some of these FHV recovered cats will manifest permanent scarring and atrophy of their nasal passages, predisposing them to lifetime of epiphora or chronic bacterial infections of the nasal/sinus passages. Chronic herpetic ulcers of the cornea are another complication. Acute FECV infection is almost always asymptomatic, with only a low incidence of acute enteritis signs (Pedersen et al., 1981). However, 5% or more of FECV infected cats, especially if kittens, will develop fatal feline infectious peritonitis (FIP) (Pedersen, 1995). The FIP virus (FIPV) is a naturally and frequently occurring mutation of FECV (Poland et al., 1996; Vennema et al., 1998). Mutations are more likely to occur, and/or cause disease, in primary infections in younger kittens (Foley et al., 1997b), in kittens with unfavorable genetic predisposition (Foley and Pedersen, 1996), or in animals that are immunosuppressed (Poland et al., 1996).

The goal of this study was to gain a basic understanding of FCV, FHV and FECV infections in shelter environments. We were particularly interested in the proportion of cats that were already shedding these agents at the time they were relinquished and how long it took for non-infected animals to become infected. We were also interested in how the sheltering experience might influence the level of virus shedding. FECV lent itself best to quantification; therefore, it was used as a model of how factors such as primary vs. secondary exposure, age, time in shelter, and the overall sheltering experience might influence these common viral agents.

## Methods and materials

### Source of animals

Studies were done on cats presented to the Animal Care and Control facilities of Sacramento

and Solano Counties, Sacramento and Fairfield, California, USA, respectively. Cats retained for possible adoption were of various ages, in outwardly good health, and not obviously feral. Relinquished animals included free-roaming intact pet cats, tame or semi-tame unowned cats from the free-roaming population, kittens of tame, feral or semi-feral queens, or tamed progeny of feral or semi-feral queens. A very small number of adult purebred-appearing cats were present in the population (3 Persian and 1 Russian Blue). Accurate ages were obtained for only a portion of the cats. Eighty-six cats were classified as adults, eight as juvenile, and 12 as kittens, with 56 cats not having any age noted.

### Sample collection

Feline herpesvirus and FCV were isolated from sterile cotton tipped swabs. Swabs for FHV isolation were taken from the conjunctival sac, while swabs for FCV isolation were from the oral fauces. Fecal samples were also collected with cotton tipped swabs inserted into the rectum. The amount of feces on each swab ranged from 1–10 mg. Swabs for FHV and FCV isolation were placed into sterile tubes containing one ml of Hank's buffered saline solution (HBSS) containing 1×penicillin/streptomycin. Fecal swabs were placed in a guanidine-based lysis buffer (L6) (Cheung et al., 1994). Fecal and virus culture swabs were frozen at  $-70^{\circ}\text{C}$  until assayed.

### FHV and FCV isolation

Crandell feline kidney (CrFK) cells (Crandell and Despeaux, 1959) were grown in 24-well disposable tissue culture plates, each well containing 5 ml of medium (one part Leibowitz-15 and one part Eagle's minimum essential medium with 1×l-glutamine/1×penicillin/streptomycin and 10% fetal bovine serum). Cultures were maintained at  $38^{\circ}\text{C}$  in 5%  $\text{CO}_2$  in air and were three-quarters confluent at the time of infection. All but 1 ml of medium was removed from each well and 100  $\mu\text{l}$  of swab fluid was then added. Medium and swab fluid were removed after 12 hours and replaced with 5 ml of fresh medium. Cultures were then examined morning and evening for typical FHV or FCV cytopathic effect and discarded after 7 days if still negative. Only FHV grew from conjunctival swabs, so a conjunctival swabs were used to assay FHV infection. Swabs for FCV isolation were taken from the oral fauces.

