Viral diseases. Herpesvirus 1 (rhinotracheitis; FHV-1) and calicivirus (FCV) are the most common viral causes of sneezing and nasal discharge in the cat. If oral ulcers are present, calicivirus is most likely. If corneal ulcers are present, herpesvirus 1 is most likely. FHV-1 has now also been associated with chronic stomatitis, facial dermatitis, and endogenous uveitis. Viral rhinitis with or without secondary bacterial infection can be recurrent. FHV-1 can be documented by direct fluorescent staining of conjunctival scrapings, virus isolation, or polymerase chain reaction. Since FHV-1 DNA can be detected in conjunctival cells of approximately 25% of healthy cats, the positive predictive value of these tests in diseased cats is low. Vaccine strains also lead to positive results in currently available assays. Quantitative PCR may ultimately prove to correlate with the presence or absence of disease. Currently used PCR assays also detect vaccine strains of FHV-1. RT-PCR assays can be used to amplify the RNA of FCV. However, these assays have the same problems with predictive value as those to detect DNA of FHV-1.

Feline viral rhinitis with or without secondary bacterial infection can be recurrent. There are no consistently effective primary therapies. I generally only use the following therapies if chronic disease is present. Lysine at 250-500 mg, PO, BID may be helpful in some cats with chronic FHV-1 and has been shown to be safe but should be given as a dose, not fed with food.

Administration of alpha interferon at 30 - 50 U, PO, daily may help some cats with suspected chronic calicivirus or FHV-1 infection. Topical administration of alpha interferon in saline to the eyes of cats with conjunctivitis or the nose may aid in the management of some cats. Lysine and alpha interferon are unlikely to lead to a cure, but hopefully will lessen clinical signs of disease.

Intranasal administration of modified live, intranasal FHV-1 and FCV vaccines has lessened disease in some chronically infected cats in one of our current Morris Animal Foundation projects. If there is a positive response to intranasal vaccination in a cat with chronic disease, I will use this form of immunotherapy up to 3 times per year. One intranasal vaccine (HESKA) has been shown to potentiate cell-mediated immunity to FHV-1 better than parenteral vaccination.

Use of alpha 2b interferon at 10,000 U/kg, SQ, once daily diluted in saline for up to 14 days has led to clinical resolution of disease in some cats with either FCV or FHV-1 in one of our current Morris Animal Foundation projects.

Acyclovir is an anti-herpesvirus drug for use in people but can be toxic to cats and should no longer be used. Famcyclovir seems to be safer and more effective than acyclovir and is now being used for long-term therapy. One dose that has been used is 1/2 tablet (62.5 mg) q12 hr for
14 days. The drug is safe at up to 90 mg/kg, PO, q8hrs and so the dose should be increased if the initial response is suboptimal and FHV-1 is still suspected. This dose does not give adequate drug levels and so increase to 40 mg/kg, PO, TID if the empirical dose is ineffective. It is acceptable to use the generic product to lessen expenses. Topical cidofovir (product for humans) can be used for the treatment of FHV-1 conjunctivitis twice daily and was effective in a controlled research project. The drug was easier to administer (twice daily) than idoxuridine or other anti-FHV-1 ocular therapies and does not cause as much irritation.

Feline leukemia virus and feline immunodeficiency virus can induce immunosuppression predisposing to bacterial rhinitis. However, there is no universally effective treatment.

**Bacterial diseases.** Almost all cats with mucopurulent or purulent nasal discharge have a bacterial component to their disease. Primary bacterial disease is rare but may be associated with *Bordetella bronchiseptica*, *Mycoplasma* spp. and *Chlamydophila felis*. In one recent Morris Animal Foundation sponsored study, we showed Mycoplasmas to be more common that FHV-1 and were associated with illness. Recently it was shown that *Bartonella* spp. are not causes of rhinitis in cats. Both *B. bronchiseptica* and *Mycoplasma* spp. can be associated with bronchitis in cats. Chlamydioidis in general, is a mild infection resulting only in conjunctivitis. If primary infections are suspected, doxycycline 10 mg/kg, PO, once daily or topical administration of tetracyclines (conjunctivitis) are usually effective. Cats with acute disease only need to be treated for 7 to 10 days. Most cases of bacterial rhinitis are secondary to other diseases including trauma, neoplasia, inflammation induced by viral infection, foreign bodies, inflammatory polyps, and tooth root abscessation. Thus, if routine antibiotic therapy fails, a diagnostic workup should be performed.

