

# Feline Calicivirus & Virulent Systemic Feline Calicivirus (VS-FCV)

Feline calicivirus is extremely common in shelters, causing a range of effects from subclinical or mild disease to Virulent Systemic Feline Calicivirus (VSFCV). Fortunately, FCV can generally be managed successfully in both individual cats and populations through vaccines, disinfection, and isolation and supportive care for affected cats. True outbreaks of VSFCV are rare - if you suspect you have one on your hands, be sure to read the information sheet in its entirety, and contact your local shelter medicine program, veterinary school or other infectious disease expert before taking drastic steps such as depopulation.

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## Recognition, management and prevention options for feline calicivirus, virulent and otherwise

With the release of the first vaccine billed as a “virulent calicivirus vaccine”, there’s been a lot of buzz lately about feline calicivirus (FCV).

While I'm happy to see increased awareness of this problematic virus, in some cases misunderstandings about what a virulent systemic calicivirus really is have led to unnecessary consternation or even depopulation when other management strategies may have sufficed. Feline calicivirus is a highly variable virus with many different manifestations, including highly virulent, fairly benign, and all points in between. Differentiation between virulent and less-virulent FCV (referred to here as "field strains") is not always straightforward.

## **To start with, here are a few key facts about feline calicivirus in general:**

**FCV infection is common even in healthy-appearing cats:** up to 25% of asymptomatic cats from multiple cat environments such as shelters and catteries, and up to 8% of pet cats, will be shedding FCV from the oral cavity at any given time. As many as half of all upper respiratory infections are caused by FCV. During acute disease from any strain - virulent or otherwise - FCV can be recovered from the oral cavity, conjunctiva, blood and/or feces. *We cannot eliminate FCV from multiple cat environments, nor exclude it from veterinary clinics.*

**FCV infection is often chronic:** as many as 50% of cats will still be shedding FCV for 75 days after recovery from acute disease. Some cats will shed for years or even for life. Chronically shedding cats may transmit infection, but risk is substantially decreased once all clinical signs have resolved, simply because there is less drool, snot, etc. to carry virus.

**FCV causes extremely variable signs:** as noted above, some strains cause no signs at all. Others manifestations of FCV include: mild upper respiratory infection without oral ulceration (indistinguishable from URI due to herpesviral infection); limping with or without URI signs; mild to very severe oral ulceration/faucitis/ulceration of the esophagus with or without URI signs; systemic signs such as fever, anorexia and lethargy in combination with one or more of the preceding signs; pneumonia; and virulent systemic calicivirus. *Not all strains of FCV that cause severe disease are truly "virulent systemic FCV".* See diagnostic section for further information.

**FCV does not always act alone:** Even relatively mild field strain FCV in combination with other pathogens – most notably Bordetella bronchiseptica and feline panleukopenia – can cause severe disease, including pneumonia and death. Not all cases of oral ulceration/URI followed by severe disease and death are VS-FCV! In fact, *it is much more common to diagnose panleukopenia with FCV or another respiratory pathogen than it is to find VS-FCV in outbreaks of URI with high mortality*

*in incompletely vaccinated cats.* An outbreak of FCV in combination with another pathogen is less of a risk to naïve cats than an outbreak in which FCV acting alone causes severe disease and death. This is because two targets are available for control; panleukopenia is much easier to control than calicivirus because the vaccine is highly effective and there is no carrier state.

**There is no genetic marker that can distinguish virulent systemic strains from any other strain.** So far, no relationship has been discovered between the genetic sequence of a particular strain of calicivirus and the level of virulence. Virulent systemic strains are not particularly closely related to one another, although within each outbreak isolates from individual cats have been similar. Specialized laboratories can only distinguish between strains that are closely related to one another or to the vaccine. Therefore, within a given outbreak it is possible to identify which cats have been infected with that particular strain, but there is no way to say what the virulence may be of any particular strain from an individual cat based on genetic sequence.

**“New” strains of FCV are the rule rather than the exception:**the virus constantly mutates within individual cats and in endemically infected populations – which is to say, virtually all densely housed feline populations. Some of these strains are more virulent, some are less, many cause no signs of illness at all. In rare cases, one of these mutants turns out to be a “virulent systemic feline calicivirus” (VS-FCV). The risk of mutations is increased when cats are over-crowded; when upper respiratory disease in general is rampant; and when kittens make up a high percentage of the population.

**Individual FCV strains tend to produce similar symptoms within exposed cats in an outbreak:** Unlike feline herpesvirus, in which the symptoms in a particular cat have more to do with the cat’s immune response than the characteristics of the virus, a given strain of FCV is likely to cause similar signs within an exposed population. So some strains consistently cause limping, others are more likely to cause mild oral ulceration, others tend to cause severe disease etc.

**To assess the risk posed by a strain of FCV, look at the worst manifestation within a population of exposed cats, not the symptoms of a particular individual.** If some exposed cats have developed severe disease in a particular outbreak, any exposed cat, no matter how mild its symptoms, may transmit severe disease. On the other hand, if an outbreak has been limited to moderate URI and oral ulceration, it is unlikely (though not impossible) that further exposed cats will develop severe disease. More on [risk assessment](#) below.

**Variant strains of FCV do not tend to remain stable within infected individuals or populations:** As noted, infected cats can chronically shed virus, and infection can be transmitted by these carrier cats. Even in outbreaks of severe, vaccine resistant VS-FCV, some cats have survived and continued to shed virus for some time. Recovered cats have been adopted out, spayed at veterinary hospitals, and sent home to naïve cats, *but in no case has a recurrence of VS-FCV been traced to any of these presumed carrier cats more than a month after recovery.* Feline calicivirus undergoes constant mutation in persistently infected cats, and it may be that strains tend to lose the mutation that conferred virulence over time. See [risk assessment section](#) for further information.