**Table 1** FHV, FCV and FECV infection status from shelters in Northern California at the time of entry and 1 and 2 weeks later

Weeks after admission	Virus infection		
	FCV	FHV	FECV
0	17/162	7/162	53/162
1	10/60	31/60	36/60
2	1/5	2/5	2/5

## FECV quantitation

FECV from fecal swabs was detected by real time PCR (TaqMan<sup>®</sup>) according to published procedures (Gut et al., 1999). Actual tests were done by the TaqMan<sup>®</sup> Service, UC Davis. The copies of viral RNA per swab were calculated; RNA copy numbers were presumed to equal numbers of actual viral particles.

## Results

### FCV, FHV and FECV shedding at the time of entry into shelters

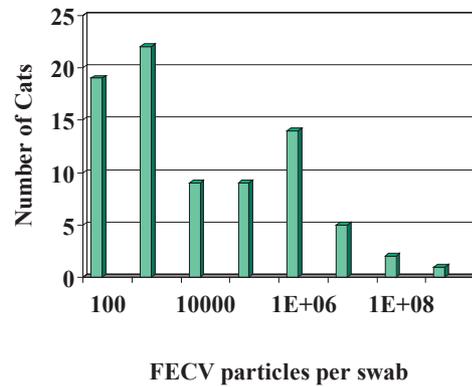
Eleven percent (17/162) of cats were shedding FCV upon admission into the shelter, compared to 4% (7/162) for FHV and 33% (53/162) for FECV (Table 1). FCV infection at the time of entry was highest in juveniles (2/5, 40%), intermediate in kittens (3/9, 33%), and lowest in adults (6/74, 7%). The pattern for FHV was similar, with the highest infection rate being in juveniles (2/5, 40%), followed by kittens less than 8 weeks of age (1/9, 11%) and then adults (2/74, 3%). FECV shedding was most common in older kittens and juveniles >8<56 weeks of age (9/10, 90%), low in adults over 56 weeks of age (39%; 29/74), and negative in kittens <8 weeks of age (0/5).

### FCV, FHV and FECV shedding after entering the shelter

Exposure to all three viruses was rapid and efficient once cats entered the shelter environment—15% (10/60) were shedding FCV after 1 week, 52% (31/60) FHV, and 60% (36/60) FECV (Table 1). Only five cats were still in the shelter at week 2—20% were shedding FCV and 40% either FECV or FHV.

### Levels of FECV shedding in uninfected and infected cats after being placed in shelters

FECV transmission was highly efficient in the shelter environment. Twenty-eight of 50 cats (56%) that

**Figure 1** The levels of FECV shedding (particles per fecal swab) in cats that were presented to shelters.

were negative for shedding at the time of entry were positive shedders after 1 week. The levels of FECV shedding during primary or chronic infections were measured in a group of adult cats. Twenty-three adult cats that were negative at the time of entry shed a mean of  $3.3 \times 10^{6.1}$  viral particles/swab 1 week after entry (primary infection), while 49 adult cats that were shedding at the time of entry (chronic infection) shed a mean of  $3.5 \times 10^{6.7}$  viral particles/swab.

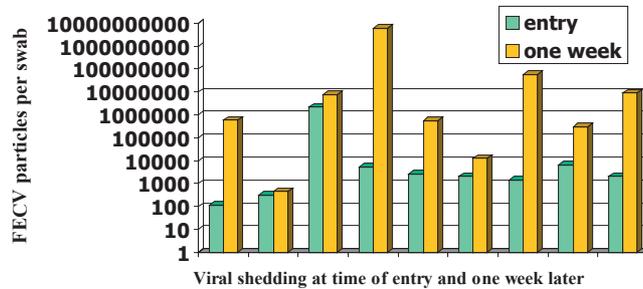
The level of fecal FECV shedding among cats that were infected at the time of entry varied greatly from one individual to another (Fig. 1). Among 79 cats of all ages that were shedding FECV at the time of admission, 41 shed from 100–1000 viral particles/fecal swab, 16 shed from 10,000 to 100,000, 19 shed 1,000,000 to 10,000,000, and 3 shed from 100,000,000 to over 1,000,000,000 particles/swab.