Since bacterial rhinitis leads to chondritis and osteomyelitis, antibiotic therapy should be continued for weeks in cats with chronic disease. I generally use drugs with an anaerobic spectrum that also penetrate bone and cartilage. Clindamycin, amoxicillin, amoxicillin-clavulanate, or metronidazole. Amoxicillin-clavulanate has the advantage of killing most *Bordetella* isolates. Clindamycin has the advantage of effective against *Mycoplasma* spp. and the drug can be used once daily for routine bacterial infections in cats. Doxycycline and metronidazole may be superior to other drugs for the treatment of chronic infections since they may modulate the immune reaction, lessening inflammation. Azithromycin (10 mg/kg, PO, q 24-72 hr) or fluoroquinolones can be used for cats with chronic disease. For cats that are difficult to treat, cephalosporin injections can be considered. However, this drug class is ineffective for *Mycoplasma* spp. and most *Bordetella* isolates and so should not be a first line therapy unless the cat is impossible to treat orally.

**Fungal diseases.** *Cryptococcus neoformans*, *C. gattii*, and *Aspergillus* spp. are the most common causes of fungal infection in cats. Cryptococcosis is the most common systemic fungal infection of cats and should be considered a differential diagnosis for cats with respiratory tract disease, subcutaneous nodules, lymphadenopathy, intraocular inflammation, fever, and CNS disease. Infected cats range from 6 months to 16 years of age, and male cats are over represented in most studies. Infection of the nasal cavity is reported most frequently (56.3 to 83.0% of cases) and commonly results in sneezing and nasal discharge. The nasal discharge can be unilateral or bilateral, ranges from serous to mucopurulent, and often contains blood. Granulomatous lesions
extruding from the external nares, facial deformity over the bridge of the nose, and ulcerative lesions on the nasal planum are common. Submandibular lymphadenopathy is detected in most cats with rhinitis. Definitive diagnosis of cryptococcosis is based on antigen testing or cytologic, histopathologic, or culture demonstration of the organism. Cats with cryptococcosis have been treated with amphotericin B, ketoconazole, itraconazole, fluconazole, and 5-flucytosine alone and in varying combinations. Good to excellent treatment responses in cats were seen with fluconazole (96.6%), itraconazole (57.1%), and ketoconazole (34.6%). Because of toxicity, I no longer use ketoconazole. I generally use fluconazole at 50 mg/cat per day because it has the least side-effects and or the azoles, has the best penetration across the blood-brain and blood-ocular barriers. If life-threatening infection is occurring or the cat is failing to respond to the azole, drugs liposomal amphotericin B should be used. Nasal and cutaneous cryptococcosis generally resolve with treatment; CNS and ocular disease are less likely to respond to treatment. Treatment should be continued for at least 1 to 2 months past resolution of clinical disease. People and animals can have the same environmental exposure to *Cryptococcus spp.* but zoonotic transfer from contact with infected animals is unlikely.

**Parasitic diseases.** While nasal mites (*Pneumonyssoides*) and a nasal worm (*Eucoleus*) occur in dogs in the United States, there are no significant nasal parasites in cats of the USA.

**Prevention of upper respiratory tract infections.** The American Association of Feline Practitioners (www.aafponline.org) recommends that all healthy kittens and adult cats without a known vaccination history should be routinely vaccinated with an intranasal or parenteral vaccine that contains FHV-1, FCV, and feline panleukopenia virus (FVRCP). Multiple modified-live products and killed products are available and the products available in the United States.

In general, modified live FVRCP vaccines are recommended for kittens housed in environments at high risk for exposure to feline panleukopenia virus (FPV). Modified live FVRCP vaccines for intranasal administration can induce protection against FHV-1 as soon as four days after administration and so this route of administration may be preferred for kittens housed in environments at high risk for exposure to FHV-1. Modified live products should not be administered to clinically ill, debilitated, or pregnant animals. Administration of intranasal FVRCP vaccines can induce transient, mild sneezing or coughing and so the owners should be informed. The vaccine marketed by HESKA Corporation in the USA induced significant protection against FHV-1 challenge as soon as 4 days after one dose.

