DIAGNOSTIC AND THERAPEUTIC APPROACH TO FELINE UPPER RESPIRATORY INFECTIONS

Michael R. Lappin, DVM, PhD, DACVIM
The Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine
College of Veterinary Medicine and Biomedical Sciences
Colorado State University, Fort Collins Colorado

Abstract. There are many causes of bacterial, viral, and fungal causes of upper respiratory infections (URI) in cats. The primary purpose of this presentation is to update attendees on management of cats with chronic disease that is likely induced by bacterial or viral causes.

Key points

1. The most common primary bacterial infections are due to Bordetella bronchiseptica, *Mycoplasma* spp., and *Chlamydia felis*.
2. The most common viral infections are feline herpesvirus 1 and feline calicivirus.
3. Amoxicillin or doxycycline are the best antibiotics to try for acute bacterial infections.
4. It can be difficult to interpret results of PCR assays on discharges in cats with upper respiratory infectious because of vaccines and subclinical carriers.
5. Lessening stress can lessen recurrent upper respiratory tract infections in cats.

Essential points in client education. In acute upper respiratory infections in cats, treatment may not be needed. If signs of infection last more than 10 days, a complete diagnostic workup should be completed. Making the home less stressful can lessen recurrent signs of upper respiratory disease.

Key words. Feline, herpesvirus, calicivirus, PCR, famciclovir

Please see the ISCAID respiratory treatment guidelines for further information on this very important topic.

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Bacterial causes. Almost all cats with chronic mucopurulent or purulent nasal discharge have a bacterial component to their disease. Diagnosis and treatment was reviewed by the International Society for Companion Animal Infectious Diseases.[1] Primary bacterial disease is rare but may be associated with *Bordetella bronchiseptica*, *Mycoplasma* spp., *Chlamydia felis*, and some *Pasteurella* spp..[1] Recently it was shown that *Bartonella* spp. are not a causes of chronic rhinitis in cats.[2]

Most cases of chronic or recurrent bacterial rhinitis are secondary to other diseases including trauma, neoplasia, inflammation induced by viral infection, foreign bodies, inflammatory polyps, and tooth root abscess. Thus, if routine antibiotic therapy fails with doxycycline or amoxicillin, a diagnostic workup should be performed.[1] If the diagnostic workup fails to find a primary disease and neutrophilic or mixed inflammation is noted, other antibiotics could be considered.[1] Pradofloxacin has been evaluated as a treatment of feline rhinitis and conjunctivitis in several studies and can be considered as a rescue drug for cats with suspected bacterial disease.[3,4] This fluoroquinolone is known to be safe for the use in cats.[5]

In a placebo-controlled, double-blind clinical trial, 39 cats with signs of bacterial upper respiratory infections or conjunctivitis were entered.[4] The cats were randomly entered into 1 of 2 treatment groups: treated orally with either 5 mg/kg pradofloxacin q24hr or 5 mg/kg doxycycline q12hr for 42 consecutive days.[4] Changes in health status and clinical scores were evaluated. The presence of *C. felis* and *Mycoplasma* spp. DNA was determined by quantitative polymerase chain reaction (PCR) and nested PCR of conjunctival swabs, respectively. Prior to treatment, DNA of *C. felis* and *Mycoplasma* spp. was amplified from samples from 23 and 20 cats, respectively. Clinical signs improved markedly within the first week for cats of both groups. Complete elimination of *Mycoplasma* spp. DNA was achieved in both groups. During treatment with either drug, *C. felis* DNA copy number declined quickly, all cats administered doxycycline became *C. felis* DNA negative and 4 cats treated with pradofloxacin remained *C. felis* DNA positive. In this study, it was concluded that both pradofloxacin and doxycycline have good efficacy against *C. felis* and *Mycoplasma* spp., resulting in a marked improvement of clinical signs. The study showed evidence that the pradofloxacin protocol studied may eliminate *Mycoplasma* spp. infections. However, since *C. felis* DNA was still amplified from samples from some cats after treatment with pradofloxacin, infection might not always be eliminated using this protocol.