**Outbreaks of severe FCV tend to be a focal population problem, not a community problem.** Focal outbreaks of VS-FCV have been identified in many areas of the country. Virtually all have arisen and spread within a particular population of cats (e.g. within a shelter, cattery, rescue home or vet clinic). While there are a few possible reports of an indoor/outdoor cat here and there spontaneously contracting a particularly virulent form of calicivirus, there is no evidence of progression from community to community, nor even any case where it has spread widely within a given community (the greatest spread occurred in one outbreak when cats were transferred directly between a rescue group and several clinics and homes – still there was no spread within the community). This is unlike, say, canine influenza, which does seem stable enough that it can become established within communities and is gradually marching from one community to another. *Pet cats within a community are at no greater or less risk if there is a particularly virulent outbreak identified within a given population (e.g. a shelter) in that community or not.*

**Not all virulent systemic feline caliciviruses behave the same way.** Although the most dramatic outbreaks have been associated with highly transmissible, vaccine resistant strains of VS-FCV, this may be an artifact of recognition rather than any particular characteristic associated with the virulent virus itself: of course we are more likely to notice situations in which many cats were affected. In particular, virulence and vaccine resistance may not be linked. Given how widespread vaccination against calicivirus is, it is logical to think that we would not necessarily recognize cases caused by strains against which vaccination is protective. In fact, there have been focal “case clusters” limited to a single household of unvaccinated cats. Although it was verified that a virulent systemic calicivirus was at fault, these cats were hospitalized with limited infectious disease precautions prior to diagnosis and no transmission to other patients at the clinic was observed. The environmental stability and transmissibility of FCV is also variable. *Any case of suspect FCV should be handled with careful infectious disease precautions, but a single case*

*does not mean an outbreak is inevitable.* The best evidence that a given strain of FCV is vaccine-resistant is observation of disease in more than one well-vaccinated cat.

## So, what does this all mean?

The bad news is this means that we need to be concerned about calicivirus at all times, especially when working with cats from a densely housed multiple cat population. We can never know when a more virulent strain will emerge. It also means we cannot diagnose virulent systemic calicivirus based on isolation of the virus (by culture or PCR) from any single cat. We must use a combination of viral isolation, history and clinical signs of all cats involved in a possible outbreak. There is some good news as well, however: VS-FCV is not marching across the United States in the way that other emerging infections such as parvovirus or canine influenza have done. While it remains a real – though rare - risk, is not likely that hypervirulent calicivirus will ever become truly endemic; the virus simply appears to be too unstable for that. However, any shelter, veterinarian or pet owner that has dealt with miserable, drooling, febrile cats with severe oral ulceration knows that even the less virulent forms can be a real problem, and measures to prevent or manage these “field strains” of FCV can have substantial benefits for cat health. In the interest of providing some more tools to manage calicivirus in general and virulent systemic calicivirus in particular, here’s a little more background on FCV.

## How is FCV spread?

Feline calicivirus is shed primarily in saliva and oculonasal discharge, but can be found in all body secretions during acute disease. Although FCV can be spread by droplets sneezed out to a distance of ~ 4 feet, **true aerosol transmission of FCV is unlikely.** In one study, naïve cats were placed in a small room in an open wire cage at least four feet away from sick cats, with strict handling order such that uninfected cats were always handled before sick cats. No transmission of FCV occurred. As soon as this order was reversed, however, the naïve cats quickly became infected. It was speculated that the lack of aerosol transmission is because cats lack the tidal volume to generate an effective aerosol, a conjecture which is supported by the fact that feline herpesvirus infection also was not transmitted to cats housed in a common air space at least four feet away from infected cats.

In addition to direct contact, fomite transmission is the primary means of spread for FCV. The importance of this and the ease with which it occurs is hard to over-state. In outbreaks of VS-FCV, technicians or visiting

owners have carried virus home, presumably via contaminated clothing or shoes. In some cases entire households of cats died from infections transmitted in this way. The study described above demonstrated that less virulent strains are also easily transmitted in this way. As well as potentially being found in all bodily excretions, virus is very likely present on hair, due to both self grooming and consequent saliva on hair, and virus clustering at the base of hair follicles (at least in some cases of VS-FCV). Strict attention must be paid to fomite control whenever a calicivirus infection is suspected; however, hospitals and shelters have successfully contained the infection without separate air supply for isolation rooms.

## What can you do to clean up/disinfect calicivirus?

Like the notorious parvoviruses, feline calicivirus are un-enveloped and therefore resistant to many commonly used disinfectants. Although not quite as durable as parvo, they can cheerfully persist for up to 28 days at room temperature (even longer at very cold temperatures). Mechanical removal or chemical inactivation is therefore required. Disinfectants that *do not* reliably inactivate calicivirus include chlorhexidine and quaternary ammonium compounds, including newer formulations. Phenol-based Lysol® solution, although effective against FCV, is not recommended for use around cats (it is both caustic and toxic in this species). Alcohols such as those used in hand sanitizers are also not absolutely reliable; of those available, 1-propanol and ethanol at 70% concentration appear to be most effective. Thorough hand washing or use of gloves is recommended when handling suspect or high risk cats.

