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Infectious Diseases Dentistry

Feline Viral Upper Respiratory Disease: Herpesvirus and Calicivirus

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There is little argument among clinicians that feline upper respiratory disease is perhaps the most common respiratory disorder for which cats are presented. In multiple-cat households and animal shelters worldwide, transmissible feline upper respiratory disease (URD) represents the most prevalent clinical disease in the population of cats at risk. The question that must be asked is: despite widespread use of vaccines against viral (herpesvirus and calicivirus) and bacterial (Chlamyphila felis and Bordetella bronchiseptica) respiratory disease, why do these infections persist? …and, what can be done to effectively manage these infections within households?

This question is important, but today there are answers that will help veterinarians manage the infected cat and minimize spread of infections among cats living within a closed population. This presentation addresses the most common cause of both acute and chronic upper respiratory infection in cats: feline herpesvirus-1 (cause of feline rhinotracheitis) and feline calicivirus. From diagnosis, to clinical management of infected cats, to vaccination…the critical issues surrounding this respiratory complex will be discussed.

Several infectious organisms are known to produce clinical signs of upper respiratory disease (URD) in cats. The most important, and most common, are:

- Feline Herpesvirus-1 (FHV-1)
- Feline Calicivirus (FCV)
- Chlamyphila felis (formerly, Chlamydia psittaci)
- Bordetella bronchiseptica

Reports on the prevalence of individual pathogens in outbreaks of feline respiratory will vary from country to country. In the United Kingdom, for example, it has been estimated that Chlamyphila felis infections constitute up to 30% of the cases of respiratory disease in cats. In North America, it’s estimated to cause fewer than 5% of cases of feline respiratory disease. Today, most authors agree that between 80% and 90% of the cases of feline viral URD are caused by one of two viral groups, either (FHV-1), cause of feline viral rhinotracheitis (FVR), or feline calicivirus (FCV). Although a number of other viruses (cat pox, FeLV and FIV) and bacteria (Haemophilus felis, Mycoplasma spp.) have been shown to be associated with clinical signs of respiratory disease in cats, their clinical importance is largely linked to either herpesvirus or calicivirus infection…and occasionally, both!

ACUTE VIRAL RESPIRATORY INFECTION

The hallmark clinical sign of acute viral URD is sneezing. Initially intermittent, the frequency and
severity of sneezing episodes increases over a 3 to 5 day period. Fever and a bilateral or unilateral serous nasal-ocular discharge typically accompany sneezing episodes. As normal respiratory bacterial flora colonize in the upper respiratory tract membranes, the serous discharge becomes mucopurulent; this represents the most common problem for which affected cats are presented to a veterinarian. Left untreated, the nares obstruct, the eyelids become adherent to each other with viscous purulent secretions, and sneezing actually stops. Oral (especially lingual) ulceration is common and may be accompanied by hypersalivation, severe dehydration, anorexia, malnutrition. Secondary bacterial infections can become life threatening (pneumonia and sepsis) therefore; empiric antimicrobial therapy is always indicated. Clinical signs are most intense during the end of the first week and the second week of infection but may persist for as long as three weeks.

In practice, a diagnosis of acute viral URD is justifiably established on the basis of history and physical signs. Seldom is it necessary to isolate the specific virus responsible for causing infection in the individual cat. Laboratory profiles are more important in monitoring patient progress during therapy than establishing a diagnosis. Although morbidity can reach 100% in multiple-cat households, mortality is more common among kittens (<6 months of age) with secondary bacterial infections than in older cats. Therefore survival rates among affected cats are expected to be high presuming antibacterial, hydration, and nutritional support can be provided.

In multiple-cat households the problem of acute viral URD in kittens does not stop despite successful management of individual cat infections, implementation of a comprehensive vaccination program, and a seropositive adult population. It is important to note that approximately 80% or more of cats that survive acute FCV infection will become chronic carrier cats. One-hundred percent of kittens that recover from acute FHV-1 infection are expected to become chronic carrier cats. Healthy appearing carriers maintained in the population serve as reservoirs and can spread virulent virus to susceptible kittens, as well as adult cats, through direct cat-to-cat contact or fomite contamination.