For kittens thought to have no more than routine risk of exposure to FPV, FCV, or FHV-1, it is currently recommended that FVRCP vaccines should be administered starting no sooner than 6 weeks of age with boosters every 3-4 weeks until 16 weeks of age. Older kittens and adult cats with unknown vaccination history should be administered two killed or two modified-live FVRCP doses 3 to 4 weeks apart. For kittens thought to have high risk of exposure to FPV, like those housed in animal shelters or pet stores, the AAFP panel currently recommends parenteral administration of modified live FPV containing vaccines as early as 4 weeks of age, particularly during an outbreak. However, intranasal administration of modified live FVRCP vaccines instead of or in addition to parenteral administration of modified live FVRCP vaccines may be superior for protection against FCV and FHV-1 in these environments. Recently, we showed
that the Pfizer FHV-1/FCV intranasal vaccine induced cross protection against *Bordetella bronchiseptica* on a Day 7 challenge study (see the abstract at the end of the proceedings). Thus, intranasal vaccination may also help protect against agents not in the vaccine. An FVRCP vaccine that contains a killed FHV-1 strain induced more rapid seroconversion to FHV-1 than a modified live FVRCP vaccine in one study.

The current AAFP Advisory Panel recommends a booster FVRCP vaccine one year later. However, a recent study showed that while there was no difference in FPV immunity, the relative efficacy of FCV and FHV-1 vaccines were lower at 1 year after initial vaccination than at 4 weeks after initial vaccination. The author concluded that the first FCV and FHV-1 booster vaccination after the completion of the initial series should be administered earlier than one year.

Based on several challenge studies, it appears that there is no need to administer FVRCP vaccines no more frequently than every third year after the one year booster vaccine; it is possible the duration of immunity is much longer. Serological test results for antibodies against FPV, FCV, and FHV-1 can be used to aid in the determination of vaccine needs.

Some variants of FCV induce systemic vasculitis in cats (virulent calicivirus) and clinical signs can be severe in some cats previously vaccinated with FVRCP vaccines. A killed, virulent FCV containing vaccine line is now available in the USA (Boehringer-Ingelheim). Whether it will be beneficial to administer this strain of FCV to cats to lessen outbreaks of virulent FCV outbreaks is currently unknown. However, this product contains two strains of FCV; serum antibodies from cats given this vaccine neutralized more FCV strains in vitro than antibodies from cats vaccinated with a products containing a single FCV stain. Thus, cats vaccinated with this, or similar 2 strain containing vaccines, may have better cross-protection. See the AAFP Informational Brief at [www.catvets.com](http://www.catvets.com) for a further discussion.

The currently available *B. bronchiseptica* vaccine for intranasal administration can be administered as early as 4 weeks of age, has an onset of immunity as early as 72 hours, and has a minimum duration of immunity of 1 year. Many cats have antibodies against *Bordetella bronchiseptica*, the organism is commonly cultured from cats of crowded environments, and there are sporadic reports of severe lower respiratory disease caused by bordetellosis in kittens and cats of crowded environments or other stressful situations. However, the significance of infection in otherwise healthy pet cats appears to be minimal. For example, in client-owned cats in north central Colorado, the organism was rarely cultured from cats with rhinitis or lower respiratory disease (approximately 3%). In addition, because the vaccine is administered by the intranasal route, mild sneezing and coughing can result. *Bordetella* vaccination should be considered primarily for use in cats at high risk for exposure and disease, such as those with a history of respiratory problems and living in humane shelters with culture proven outbreaks. Since the disease is apparently not life-threatening in adult cats, is uncommon in pet cats, and responds to a variety of antibiotics, routine use of this vaccine in client-owned cats seems unnecessary.

Killed and modified live *C. felis* containing vaccines are available. Infection of cats by *C. felis* generally only results in mild conjunctivitis, is easily treated with antibiotics, has variable prevalence rates, and the organism is of minimal zoonotic risk to people. In addition, use of
FVRCP vaccines that also contained *C. felis* was associated with more vaccine reactions in cats when compared to other products. Thus, whether *C. felis* vaccination is ever required is controversial. The use of this vaccine should be reserved for cats with a high risk of exposure to other cats and in catteries with endemic disease. Duration of immunity for *Chlamydophila* vaccines may be short-lived, so high-risk cats should be immunized before a potential exposure.

**References available on request**

INTRANASAL ADMINISTRATION OF A MODIFIED LIVE FELINE HERPESVIRUS 1 AND FELINE CALICIVIRUS VACCINE INDUCES CROSS PROTECTION AGAINST BORDETELLA BRONCHISEPTICA. A Bradley¹, J Kinyon², T Frana², D Bolte³, DR Hyatt³, MR Lappin¹. ¹. Department of Clinical Sciences, Colorado State University, Fort Collins, CO. ². Veterinary Diagnostic Laboratory, Iowa State University, Ames, IA. ³. Veterinary Diagnostic Laboratory, Colorado State University, Fort Collins, CO.