Accelerated hydrogen peroxide (Rescue™), potassium peroxymonosulfate (Trifectant®, Virkon-S®), and sodium hypochlorite and other products in that family (e.g. 5% bleach diluted at 1/2 cup per gallon) have been proven effective against FCV. One of these disinfectants should be used routinely to clean surfaces and instruments after any cat has had contact, particularly a cat from a high risk background (shelter, rescue group, cattery, pet store) or showing *any* signs of URI or FCV infection. Kittens are particularly likely to shed calicivirus, and may shed virulent virus without showing overt signs. Because of the ease of fomite transmission, strict isolation precautions including gowns, gloves and shoe covers are required when handling suspect cases. In rare cases, mildly affected cats have been documented to transmit fatal disease; therefore these precautions should apply to *any* suspect case of calicivirus, especially in an outbreak in which some cats have been severely affected. Accelerated hydrogen peroxide has good activity in the face of organic matter, and can even be used (with care) to

clean carpeted areas. This makes it a good choice for decontaminating outdoor areas, homes, or other difficult to clean areas. After a severe outbreak in a home, waiting one month before obtaining a new cat may be a prudent precaution to let any remaining virus die off naturally.

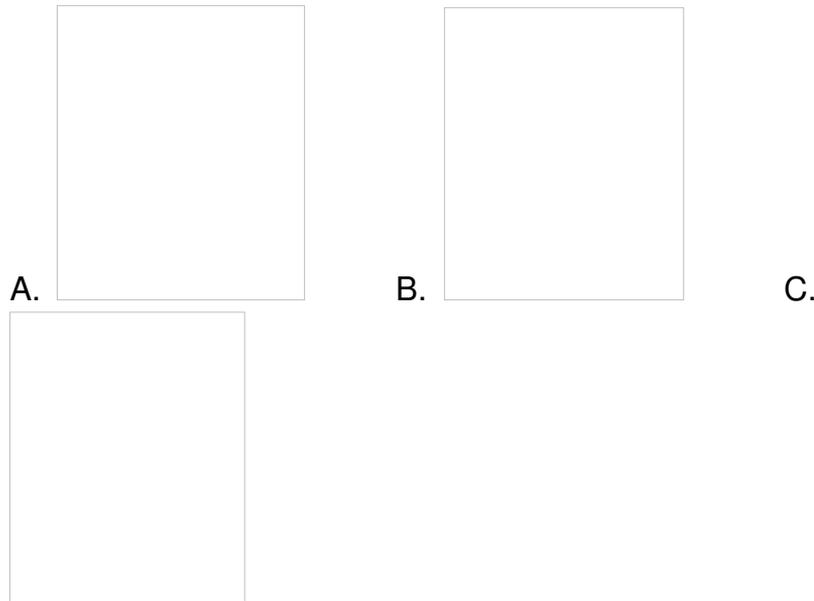
Because of the frequent carrier state, simply decontaminating the environment may not be effective if exposed cats remain present. Whether or not they are showing clinical signs, these cats may re-contaminate the environment or directly spread disease to naïve cats. Therefore, risk assessment and appropriate isolation/quarantine/removal of possible carrier cats in addition to thorough disinfection may be necessary to halt a severe outbreak. In one case, a veterinary clinic cleaned and disinfected very thoroughly following an outbreak of VS-FCV and sent all patients home or off site. The only remaining cat was the clinic cat who had appeared healthy throughout. When the clinic re-opened, new patients developed VS-FCV. A careful examination of the clinic cat detected minor oral ulcerations, and he was culture positive for the strain of VS-FCV implicated in that particular outbreak. Removal of that cat (to a single cat home) and repeated cleaning/disinfection led to complete resolution of the outbreak. In another case, endemic FCV pneumonia persisted in a cattery until all carriers were identified by viral culture and removed. See risk assessment section for discussion of when removal of all exposed cats may be necessary.

## **How is FCV diagnosed? How is VS-FCV distinguished from other strains of FCV?**

*The most important thing to realize is that neither field strain nor VS-FCV can be diagnosed based on clinical signs alone.* Just as it is not possible to reliably rule parvo in or out based on the smell of diarrhea, it is not possible to look at an individual cat and know for sure whether FCV is the cause of its problems. FCV can manifest in many different forms, every one of which can also be caused by other pathogens (see table one for a listing of clinical signs potentially associated with FCV). Even oral ulceration, which is often thought of as characteristic of FCV infection, is not present in every case, nor is every case of oral ulceration caused by FCV. For example, our old friend feline herpesvirus can cause severe oral ulcers, although this is seen less commonly than with FCV. Incorrectly diluted quaternary ammonium and phenol disinfectants can also cause severe oral ulceration, respiratory signs, pneumonia and death – this can look an awful lot like a calicivirus outbreak, as multiple cats are often affected.

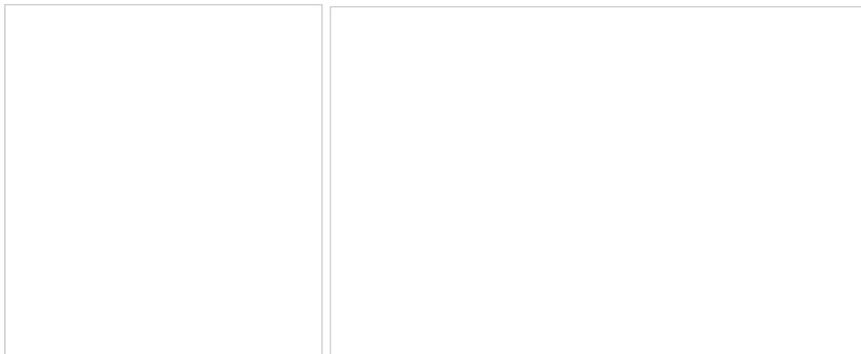
**Example 1:** The lesions on tongue A were caused by feline calicivirus, on

tongue B by quaternary ammonium toxicity, and on tongue C by feline herpesvirus. The moral of the story? Oral ulcers do not equal FCV!



