One of the most common and frustrating syndromes causing sneezing and nasal discharge in cats is chronic rhinosinusitis (‘chronic snufflers’, ‘chronic cat flu’). While chronic rhinosinusitis (CRS) is commonly associated with viral infection, many affected cats have no history of viral infection or other predisposing causes. A complete diagnostic workup is important to identify the underlying etiology when possible. Unfortunately, for most cats, a cure is not possible and treatment is often life-long. Part of client education is setting realistic expectations.

Clinical Signs
Cats with CRS are typically presented for sneezing and noisy breathing. Nasal discharge may be serous or mucopurulent, if secondary bacterial infection occurs, and is usually bilateral. Unilateral nasal discharge is more likely to be associated with a foreign body or neoplasia. Serous discharge is most likely associated with viral or allergic etiologies. Sanguineous discharge may be associated with intermittent hemorrhage due to inflammation. Occasionally, affected cats are lethargic and anorectic, but generally they are otherwise well. Other clinical signs include ocular discharge, epiphora, dysphagia and halitosis. Clinical signs often persist for years, and in some cases, they are seasonal, suggesting an allergic component.

Etiology
Some, but not all, cats with CRS have a history of infection with feline herpesvirus (FHV-1) or feline calicivirus (FCV) at a young age. Early severe viral infection, particularly with FHV-1, may trigger chronic disease although the role of FHV-1 in CRS remains unclear. In one study of 10 cats with CRS and 7 normal cats, FHV-1 was not found on virus isolation, but was detected by PCR in both groups of cats, indicating actively replicating virus was not present. One theory is that FHV-1 is the inciting cause of CRS, but active infection is not present in symptomatic cats. FHV-1 infection of the respiratory epithelium causes areas of multifocal epithelial necrosis as well as osteolytic changes in the turbinate bones that may be permanent. The damaged turbinates seem to be prone to secondary bacterial infections, possibly because loss of normal nasal architecture disrupts mucociliary function and results in trapping of mucus and bacteria. Latency occurs in approximately 80% of cats infected with FHV-1 and recrudescence may be triggered by stressful events, such as crowding in multi-cat environments, rehoming, immunosuppressive drug therapy, concurrent diseases, etc.

Many affected cats improve when treated with broad spectrum antibiotics but relapse once therapy is discontinued, implying that bacterial infection plays at least a contributory role in CRS. Both aerobic and anaerobic bacterial species can be cultured from biopsy samples and nasal flush samples from cats with CRS. The normal bacterial flora of the feline nasal cavity includes *Pasteurella*, *Staphylococcus* and *Streptococcus*, as well as anaerobic bacteria. Primary bacterial causes of upper respiratory tract disease in cats are uncommon, and include *Bordetella bronchiseptica*, *Mycoplasma* spp., *Streptococcus canis*, and *Chlamydophila felis*. A recent study failed to link *Bartonella* spp to CRS in cats. However, *Mycoplasma felis* may be a more important upper respiratory tract pathogen in the cat than previously thought.