Vaccination against all feline upper respiratory pathogens is not possible. Results of previous studies suggest that intranasal vaccination may stimulate nonspecific immunity against agents not contained within the vaccine, but no study has directly examined this in cats. The authors hypothesized that cats administered a modified live feline herpesvirus-1 (FHV-1) and feline calicivirus (FCV) intranasal vaccine would have fewer clinical signs after challenge inoculation with *Bordetella bronchiseptica* than unvaccinated controls.

Twenty specific pathogen free 12 week-old kittens were randomized into 2 groups of 10 cats each. The vaccinated group was administered a single intranasal dose of a commercially available vaccine (FELOMUNE CVR®; Pfizer Animal Health, New York, NY) containing modified live strains of FHV-1 and FCV, and the control group remained unvaccinated. All 20 cats were administered *B. bronchiseptica* by nasal inoculation seven days later and were observed daily for clinical signs of illness for 20 days.

In the first 10 days after *B. bronchiseptica* challenge, vaccinated cats were less likely to be clinically ill (indicated by lower cumulative clinical scores) than control cats (*p* = 0.01). The most commonly observed clinical sign was sneezing. Overall, 9 of 10 control cats and 2 of 10 vaccinated cats were noted to sneeze at least once during days 1-10 after inoculation with *B. bronchiseptica* (*p* = 0.006). These differences were no longer apparent during days 11-20. Finally, the percentage of observation points with sneezing recorded was significantly greater in control cats than in vaccinated cats over days 1-10 (*p* < 0.0001) and days 1-20 (*p* = 0.02).

Intranasal vaccination against FHV-1 and FCV decreased signs of illness due to an infectious agent not contained in the vaccine. This nonspecific immunity could be beneficial for protection against organisms for which vaccines are not available and as early protection while specific adaptive immunity is developing.

Presented at the ACVIM Forum in New Orleans on June 1, 2012. Dr. Bradley won a Resident Award for best presentation at the meeting.
Feline upper respiratory tract disease is a leading cause for euthanasia in shelter cats and can be frustrating to treat. The purpose of this study was to evaluate novel treatments for cats from shelters with suspected chronic viral rhinitis that have failed conventional therapy.

Cats from shelters that failed traditional therapy (lysine; antibiotics) for 2-3 weeks were transported to CSU and randomly assigned to one of two treatment groups. Group A was administered human interferon alpha (10,000 Units/kg SQ) once daily for 14 days. Group B was administered an intranasal FHV-1/FCV vaccine (HESKA Corporation, Loveland, CO) on Day 1 as immunotherapy followed by 1 mL of saline SQ once daily for 14 days. A clinical score for each cat was determined daily by a trained, blinded individual. Cats who improved (clinical score < 3) by day 14 were eligible for adoption. Cats with a score of ≥ 3 on Day 14 were entered into the crossover group. Cats who failed both therapies and/or had severe ocular signs were administered famciclovir as a rescue drug for FHV-1. Total DNA and RNA was extracted from nasal or pharyngeal swabs collected prior to the first treatment and evaluated for the presence of FHV-1 DNA and FCV RNA using previously reported molecular assays.

A total of 47 cats were transferred from the shelters to the research facility to enter the treatment study. Of these cats, 16 had clinical signs resolve spontaneously during the final equilibration period before treatment, three cats required famciclovir treatment immediately due to ocular ulcers, one cat had to be euthanized prior to treatment because of severe stomatitis, and one cat was euthanized early during the first treatment period because of severe stomatitis. One cat had a clinical score > 3 after both treatments and famciclovir rescue therapy and was found on workup to have a severe proliferative rhinitis. All other cats (n = 25) had a clinical score of < 3 during the first treatment period or soon after crossover. Response rates to primary treatment with interferon alpha or intranasal vaccine administration were 66.7% (8 of 12 cats) and 100% (13 of 13 cats), respectively (p = 0.039). All four cats with clinical scores > 3 after alpha interferon therapy had clinical scores < 3 two to seven days after the crossover to intranasal vaccine administration. Mean time to response for those cats developing clinical scores < 3 during the first treatment was not significantly different between groups. All six cats positive for nucleic acids of FHV-1, FCV, or both responded to the primary treatment (2 cats-interferon alpha; 4 cats-intranasal vaccine).

Administration of human interferon alpha or a topical FHV-1/FCV vaccine as immunotherapy may be beneficial in alleviating chronic clinical signs of suspected feline viral URTD in some cats.

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