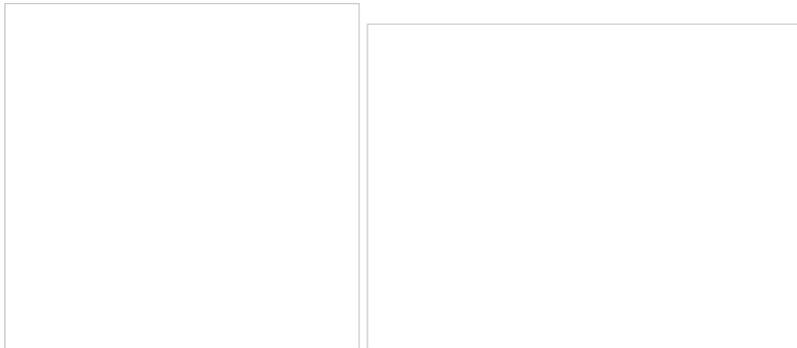
Virulent systemic calicivirus often starts with similar signs to other field strain caliciviral infection, such as oral ulceration, fever, and limping. However, by definition VS-FCV is characterized by progression in some cats to more severe disease, including vasculitis leading to marked edema and/or extensive hair loss, oozing and ulceration of the skin. See table two for characteristics suggestive of VS-FCV versus field strain FCV infection.

**Example 2:** Marked facial edema and extensive hair loss, oozing and ulceration of the skin in two cats affected by VS-FCV. Less virulent strains can cause slight crusting on the muzzle and feet.



**Example 3:** Hair loss, crusting and edema of the face and feet in a cat that did not have VS-FCV; this cat had vasculitis secondary to sepsis. This cat also had oral ulceration due to vasculitis; however, this symptom appeared late in the course of disease rather than prior to development of

the other signs of vasculitis. Remember to rule out look-alike causes of vasculitis!



Diagnosis of calicivirus is further complicated by the fact that calicivirus can be isolated from the oral cavity of as many as 1 in 4 healthy cats, so simply detecting the virus in saliva does not provide a definitive diagnosis – its presence could be completely coincidental. Finding calicivirus in other samples such as serum or tissue is more suggestive that an acute infection is present, but does not rule out the possibility that a co-pathogen such as *Bordetella bronchiseptica* or panleukopenia is responsible for severe manifestations of disease. So while there is some value in looking for the virus in various samples as described below, the results must be taken in context with the history and clinical signs of affected cats. See table 3 for elements of the history that would increase suspicion of caliciviral infection leading to disease.

### **Table 1. Clinical conditions sometimes associated with FCV infection**

- Fever
- Ulceration of the oral cavity (including tongue and palate) and nasal planum
- Rhinitis
- Conjunctivitis
- Acute and chronic gingivostomatitis
- Acute arthritis/"limping kitten syndrome"
- Pneumonia
- Systemic vasculitis with multi-organ involvement

### **Table 2. Increased suspicion of VS-FCV versus more benign field strain if:**

- More than one cat with exposure history and signs consistent with

general caliciviral infection (fever, oral ulceration, URI, limping) which preceded the appearance of the signs listed below in at least one case.

- Signs of vasculitis not explained by another cause, including facial or limb edema or extensive crusts/scabs/alopecia or ulceration on body, feet or haired skin of face/pinnae
- Individualized hepatocellular necrosis on biopsy or necropsy
- Death in some affected cats
- Adults affected more severely than kittens

### **Table 3: Elements of history that would increase suspicion for FCV infection**

- Recent (within 1-2 weeks) exposure to a multi-cat environment such as an animal shelter, boarding clinic, or veterinary hospital; or recent addition of a new cat to the household.
- Clinical signs of typical FCV such as oral ulceration and limping preceded more severe systemic signs.
- More than one cat affected (suspicion is decreased if only one cat is affected if many were closely exposed)
- Fully vaccinated, otherwise healthy adult cats affected
- Evidence of fomite transmission in cats not directly exposed to the suspect case/environment, e.g. cats belonging to clinic/shelter staff affected, housemates of cats visiting a vet clinic exposed (this rules out disinfectant toxicity)

### **Detecting calicivirus and deciding what to make of the results**

Because results of viral isolation/PCR are difficult to interpret, it is often more efficient to first rule out other possible causes of the observed signs before pursuing specific diagnostics for FCV. It is also worth asking whether the diagnosis will make a difference in management of a given case. In an outbreak, clearly there is value in establishing a cause so that appropriate measures can be taken to prevent further spread; however, in an individual cat it may add to the expense without changing the treatment plan. Assuming that you are going to pursue additional diagnostics, read on...

### **Obtaining samples**

Calicivirus can be detected by either viral culture or RT-PCR (reverse transcriptase PCR). Both methods are equally sensitive; however, PCR is

more readily obtained in most areas through commercially available respiratory panels. Calicivirus is most commonly isolated from oropharyngeal swabs, particularly during chronic infection. Sampling conjunctiva in addition to the oropharynx will increase the likelihood of detecting FCV. During acute disease, FCV may also be isolated from serum, feces, urine, and affected organs. In general, samples should be taken from the area or organ showing most evidence of disease; therefore, nasal swabs may be preferable when rhinitis is the primary sign, oropharyngeal swabs when gingivostomatitis is present, and so on. Samples from multiple sites can be pooled to increase the likelihood of detecting the virus.