THE CHRONIC CARRIER STATE

Unlike the feline panleukopenia virus, FHV-1 and FCV are relatively unstable outside the host cat (<18 hours for FHV-1 and about 2 weeks for FCV assuming ideal conditions of temperature and humidity). Therefore, the persistence of viral URD within a population depends on the ability of these viruses to sustain themselves in adult carrier cats.

NOTE: the FCV carrier cat sheds virulent calicivirus from the oropharynx continuously! FCV carrier cats, therefore, pose a substantial threat to susceptible kittens in multiple-cat population. It has been estimated that as many as 25% of clinically healthy breeding cats and approximately 10% of healthy household cats are FCV carriers. On the other hand, the FHV-1 carrier cats have a truly latent infection. Viral shedding is not continuous, but can occur subsequent to physiological stress (e.g., general anesthesia, boarding) or pharmacological stress (e.g., administration of corticosteroids). Although the virus is consistently recovered from tonsils of affected carriers, tonsillectomy does not eliminate virus excretion. Obviously, other sites of persistence in the oropharynx must exist.

The occurrence of repeat outbreaks of feline viral upper respiratory disease within a multiple cat household, particularly when kitten morbidity is high, supports the hypothesis that one or more chronic carrier cats live within the population. Diagnosis of the chronic carrier cat can be quite difficult even when virus isolation is attempted. Clinical signs in affected cats are variable to nonexistent. When present, however, they may provide important clues regarding the presence of a chronic carrier within a given population.

Clinical signs associated with the chronic carriers state, if present, typically manifest as paroxysmal sneezing episodes with continuous or intermittent mucopurulent nasal and/or ocular discharge. Characteristically, the sneezing and nasal discharge respond, usually completely, to empiric antibiotic treatment. However, resolution of clinical signs is only effective during the time of treatment. Within 3
days following discontinuation of the antibiotic, clinical signs typically re-occur. In addition to paroxysmal sneezing and nasal discharge, stomatitis, chronic gingivitis, gingival ulceration, and periodontal disease with premature loss of teeth will be evident. In our experience, this is especially true in cats with FCV and FIV infections. Radiographs may reveal secondary frontal sinusitis.

Recrudescent FHV-1 infections in adult cats manifest in a variety of ways: herpesvirus keratitis, corneal ulceration, and symblepheron in severe cases. Sneezing and nasal discharge is relatively uncommon. The author has proposed that feline vestibular syndrome is, in fact, yet another manifestation of feline herpesvirus-1 recrudescence.

Both FeLV and FIV infection are reported to be common concomitant (predisposing?) infections in cats determined to be chronic respiratory virus carriers. Routine testing of suspected carriers for both FeLV and FIV is highly recommended.

**MANAGEMENT CONSIDERATIONS: THE CHRONIC CARRIER HOUSEHOLD**

Unfortunately, even the most comprehensive vaccination program will not guarantee protection against persistent virus infections occurring within a household. Objectively, management of chronic feline viral URD within a household or cattery, must be directed at effective control: strategic vaccination programs, strict environmental regulation, minimizing exposure, and, when possible, identification and isolation of carrier cats. Although parenterally vaccinated cats do develop significant, sometimes referred to as "protective," circulating antibody levels, immune carrier cats are commonplace. Use of intranasal vaccination, if available, has been shown to mitigate the risk of outbreaks within a closed household and for reducing kitten losses associated with enzootic viral URD.

Several drugs have been used in an attempt to manage clinical signs of chronic, intermittent upper respiratory disease attributed to a chronic FCV or FHV-1 carrier state. For example, any broad spectrum antibiotic will control the clinical signs but, as described above, the response is typically limited to the time the cat is receiving the drug. Amoxicillin-clavulanate, metronidazole, and doxycycline have been recommended. In our experience, azithromycin, administered at 5 mg/kg, orally, once daily for 10 to 14 weeks (a liquid preparation is now available) has effectively managed clinical signs for periods longer than other conventional antimicrobials. Immunomodulation has been attempted using human recombinant interferon (30 I.U. per day, orally, indefinitely). In our experience, little to no discernable response has been detected. A new recombinant feline-origin omega interferon (Virbagen Omega) is being studied at this time (10,000 I.U. per day, administered orally) in chronically affected cats (NOTE: this product currently has limited availability and is not licensed for use in the United States). Administration of L-lysine (a non-prescription amino acid available in ‘health food stores’), 250 mg administered orally, with food, once daily, for an indefinite period, has been recommended to prevent the consequences of viral recrudescence in FHV-1 carrier cats. Lysine is reported to compete, pharmaceutically, with arginine, which is required by herpesviruses to replicate. However, diagnosis of the FHV-1 carrier states requires isolation of the virus... and... viral shedding is intermittent. In clinical practice, therefore, the decision to treat with lysine is seldom based on diagnostic confirmation of FHV-1 infection. Anecdotal reports of response to lysine therapy have been difficult to assess.