Diagnosis
Diagnosis is often one of exclusion, after ruling out other etiologies, such as trauma, neoplasia (especially lymphoma), fungal infection (e.g., *Cryptococcus*), periodontal disease, nasal foreign body, and nasopharyngeal polyps. A careful physical examination and medical history are very important for the diagnosis of CRS. The face, especially the nose, should be examined carefully for deformity, pain or swelling. The oral cavity should be evaluated for periodontal disease, especially tooth root abscesses. Nasal patency can be evaluated with a chilled glass slide or plucked cat hairs.
A minimum database should be collected (complete blood cell count, serum chemistry panel, urinalysis, FeLV/FIV testing). Fungal serology may be appropriate in certain geographic areas. Cats with recurrent signs may require further diagnostic testing, such as rhinoscopy and skull radiography. Radiographs should include dorsoventral, skyline and lateral views. Common radiographic changes include soft tissue/fluid densities in the nasal cavity and frontal sinuses and destruction of the turbinate bones. Rigid or flexible scopes (<2mm) can be used to examine the rostral feline nasal cavity. Flexible endoscopes can be used to examine for caudal rhinoscopy by retroflexing around the soft palate. If rhinoscopy is planned, biopsy samples should be obtained rather than brush or flush cytology, as biopsies produce a better diagnostic yield. Biopsies should be obtained during rhinoscopy even if the mucosa appears normal. Ideally, biopsies should be obtained with visualization through rhinoscopy, but can also be performed blindly with cup biopsy forceps. The caudal nasopharyngeal cavity can also be examined under sedation with the use of a dental mirror and a spay hook to retract the soft palate. Histopathologically, affected cats are categorized as having lymphocytic-plasmacytic, eosinophilic, or idiopathic rhinosinusitis. Nasal flushing is useful to remove mucus. Nasal flush samples can be submitted for bacterial culture, but the results are typically difficult to interpret due to the normal flora found in the feline nasal cavity. In some areas, advanced imaging modalities are available, such as computed tomography (CT) that may prove useful for selected cases. Full evaluation for nasopharyngeal polyps will require sedation or anesthesia, and retraction of the soft palate.

Virus isolation can be used to document current infection but results are not available for several days and virus culture is not performed by all laboratories. PCR testing of oropharyngeal or conjunctival swabs for respiratory pathogens is widely available. Acquiring adequate material for submission can be challenging in cats; samples should be collected by deep pharyngeal swabbing. Conjunctival swabs may also be used if there is ocular involvement. False positive results may occur due to:
1. Sample contamination either at the source clinic or at the laboratory
2. Previous vaccination
3. Poorly designed tests (e.g., nonspecific primers)

False negative results may occur due to:
1. Poor quality sample
2. Inappropriate sample handling either at the source clinic, during shipping, or at the laboratory
3. Intermittent shedding of the organism

In addition, many respiratory pathogens can be detected in both symptomatic and clinically normal cats, making interpretation of a positive test result difficult. The negative predictive value of the FHV-1 PCR assays is in question because many cats that are likely to have FHV-1 associated disease are PCR-negative. This may relate to clearance of FHV-1 DNA from tissues by the immune reaction. Treatment does not eliminate FHV-1 infection so there is no benefit to follow-up culture or PCR testing. Given the limitations of PCR testing, it may be best to reserve testing for certain situations, such as recurrent disease or outbreaks of disease in multi-cat environments where the results of testing may change treatment plans.

The diagnostic plan can be thought of in phases. Phase 1 (initial presentation): Thorough physical examination, good medical history, minimum database collection, therapeutic trials
Phase 2 (when initial findings indicate further investigation or failure to respond to therapeutic trials): Oropharyngeal exam under sedation, skull imaging (radiography, CT, MRI), rhinoscopy with collection of samples for histopathology and cultures, virus culture or PCR

Treatment
CRS is often resistant to therapy, and control of clinical signs, rather than cure, is the goal of therapy. Broad spectrum antibiotics (e.g., amoxicillin-clavulanate, clindamycin, doxycycline or pradofloxacin) may be used to control secondary bacterial infections. Clindamycin penetrates bone well and has a good spectrum of activity against anaerobes. In a study of 31 shelter cats with upper respiratory tract disease, azithromycin did not perform
better than amoxicillin.\textsuperscript{11} In addition, azithromycin is not effective against \textit{Chlamydophila}.\textsuperscript{12} If there is a positive response to antibiotic treatment, therapy should be continued for 6 weeks or longer, especially if osteomyelitis exists.\textsuperscript{13} Pulse therapy cannot be recommended due to the risk of developing resistant bacterial infections. However, many cats will relapse when therapy is discontinued. Some cats benefit from administration of antihistamines such as chlorpheniramine (1-2 mg/cat, PO, BID). Many other antihistamines are now available, and if one drug is not successful, another should be tried.