The mean level of primary FECV shedding from six 8–16-week-old kittens was 10,000 times higher than for 23 older cats with primary infections ( $5.9 \times 10^{10}$  particles/swab vs  $3.3 \times 10^{6.1}$  particles/swab). The act of sheltering for 1 week enhanced virus replication from 10- to 1,000,000-fold in 9/9 adult cats that were infected at the time of entry and retested 1 week later (Fig. 2).

## Discussion

### FCV infection in shelter cats

The 11% FCV shedding rate of cats coming into shelters was virtually the same as the 12.3% shedding rate reported for household pet cats of all ages in England (Couts et al., 1994). The highest FCV shedding rate in the present study was among juveniles (40%), followed by kittens (33%), and then adults (8%). This age pattern was also typical of



**Figure 2** The levels of FECV fecal shedding (particles per fecal swab) in nine adult cats that were infected at the time of relinquishment to shelters and 1 week later.

what has been previously reported for cats from high density environments; 37.3% of English show cats less than 12 months of age were shedding FCV compared to 17% of older cats (Couts et al., 1994). The 15% FCV shedding rate among cats kept in shelters for a week or more was also similar to the 24–25% shedding rates described for high-risk cats in England (Couts et al., 1994; Wardley et al., 1974). FCV is an infection mainly of young kittens (Pedersen, 1988a). The fact that the FCV shedding rate only increased from 11% to 15% after 1 week in the shelter indicates that most cats in this region had been exposed prior to entry into a shelter.

### FHV infection in shelter cats

The low incoming shedding rate for FHV was anticipated. Only 0.6%–1.75% of healthy cats in England were shedding FHV (Couts et al., 1994; Wardley et al., 1974). Most acute FHV disease is seen in the post-weaning period (Pedersen, 1988b). Therefore, it was not surprising to observe the highest FHV shedding rate in juveniles and the lowest in young adults and kittens. The rapid increase in virus shedding, from 4 to 52% after 1 week in the shelter, was much higher than anticipated. FHV is very efficiently spread from cat-to-cat and every cat that has been previously infected is a potential latent carrier (Hickman et al., 1994). Stresses as simple as moving a cat into a new environment can convert latent to active infections in a few days (Gaskell and Povey, 1977; Hickman et al., 1994). Therefore, it was not possible to determine how much of the increased rate of FHV shedding during the first week in the shelter was due to virus exposure and how much to activation of pre-existing latent infections. The marked increase in virus shedding after only 1 week clearly demonstrates why FHV is one of the most important causes of disease in shelter environments.

### FECV infection in shelters

FECV infection was much higher (33%) among cats coming into shelters than expected. Most of the cats were from outdoor type environments, which should reduce FECV spread. Outdoor cats tend to bury their feces in distinct territories, thus limiting fecal–oral contact. However, the cats that were being relinquished to the shelters and included in this study were not feral in behavior. They also tended to come from urban areas, where the density of outdoor cats is high. These factors often lead to the common use of gardens, sand boxes, etc. FECV is relatively stable, lasting up to 7 days in the environment. FECV is somewhat unique because immunity is not long-lasting and re-infections are common (reviewed by Pedersen, 1995). About one in ten infected cats will persistently shed the virus, eight in ten will undergo repeated re-infections, and one in ten will develop solid immunity (Foley et al., 1997a). Two cats that appeared to be immune to FECV were observed in the present study. These animals remained non-infected even after 2 weeks of stress and exposure.