Many commercial laboratories offer viral culture and/or RT-PCR for FCV. Careful sample handling is important to prevent cross contamination and preserve virus during transport. Sterile swabs should be used to vigorously swab the pharynx, including the fauces, and a separate swab used for the conjunctiva if desired. These swabs can then be pooled and transported as per instructions from the laboratory to which samples will be submitted. If necessary, viral transport media can be made by adding 10 mgs of injectable Amoxicillin and 6 mgs of Gentamicin sulfate to 500 mls of sterile saline. (Injectable drugs with similar spectrum may be substituted; for example Ampicillin for Amoxicillin and Amikacin for Gentamicin. The recommended dose per kilogram should be added to 500 mls of sterile saline.)

## **Interpreting results**

Both negative and positive diagnostic test results for FCV must be interpreted with caution. This is particularly true when samples are available from only a single cat – a single oropharyngeal sample can help rule out calicivirus if negative, but can not rule it in. This is because up to 25% of clinically normal cats will test positive for FCV infection via oropharyngeal swab, especially cats from a multiple cat household or those recently adopted from a shelter, pet store, or breeder. Recent vaccination with a modified live vaccine can also cause positive results. Therefore, simply isolating the virus does not confirm that FCV is the cause of the cat's clinical signs. Further complicating diagnosis, highly virulent isolates are genetically distinct from one another, and no currently available test can differentiate relatively benign field strain calicivirus from more virulent forms. A positive result on tissue or serum (as opposed to oropharyngeal swabs) suggests that caliciviral infection is causing or contributing to clinical disease as FCV is likely present in these samples only during acute infection. However, isolation from serum or tissue does not particularly indicate virulent systemic disease – even field strain FCV can cause viremia.

A negative result must also be interpreted with care. Sensitivity is variable, and depends on the location sampled, the viral strain, and the time with respect to disease onset. Negative results are common on blood or serum even during acute disease. Only 2/7 acutely obtained serum samples were positive from known cases of VS-FCV in one outbreak. A negative oropharyngeal swab result obtained from an acutely ill cat is suggestive that calicivirus is not involved, but does not rule it out absolutely. Although sensitivity of close to 90% was observed on acutely collected oropharyngeal swabs in one outbreak of VS-FCV, it dropped to approximately 30% or less when samples were collected greater than a week after onset of signs. Other studies have shown 68%-100% sensitivity on oropharyngeal samples obtained within the first week post-infection, depending on the strain of infecting virus. Recovering or chronically infected cats may shed constantly or intermittently in a pattern that is unaffected by stress (unlike feline herpesvirus, which is stress associated). In order to detect low-level or recovering carriers, 2-3 oropharyngeal swabs obtained at least a week apart are recommended. (See quarantine section for details.)

In order to establish feline calicivirus as the probable cause of death in a cat, a full necropsy should be performed. The value of this is to rule out other causes or co-pathogens as well as to look for calicivirus. If virulent systemic feline calicivirus is suspected, tissues of particular interest include skin (particularly footpads, nasal planum, and any areas of obvious ulceration), tongue, lung, liver, spleen, GI tract, pancreas, and lymph nodes. Ideally the necropsy should be performed on a fresh or refrigerated specimen; if this is not possible, dual frozen and formalin fixed samples of the above listed tissues should be obtained. Although variable among cases and isolates, pancreatic necrosis and "individualized hepatocellular necrosis" have been found in several outbreaks of VS-FCV, and would be cause for further investigation. Note that while identification of the virus from an internal organ by PCR does indicate that the cat was likely viremic at the time of necropsy, it does not establish whether calicivirus was the cause of death of the animal or whether it was a co-pathogen at the time of death. Immunohistochemical examination of tissues demonstrating the presence of the virus in the viscera and its association with lesions is required to confirm VS-FCV. This is only available through specialized laboratories.

Panleukopenia should always be ruled out in cases of severe illness or sudden death - with or without respiratory signs - in any shelter cat or other cat with an incomplete vaccination history. Calicivirus and panleukopenia may cause synergistic infections and very severe signs; unlike calicivirus, however, panleukopenia can be largely controlled with a rigorous vaccination program.

## **Summary: diagnostic criteria for an FCV outbreak**

- History and clinical signs suggestive of FCV
- Other common causes ruled out
- The majority of affected cats positive by culture/PCR on oropharyngeal swabs and/or
- Culture/PCR positive on serum or tissue samples (especially if from more than one cat) and/or
- Evidence of viral infection on necropsy or...
- Gold standard: Immunohistochemical examination of tissues demonstrating the presence of the virus in the viscera and its association with lesions. This is the only way – other than based on clinical signs – that VS-FCV can be distinguished from field strain infection.

## **Can we ship samples to the Shelter Medicine Program for diagnostic testing?**

No, we are not able to receive samples at the shelter medicine program. Samples can be sent to commercial diagnostic or university laboratories for PCR testing and/or viral isolation. See our [diagnostic testing page](#) for more information.

## **If cats are getting horribly sick, does it really matter if it's VS-FCV or not?**

That's a good question! Virulent systemic feline calicivirus is a distinct syndrome characterized by vasculitis and consequent edema and skin ulceration. True outbreaks of VS-FCV remain quite uncommon. However, distinguishing between VS-FCV and strains of FCV causing severe disease for other reasons is somewhat of an academic exercise. We know vaccine resistance or easy transmission is not necessarily a characteristic linked to virulent systemic strains. Some field strains are not technically "virulent systemic" but are vaccine resistant, highly transmissible and cause very severe signs such as extensive oral and esophageal ulceration and/or pneumonia. If any calicivirus has been implicated in an outbreak and is wreaking havoc within a shelter or clinic, similar measures will need to be taken regardless of whether it meets the definition of VS-FCV per se. Since there is no vaccine thought to be particularly more likely to protect against virulent versus other strains of FCV, even the vaccination strategy is no different whether dealing with a field or VS-FCV

strain. (See vaccine section for more info.)