In cats with a history of infection with FHV-1, therapies may include lysine, antivirals and immunomodulators. One study found subjective improvement in clinical signs in response to cationic liposome DNA complexes (CLDC) immunomodulatory therapy.\textsuperscript{14} Further research is underway at Colorado State University. Another pilot study evaluated the effect of oral supplementation of \textit{Enterococcus faecium} SF68 (FortiFlora\textsuperscript{®}, Purina Veterinary Diets\textsuperscript{®}) on a small number of cats with chronic FHV-1 infection.\textsuperscript{15} While the results were variable, the findings suggested that the probiotic lessened morbidity and that further studies are warranted.

Feline interferon omega (Virbagen\textsuperscript{®} Omega, Virbac Animal Health) is often recommended for cats with acute and chronic upper respiratory tract disease, but results of controlled studies evaluating efficacy in clinically affected cats with respiratory disease are not available. Low dose oral human recombinant interferon therapy (30 U/kg, PO, daily alternating 7 days on, 7 days off) may be helpful through mediation of inflammatory cytokines. Controlled data on efficacy for treatment of FHV-1 and FCV are lacking. Topical administration of human recombinant interferon in saline to the eyes of cats with conjunctivitis or the nose has been recommended by some veterinarians as an aid in the management of some cats with acute or chronic FHV-1 or FCV infections, but again data on efficacy are lacking.

Antiviral drugs have become more popular in the management of cats with acute or chronic FHV-1 infections. Currently available antiviral medications are only efficacious for DNA viral infections such as FHV-1 and not RNA viruses like FCV as they interfere with viral DNA synthesis and thus viral replication. Famciclovir is safe and effective and is used for both acute and long-term therapy for cats with FHV-1 infections. Recent pharmacokinetic studies suggest that a dose of 40 mg/kg, PO, TID may achieve effective concentrations of the active drug in tears and at the ocular surface.\textsuperscript{16-18} Lysine at 250-500 mg, PO, BID may be helpful in some cats with acute or chronic rhinosinusitis from FHV-1 infection (not FCV).\textsuperscript{19} There is some evidence that lysine is not effective as a dietary supplement, and that bolus administration is more effective.\textsuperscript{20}

Intranasal administration of modified live FHV-1 and FCV vaccines may lessen disease in some chronically infected cats but controlled data are lacking. In one study, a modified live FHV-1 and FCV intranasal vaccine decreased signs of illness in cats experimental infected with \textit{Bordetella bronchiseptica}, suggesting intranasal vaccination can stimulate short-lived nonspecific immunity.\textsuperscript{21} If there is a positive response, this form of immunotherapy can be administered up to three times per year.

Therapy with immunosuppressive medications, such as corticosteroids, should be used with caution as they may exacerbate viral and bacterial components of the disease. However, since CRS is likely multifactorial and is poorly understood, patients diagnosed with lymphocytic-plasmacytic rhinitis may respond to immunosuppressive drug therapy, such as prednisolone (1-2 mg/cat, PO, BID). The lowest dose and the longest dosing interval that is effective should be determined by adjusting the dose over time. Beclomethasone and fluticasone are available as inhaled formulations and may have direct beneficial effects on the nasal mucosa in some cases. They can be administered via metered dose inhaler with a feline inhalation chamber at 1-2 puffs once to twice daily. Finally, some cases will respond to cyclosporine (25 mg/cat, PO, once daily to once every other day). Trough blood levels should be checked two weeks after initiation of therapy to ensure that excessive blood levels are not achieved which may activate latent infectious diseases such as toxoplasmosis. Caution should be used in cats that are FeLV- or FIV-positive.
Nonspecific therapies include nebulization with saline and the use of saline nasal drops to help loosen secretions, especially in dry environments. The nares should be kept free of dried discharges. Some authorities recommend the use of pediatric nasal decongestant drops. Inappetent cats must be coaxed to eat or treated with appetite stimulants (e.g., cyproheptadine). In multi-cat environments, CRS can be a significant problem and measures to reduce environmental stressors may be beneficial. Feline facial pheromone may also be helpful.

References