Since bacterial rhinitis leads to chondritis and osteomyelitis, antibiotic therapy may need to be continued for weeks in cats with chronic disease. Drugs with an anaerobic spectrum that also penetrate bone and cartilage well are often effective. Clindamycin or amoxicillin-clavulanate are frequently used. Amoxicillin-clavulanate has the advantage of killing most *B. bronchiseptica* isolates. Clindamycin has the advantage of effective against *Mycoplasma* spp. and is effective against many anaerobes. After being administered twice daily on the first day, azithromycin can be administered every third day.[1] Cefovecin can be used in cats that are difficult to treat orally, but since it is a beta-lactam, there is no effect against *Mycoplasma* spp..[6] Topical administration of antibiotics by drops or nebulization may be beneficial for some cats but controlled studies are generally lacking. Lessening stress and immune stimulants as discussed for viral disease may be of benefit.

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 amplified in conjunctival cells of

approximately 25% of healthy cats, the positive predictive value of these tests in diseased cats is low.[7] Quantitative PCR may ultimately prove to correlate to the presence or absence of disease but some cats with chronic FHV-1 infections do not have high values.[8,9] 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. For FHV-1, lysine at 250-500 mg, PO, once or twice may be helpful in some cats lessening recurrent disease and has been shown to be safe but should be given as a dose, not fed with food and is not a treatment for active disease. Lysine has been shown to be ineffective for prevention of upper respiratory tract infections in shelter studies and so should not be used for this purpose.[10]

Administration of human alpha 2b interferon at 50 U, PO, daily may help some cats with suspected chronic calicivirus or FHV-1 infection. This can now be formulated for practitioners by prescription at some pharmacies (www.roadrunnerpharmacy.com/) in the USA. In Europe, feline interferon may been beneficial in the management of some cats. Intranasal administration of modified live, intranasal FHV-1 and FCV vaccines may lessen disease in some chronically infected cats.[11] 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.

Famciclovir is currently the orally administered drug of choice for management of acute (and possibly chronic) FHV-1 infections in cats.[12-14] The drug has been prescribed mostly at 40 or 90 mg/kg and is safe at up to 90 mg/kg, PO, q8hrs and so the dose should be increased if lower doses were used and the initial response is suboptimal and FHV-1 is still suspected. Administration of one dose of famciclovir (125 or 500 mg) on admission to an animal shelter was ineffective in lessening clinical signs of disease.[15]

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.[16] The drug is easier to administer (twice daily) than idoxuridine or other anti-FHV-1 ocular therapies and does not cause as much irritation. This drug is available in some compounding pharmacies (www.rxfixer.com). In a recent research study, raltegravir was effective for the management of FHV-1 associated clinical signs in a model.[17]

Immune modulation with a the probiotic *Enterococcus faecium* strain SF68 (FortiFlora®, Purina Pet Care) was effective in lessening stress reactivated FHV-1 signs in a model.[18] Field studies with this probiotic are in progress. Recently, the use of an intranasal product containing 2 Toll-like receptor agonists was beneficial in lessening signs and shedding of FHV-1 in a model.[19] Field studies with this compound are in progress.

Stress relief. Many of the cats with chronic recurrent signs of upper respiratory disease are likely to be infected by FHV-1 or FCV. Stress reactivation of feline viral infections is thought to be common, in particular for FHV-1. All the principles of stress relief for management of feline interstitial cystitis also apply to cats with recurrent signs of URI. In a recent study, use of a

facial pheromone diffusor could lessen recurrent signs of FHV-1 in a mild stress model in experimentally inoculated cats.[20]

Fungal diseases. *Cryptococcus neoformans*, *C. gattii*, and *Aspergillus* spp. are the most common causes of fungal infection in cats. Aspergillosis in cats carries a grave prognosis.

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. Care should be taken if voriconazole is used as it has been associated with neurotoxicity in cats. 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.