## What is the role of vaccination?

At best, vaccines against FCV do not protect against infection or establishment of a carrier state, though ideally they will mitigate the severity of disease. Three general types of FCV vaccines are available: modified live (MLV) or killed subcutaneous (SC), and modified live intranasal. The advantage of the modified live intranasal vaccine is the possibility of a more rapid onset of protection compared to subcutaneous delivery, which may be an advantage in the face of an outbreak <sup>[1]</sup>. Unlike the SC MLV vaccine for panleukopenia, both MLV and killed vaccines for calicivirus (and feline herpesvirus) need to be boosted 2-3 weeks after initial administration to provide full protection. Therefore, the ability of the vaccine to cross-protect against multiple strains is a more important consideration than whether the vaccine is MLV or not. Ideally, cats would receive the two vaccine series at least two weeks prior to entering a shelter. In reality this is often impractical. Fortunately exposure to calicivirus may not be as rapid as to the more ubiquitous feline herpesvirus. Vaccination can still be a helpful adjunct to control caliciviral infection, especially in shelters where cats tend to stay for weeks or longer, but can't be relied on as the sole tool to prevent this disease.

Some studies have suggested that vaccine protection against respiratory viruses partially wears off over time. Although vaccination remains somewhat protective three years after administration (the currently recommended standard revaccination interval), there may be some benefit to earlier revaccination for cats prior to exposure to a high risk environment, particularly if the cat has been leading a secluded lifestyle for some time. For instance, a formerly isolated indoor pet cat who is going to stay at a boarding kennel or whose owner is about to embark on a career as a foster kitten-raiser might benefit from a booster vaccine one month prior to exposure.

Unfortunately, there is an increasing number of strains against which vaccination does not provide even limited protection ("vaccine resistant strains"). That same tendency to mutate that results in so many different clinical manifestations of FCV means that vaccine resistant strains are constantly emerging, and most FCV vaccines contain strains that have not been updated in decades. Although new vaccine strategies such as polyvalent vaccines are under investigation, at this point it is prudent to assume that even vaccinated cats will be susceptible to infection and severe disease from some strains of calicivirus. For this reason, clients should take careful isolation precautions to protect pet cats should they choose to adopt or provide foster care for cats with signs of FCV infection.

This is particularly true in any outbreak in which otherwise healthy, well vaccinated adult cats have been affected.

<sup>1</sup> *Regardless of choice of respiratory vaccine, all cats > 4 weeks of age entering shelters should receive a subcutaneous modified live panleukopenia vaccine immediately on intake. This may be given in conjunction with a three way SC FVRCP vaccine and/or simultaneously with a 2 or 3 way FVRC(P) intranasal vaccine.*

## **What about two strain caliciviral vaccines?**

There are vaccines now available in the United States and Europe that incorporate two strains of calicivirus. One of these contains a strain of calicivirus known to cause virulent systemic disease in addition to the more traditional strain. The vaccine provided significant protection when cats were challenged with the *same* strain it was made from 3 weeks after completion of a series of two vaccines administered 3 weeks apart. So far each known VS-FCV strain has arisen as a new mutation within a group of cats, and the strains we've checked at UC Davis have not been genetically closely related nor serologically cross reactive. This suggests that infection or vaccination with one VS-FCV strain is not particularly likely to confer cross protection against other VS-FCV or field strains. We've even found one cat simultaneously infected with a VS-FCV and less virulent field strain (shedding one from the nose and the other from the mouth).

So the bad news is there is no evidence that any currently available vaccine provides better protection specifically against highly virulent strains. However, the good news is that there is evidence that the two-strain (bivalent) vaccines DO provide broader cross protection against calicivirus generally. In communities where panleukopenia is a threat, *the single most important thing is to ensure that all cats over 4 weeks of age receive a modified live subcutaneous panleukopenia vaccine immediately on intake.* Bivalent MLV vaccines are available in combination with MLV panleukopenia and herpesvirus and should be used where broader calici protection is desired in a shelter environment. While all cats may benefit from the increased protection of a bivalent vaccine, the benefit is likely to be greatest in sanctuaries and long-stay shelters, for pet cats at high risk of calicivirus exposure (e.g. pets of feline foster care providers and shelter or veterinary professionals) or for individual cats likely to stay for a prolonged period in a shelter (e.g. due to a legal hold).

## **What is the best vaccination strategy in the face of an outbreak?**

Unlike panleukopenia vaccination which provides rapid protection after even a single MLV vaccine in many cats, either MLV or inactivated calicivirus vaccine may need to be boosted to provide full protection. Therefore, no vaccine is likely to be very helpful in the face of an active outbreak unless cats can be isolated from exposed/at risk cats for some time.

For VS-FCV specifically, as noted most recognized outbreaks have involved well vaccinated cats. In one outbreak for which data were available for a limited number of kittens, no difference in disease risk was seen between those previously vaccinated with a subcutaneous versus intranasal vaccine. A small trial was performed which compared clinical signs in 4 kittens orally immunized with a typical vaccine strain (FCV-F9, Heska strain) with two unvaccinated littermates. Kittens were challenged with FCV-Ari (a highly virulent calicivirus) six weeks after vaccination. Although no statistical significance was reported, it appeared that the recently vaccinated cats were not as severely affected as the unvaccinated kittens. Vaccination did not generate cross protective antibodies against this strain of calicivirus. The protective effect may have been the result of direct competition between vaccine strain and field strain virus in these recently vaccinated kittens, or some other effect. It is possible (but unproven) that intranasal vaccination shortly before exposure, or perhaps even concurrent with exposure, will provide a degree of protection against more virulent strains by direct competition. This would be a reasonable adjunct strategy in the face of an acute outbreak, but should not be relied upon. Remember that cats recently vaccinated with an intranasal vaccine are very likely to culture positive for FCV, and RT-PCR followed by genetic sequencing would be required to distinguish vaccinates from truly infected cats.