### FCV, FHV and FECV disease in shelters

A significant proportion of cats in this study were shedding one or more of these viruses at the time of entry. Therefore, shelters are not the ultimate source of these particular viruses, but the shelter environment appears to amplify and efficiently spread these agents and enhance clinical disease. The impact of infection by FCV, FHV and FECV can have immediate and long-term consequences to a shelter, depending on the relative importance of acute and chronic disease manifestations. Acute disease is the most obvious problem for shelters, while chronic disease is largely a problem for cats that have been adopted into homes. Acute FCV disease may not be as great of a problem in shelters

in this area as believed, because most cats have been exposed to FCV prior to relinquishment and the virus can persist in the face of routine immunization (Pedersen and Hawkins, 1995). Furthermore, acute FCV disease tends to be mild or inapparent in nature, even in similar high cat density environments (Johnson, 1984). However, under certain conditions, FCV infection can greatly increase the mortality to feline panleukopenia (FPV) virus infection (Bittle et al., 1961), and we have also observed that many shelter cats dying of panleukopenia are coinfecting with FCV. FCV can infrequently mutate or recombine with other strains in the shelter milieu to produce a highly virulent virus associated with outbreaks of fatal hemorrhagic fever (Pedersen et al., 2000). The most important clinical manifestation of FCV infection is probably chronic ulceroproliferative faucitis, a progressive disease that occurs in some FCV carriers (Reubel et al., 1992). This disease is a major cause of euthanasia.

Upper respiratory infections caused by FHV are serious problems in shelters (Pedersen, 1988b). Some of the reasons for this are demonstrated by findings of the present study. Although only 4% of cats entering the shelter are shedders, over one-half of them will shed FHV within the next week. The shelter environment is ideal for reactivation of latent infections, spread of the virus from cat-to-cat, and for enhancing the severity of disease signs through stress and increased exposure. Acute FHV infection is probably the single leading cause for shelter cats to be destroyed or to receive veterinary care. As bad as acute FHV infection is in shelters, there are also serious chronic sequelae to the infection that must be borne by recovered cats. Long term effects of acute FHV disease include scarring of the nasolacrimal and chronic epiphora, persistence of replicating virus in the nerves of the cornea and indolent ulcers, and chronic scarring and atrophy of the nasal mucosa and turbinates resulting in chronic rhinosinusitis (Pedersen, 1988b).

The acute stage of FECV infection is of little consequence. Except for the unusual cat with an acute gastroenteritis, the infection is largely asymptomatic (Pedersen, 1995). However, during bouts of virus replication in the gut, macrophage-tropic mutants are frequently generated (Poland et al., 1996; Vennema et al., 1998). Some of these mutant viruses leave the gut and are carried systemically by their macrophage hosts. Such mutant viruses cause feline infectious peritonitis (FIP), a disease that ultimately kills upwards of 5% of shelter kittens (Pedersen, 1995). Anything that in-

creases virus replication in the gut will increase the likelihood of this mutation to occur (Poland et al., 1996). Young kittens, which are at greatest risk, produce the highest amounts of virus. Most kittens less than 8 weeks of age coming into shelters have not been exposed to FECV, but virtually all are shedding after 1 week. The amount of virus replication is also enhanced ten to a million fold by the mere fact of being placed in a shelter, an environmental influence that is probably similar to that which increases FHV shedding. It is not surprising; therefore, that FIP is one of the most important diseases of cats coming from shelter environments.

## Conclusions

Feline calicivirus, FHV and FECV infections are brought into shelters with relinquished animals, which are shedding these viruses to varying degrees at the time of entry. FCV is brought in mainly by young kittens, whereas FECV and FHV are more apt to be introduced by older kittens and juveniles. Although shelters are not the primary source of these viruses, the shelter environment serves to spread the viruses between infected and non-infected individuals and to amplify shedding, in particular for FHV and FECV. The proportion of cats shedding FHV can go up over ten-fold in 1 week, while the incidence of FECV shedders will almost double. Factors intrinsic to the sheltering experience appear to increase FECV shedding from 10- to 1,000,000-fold after 1 week. Similar factors probably account for the dramatic increase in FHV shedding. Feline calicivirus infection is least affected by the shelter experience, probably because most cats have already been exposed prior to relinquishment.

## Acknowledgements

This study was supported by funds from the Center for Companion Animal Health and the Maddie's shelter Medicine program, School of Veterinary Medicine, University of California, Davis, CA, 95616, USA.

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