**NOTE:** antiviral drugs used to treat herpesvirus infections in humans (e.g., acyclovir) are not effective against feline herpesvirus and, in fact, are contraindicated. Likewise, ribavirin is an antiviral drug effective against FCV, however the drug is quite toxic to cats and should not be used.

**IMMUNIZATION**

Serologic response following vaccination with modified-live virus bivalent (FHV-1 and FCV) vaccines, whether administered parenterally or topically, is consistently characterized by the development of
high titers. Vaccinated cats, however, do not necessarily enjoy complete protection. The immunity derived from vaccination does protect cats against developing severe disease following exposure. Vaccination, however, does not protect cats against infection. Even if immunized prior to exposure, vaccinated cats can become infected and develop a chronic carrier state. Efforts to prevent development of the chronic carrier state through the use of topical FHV-1/FCV vaccines has not been consistently successful.

Although immunization cannot guarantee complete protection from respiratory infection nor from the development of a chronic carrier state, routine vaccination of kittens using a modified-live bivalent (FHV-1 and FCV) vaccine, is recommended, particularly in multiple-cat households. An extensive review of available data on the immunogenicity of FHV-1 and FCV vaccines by the AAFP Panel on Vaccine Recommendations (SECOND EDITION: 2000) has led to significantly revised vaccination protocol. Whether using a parenterally administered vaccine or topically administered vaccine:

**Initial Series:** First dose at 9 weeks of age; a second dose is administered 3-4 weeks later.

**1st Booster Inoculation:** 1 year following the last dose in the initial series.

**Subsequent Boosters:** Administer 1 dose every 3 years thereafter.

The minimum duration of immunity in adult, vaccinated cats has been shown to be at least 5 years.

There are three key advantages to intranasal administration of FHV-1/FCV vaccination. First, the onset of protection is rapid, generally occurring within 24-48 hours. Secondly, intranasally administered vaccines are not interfered with by circulating maternal antibody. Third, intranasal vaccines appear to actively stimulate local immunity within the nasal cavity, the most likely site of infection. Although parenterally administered vaccines produce high titers, their ability to stimulate local immunity is limited and, in kittens, maternally derived antibody can interfere with initial vaccination in kittens under 9-10 weeks of age.

Topical vaccination, although having limited global distribution, has been recognized to lessen, and in some cases eliminate, clinical signs of rhinitis in chronic carrier cats. Prior to administering vaccine, 2-3 days of pretreatment with an antimicrobial may be necessary to reduce the amount of nasal discharge. A single dose of intranasal vaccine is administered in accordance with manufacturers’ recommendations: 1 drop in each eye and the remaining volume onto the nose-web. A response is expected within 10 to 14 days as the volume of discharge and associated sneezing diminishes significantly. If there is no initial response, some cats may respond to a second dose administered 30 days following the first dose. We have routinely re-isolated virus from cats despite the diminution of clinical signs. Topical administration of vaccine to chronic carrier cats is NOT expected to eliminate the chronic carrier state.

**TOPICAL UPPER RESPIRATORY VACCINES**

(FHV-1 and FCV)

- **Felomune CVR (Pfizer Animal Health):** modified live, herpesvirus-1 and calicivirus. (0.5 ml)
- **Feline Ultranasal FVRC Vaccine (Heska):** modified live, feline herpesvirus-1 and calicivirus. (0.2 ml)
- **Feline Ultranasal FVRCP Vaccine (Heska):** modified live, feline panleukopenia in addition to herpesvirus-1 and calicivirus. (0.2 ml)
Recommended Reading


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