## **Outbreak intervention**

Controlling a true outbreak of severe or virulent-systemic FCV is one of the most challenging infectious disease control situations a shelter can face. All exposed cats must be considered at risk for transmitting severe disease to others; there is no clearly defined “quarantine period” after which we know cats are safe; and we cannot assume that vaccination will be protective. This creates a real dilemma for adoption – once we get cats through the illness, do we send them out for adoption? The last thing we want to do is have an adopter’s pet end up infected by the newly adopted pet. Do we make them available to single cat homes only? That’s a big strike against adoption in some communities, meaning the cats will linger in the shelter longer and possibly infect new incoming cats. Even if cats are adopted into single pet homes, they will inevitably go to vet clinics for vaccines or other wellness care, and other people’s pets may end up

exposed. It's very likely that cats will no longer be a risk 2-3 months after clinical signs have fully resolved, but that's a long time to care for – and strictly isolate – cats with a potentially deadly illness. A responsible, duly advised foster home with no other pet cats may be a good option, but these can be hard to come by.

FCV outbreak control measures are expensive, labor intensive, and may even cost some cats their lives. That's why it's SO important to ask the question: *does this really need to be approached as an FCV outbreak?* Remember FCV infected cats leave shelters and catteries every single day, very rarely with ill effect. There is no possible way we can avoid sheltering or adopting out cats with FCV, nor is it necessary to do so. Our goals are to minimize the risk that adopted cats will transmit severe disease to adopters' pets or community cats, and to reduce the likelihood that a severe outbreak will persist and infect new incoming cats.

## **Making the decision: risk assessment for FCV**

The obvious first step in deciding whether outbreak control measures are necessary is to definitely diagnose FCV and rule out other common causes of the observed signs, such as feline panleukopenia. Even if FCV is a contributing factor, the outbreak can often be resolved by controlling the co-factor, which may be more amenable to intervention. In the meantime, of course, affected and exposed cats should be isolated as with any possibly infectious outbreak. Once FCV has been clearly implicated in an outbreak, consider the following to evaluate risk:

### **Have contributing co-factors really been ruled out?**

I can't stress this enough: **the vast majority of suspected VS-FCV cases or outbreaks we are contacted about turn out to have another primary cause** such as panleukopenia, disinfectant toxicity, or the cumulative effects of severe crowding, poor sanitation, problems with air quality, and rampant disease from many causes, adding up to a picture that looks a lot like VS-FCV. While none of these conditions is desirable, any of them pose less of a risk to community cats and are more straightforward to correct than an outbreak of VS-FCV.

### **How severe is the worst manifestation of disease?**

If the worst signs in an affected *population* are limited to mild to moderate oral ulceration, limping and/or URI, then even in the worst case scenario in which an adopter's pet gets sick, the consequences will likely be limited to a nuisance rather than a life threatening illness. On the other hand, if some cats are getting very sick or dying – whether from virulent systemic disease or “just” horrible oral ulceration - then any exposed cat could transmit severe disease if exposed to a naïve cat.

## **Are otherwise healthy adult cats affected?**

One of the reasons an adopter's pet at home rarely contracts severe disease from newly adopted shelter animals is that the pet's overall health is good, the animal is not overly stressed, and the pet has not been subjected to the additional environmental factors common in shelters (such as poor air quality) that predispose to serious disease even from relatively mild pathogens. These advantages protect against many infections but not against VS-FCV, which tends to affect otherwise perfectly healthy adults. If severely affected cats in an outbreak are generally kittens or otherwise immune-compromised, then the risk to community pets is lower. If the FCV appears able to cause severe disease even in adult cats that otherwise appeared to be in vibrant good health, this is more of a concern.

## **Are well-vaccinated cats affected?**

“Well vaccinated” in this case would include any cat over 6 months of age that had received at least two vaccines 2-4 weeks apart > 4 weeks and < 3 years before exposure. In a shelter, this would most often include resident cats or pet cats belonging to staff or volunteers. If these well vaccinated cats are severely affected, then much greater concern about spread to community cats is warranted.

Taking these factors into account, the shelter manager and veterinarian must weigh the known risk and cost of quarantine/depopulation versus the possible risk to community pets and newly admitted cats should quarantine measures not be taken. If FCV is clearly implicated as a sole pathogen causing severe disease in otherwise healthy, well-vaccinated cats, then stringent control measures are warranted.

## **The basics of FCV outbreak control**

If you've reviewed the diagnostic testing and risk assessment information above and you're convinced you have an FCV outbreak meriting serious control measures, read on. As noted above, before depopulating, contact

your friendly local shelter medicine program, veterinary school or other infectious disease expert to double check the diagnosis, if you haven't already done so.

Control of an FCV outbreak is similar to control of any other outbreak, with a couple of twists. As in any outbreak, the first steps are to:

- **Create a communication plan**, including notifying area veterinary clinics (especially those who may have seen affected cats adopted from the shelter); other shelters and rescue groups; shelter staff and volunteers; and media.
- **Identify exposed/at risk cats**
  - If the strain has only affected poorly vaccinated cats, then it may be possible to divide exposed cats into lower and higher risk based on vaccination history. In some cases, infection may be limited to a single building, depending on how the facility is set up. However, given the ease of transmission, “exposed/at risk” is likely to mean all cats on the premises at the time of the outbreak unless outstanding infectious disease control measures were already in place. Even at veterinary clinics, cats simply housed on the same premises have been infected and gone home to transmit fatal disease to other pets in the household.
- Create an immediate and complete break between exposed cats and newly admitted cats.
  - Carefully isolate/quarantine exposed cats (or euthanize if resources for quarantine do not exist). For more information on quarantine, see below.
  - Create clean intake areas for newly admitted cats (close to admissions until this can be done).
    - Thoroughly clean all surfaces, followed by application of a disinfectant active against unenveloped viruses (Accelerated hydrogen peroxide (Rescue™), potassium peroxymonosulfate (Trifectant®, Virkon-S®), and sodium hypochlorite and other products in that family (e.g. 5% bleach diluted at 1/2 cup per gallon). Pre-cleaning is especially critical with bleach, as bleach is substantially inactivated by organic matter. Allow to dry thoroughly and repeat before admitting new cats.
- Consider temporarily adding a two-way intranasal herpes/calici (FVRC) vaccine for all exposed and new incoming cats, in addition to continuing vaccination with modified live subcutaneous panleukopenia vaccine (either as part of a 3 way FVRCP or single antigen).

## **The quarantine dilemma**

Quarantine for FCV is exceptionally problematic because the period for which exposed cats are a risk to others is unknown (and probably variable). We know that shedding persists in many cats for weeks or months; what we don't know is how long the virus maintains its original virulence under these circumstances. Following outbreaks of VS-FCV, recovered or asymptomatic cats are known to have transmitted fatal disease within 2 weeks of being released. On the other hand, in a few known cases, cats shedding a formerly virulent systemic strain have been released to homes or adopted out 10 weeks or more following resolution of an outbreak and no further transmission of disease was seen. In these cases, it appears that although the cats were still carriers, the virus had lost the mutation conferring increased virulence. This may be the reason that no outbreak of very severe disease has persisted for more than ~2 months even in the face of incomplete control measures. Unfortunately, not enough cases have been closely followed to know the exact amount of time required for exposed cats to be safe around others.

Because of the uncertainty with respect to risk for adopter's pets; the length of quarantine required to be reasonably sure no further transmission will occur; and the difficulty of preventing spread of this highly transmissible infection, some shelters elect to euthanize rather than quarantine exposed cats. Overall, this may be a life-saving choice if the alternative is insufficient quarantine leading to continued spread within the shelter or into the community; or monopolization of the shelter's resources by the quarantine cats such that the shelter is unable to serve the rest of their population adequately. This does not need to be an all-or-nothing choice. In some cases, shelters may invest in quarantine for selected highly adoptable cats; cats in which the shelter has already invested heavily (e.g. those returned from foster care); or of course cats in legal holding periods.

## **Length of quarantine**

As noted above, the exact length of time required for quarantine is unknown. The more severe the original disease was (overall, not in any particular cat), the farther on the side of caution one would want to err, of course. If severe disease was limited to unvaccinated cats, then there is less reason for concern about placing recovered cats into adoptive homes, but still reason to avoid exposing them to new incoming cats who do not have complete vaccine protection. In that situation, quarantine until clinical signs are completely resolved followed by adoption out of a separate venue from the general shelter population may be sufficient. For

severe disease in vaccinated cats, a 3 month quarantine is probably safest. In each case, the shelter management and veterinarian must balance the risk and cost of quarantine versus the risk to newly admitted and community cats.

## **Quarantine details**

Quarantined cats should be removed to a *separate* isolation ward, separate building, or experienced, well trained foster care who have no cats of their own (especially if vaccine resistance is suspected). Foster parents should be counseled carefully about the need to prevent contamination of their homes, the risk of transmission to pet cats even by contaminated clothing during acute stages, and the prognosis should the cats become ill. Because quarantine may be lengthy, cats should be housed in comfortable quarters that are easy to maintain, such as an easily-cleaned group room or garage. It is unduly labor-intensive and inhumane to house cats in small cages for this length of time. Any area where cats are quarantined must be able to be decontaminated following completion of the quarantine. If the area cannot be thoroughly cleaned and disinfected then the area should be kept off limits to cats for 4 months following quarantine to allow the virus to die off naturally (possibly longer in very cold climates). Fortunately, with newer disinfectants such as accelerated hydrogen peroxide (e.g. Rescue<sup>TM</sup>) that have good penetration and activity in the face of organic matters, even areas with carpeting or other organic material can be more readily decontaminated.

Precautions for quarantine include:

- Limit access to a few highly trained staff members or volunteers
- Wear full protective clothing (jump suits, boots or shoe covers, and gloves)
- Shoe covers or dedicated boots are required – foot baths are insufficient
- Use supplies (brooms, feeding carts, scrub brushes, thermometers, stethoscope, etc.) dedicated to quarantine and used only in that room.
- Handle cats in quarantine only after caring for healthy cats.

## **Role of viral culture to identify low risk cats**

In some cases, viral culture/PCR may be used as an adjunct to quarantine to identify cats that are no longer shedding FCV. This is generally not cost effective in a large outbreak but may be a good strategy to hasten release of some cats. Because viral shedding may be

intermittent, 3 oropharyngeal swabs obtained at least a week apart are required to call a cat truly negative (therefore cats will still have to be held in quarantine at least 3 weeks).

Regardless of choice of respiratory vaccine, all cats > 4 weeks of age entering shelters should receive a subcutaneous modified live panleukopenia vaccine immediately on intake. This may be given in conjunction with a three way SC FVRCP vaccine and/or simultaneously with a 2 or 3 way FVRC(P) intranasal vaccine.

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