CHRONIC CANINE RHINITIS

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Chronic nasal disease is an infrequent problem in dogs. However, when present, it commonly may become a frustrating problem to properly diagnose and in some situation to clinically manage. Attempts to achieve an early diagnosis should be made. Symptomatic therapy will unnecessarily delay diagnosis and may lead to situations where treatment becomes either exceedingly difficult or essentially impossible. This is especially important in dogs with fungal rhinitis or nasal neoplasia, where early diagnosis will potentially improve response to therapy.

CAUSES FOR CHRONIC NASAL DISEASE IN DOGS

The principle diseases associated with chronic rhinitis in dogs are sinonasal neoplasia, idiopathic lymphoplasmacytic rhinitis, fungal rhinitis, dental disease and chronic nasal foreign bodies. Nasal discharge is not limited to primary nasal disease, but also may occur with systemic and extranasal disorders. Very often extranasal disorders have systemic signs (e.g. depression, pyrexia, hemorrhage) and a history of acute onset whereas primary nasal disorders (other the initial phase of nasal foreign bodies) have a more chronic duration. Important extranasal disorders that may present with nasal discharge include coagulopathies, vasculitis, hypertension, hyperviscosity syndrome, and pneumonia.

The character and type of nasal discharge may be helpful in developing a list of potential causes, but is not characteristic for specific diseases. Unilateral discharge is often associated with neoplasia, fungal and foreign body rhinitis, and dental disease. Bilateral discharge is typical of systemic disorders, advanced neoplasia or fungal rhinitis, idiopathic lymphoplasmacytic rhinitis, and allergic rhinitis. However, it also is possible for systemic disorders and idiopathic lymphoplasmacytic rhinitis to present with only unilateral nasal discharge. Serous nasal discharge may be seen initially with a variety of nasal disease, but often becomes mucopurulent as disease progresses and secondary bacterial invasion occurs. Mucopurulent nasal discharge is most common and indicates bacterial infection ***secondary*** to an underlying disorder that has damaged the nasal mucosa with resultant bacterial invasion. **Primary bacterial infection is an exceedingly rare cause of chronic rhinitis in dogs.** Mucopurulent and serous discharges may be blood-tinged as a result of mucosal erosion. Epistaxis usually results from an underlying nasal disorder causing erosion of a major blood vessel, but also may be seen with systemic disorders such as coagulopathies, hypertension, vasculitis or hyperviscosity syndrome.

APPROACH TO THE DIAGNOSIS OF CHRONIC NASAL DISEASE IN DOGS

Clinical history and physical examination findings generally offer an indication for primary nasal disease as opposed to systemic or extranasal disease. Routine laboratory tests (complete blood count, serum chemistries, urinalysis), coagulation profile, blood pressure and thoracic radiographs are important to rule out most of the systemic or extranasal causes for nasal discharge. Cytologic evaluation of nasal discharge is rarely helpful other than possibly for identification of Eucoleus [Capillaria] boemhi parasitic ova. Bacterial and fungal cultures of nasal discharge are not recommended as they are nonspecific and frequently simply represent resident bacteria and fungi within the nose. Serologic tests for aspergillosis and penicilliosis should be delayed because some normal dogs and some dogs with nasal neoplasia will have positive results. Empirical antimicrobial treatment is not advised and merely delays definitive diagnosis unless Bordetella bronchiseptica or Pasteurella multocida rhinitis (both very rare), or pneumonia is present. Mucopurulent nasal discharge is next to always a result of secondary bacterial rhinitis due to an underlying primary nasal disease.

Anesthesia is required for further evaluation of most dogs with rhinitis. A thorough oral examination with inspection of the hard palate, oropharynx and dental structures should be performed. A periodontal probe should be used to inspect the gingival sulci of maxillary teeth. Oronasal fistulae are often associated with the maxillary, third incisors, first and second premolars, and the mesial root of the third premolar. Diagnostic imaging studies and rhinoscopy require general anesthesia. Nasal computed tomography is the imaging modality of choice in dogs with chronic rhinitis. Rhinoscopy may have limited utility depending on the nature and severity of nasal discharge present. Retroflex nasopharyngoscopy is of value to examine the nasopharyngeal region for the presence of foreign

bodies. Following evaluation of the nose, nasal biopsy is required for definitive diagnosis. Nasal flushing may be done if foreign material is suspected to be present within the nose.

COMMON CASUSES OF CHRONIC RHINITIS IN DOGS

Geographic locality will play role, but excluding nasal foreign bodies and dental disease, the most common causes for chronic rhinitis in dogs are neoplasia, idiopathic chronic (lymphoplasmacytic) rhinitis and fungal rhinitis. Parasitic rhinitis is uncommon. The treatment for nasal mites (Pneumonyssus caninum) is ivermectin 0.2 mg/kg, PO with the dose repeated in 2-3 weeks. The treatment for nasal nematodes (Eucoleus [Capillaria] boehmi) is not clearly defined although ivermectin 0.2 mg/kg, PO once has been reportedly effective. Allergic rhinitis is often mild, but if severe, antihistamines such as diphenhydramine, chlorpheniramine, or trimeprazine-prednisone (Temaril-P®, Pfizer Animal Health) may be prescribed to control symptomatology. In the rare situation of bacterial rhinitis due to Bordetella bronchiseptica, doxycycline 5-10 mg/kg q12h, PO for 2 weeks may be effective.

Fungal Rhinitis

Fungal rhinitis is a relatively common cause of chronic rhinitis in the dog within various geographic regions throughout North America. Aspergillus fumigatus is the most common cause of fungal rhinitis in dogs, but occasionally Penicillium species and Rhinosporidium seeberi and very rarely Cryptococcus neoformans may cause disease. Rhinosporidium seeberi is associated with the growth of a granulomatous mass within the rostral nasal cavity. Cytology of tissue from these granulomatous masses is often diagnostic. Treatment for rhinosporidiosis is best accomplished by aggressive surgical resection of the granulomatous mass.

Nasal aspergillosis is most commonly seen in young to middle-aged dolichocephalic dogs with German Shepherd and Rottweiler breeds reported to be predisposed. Affected dogs present with copious unilateral or bilateral mucopurulent nasal discharge. Sneezing is common and may be accompanied by mild to severe epistaxis. Facial pain and depigmentation and ulceration of the nasal planum may be present. In contrast to nasal neoplasia, facial distortion is unusual in all but advanced cases of fungal rhinitis. Nasal CT images along with rhinoscopic visualization of the nasal cavity is noteworthy for the presence of dramatic turbinate loss within the nasal cavity. Sinus involvement may be present. Invasion through the maxillary or palatine bones with extension into surrounding soft tissue structures is occasionally seen. Nasal CT scan is preferred over radiographs so that the integrity of the cribriform plate prior may be evaluated prior to local antifungal therapy. A noninvasive form of nasal aspergillosis infrequently occurs in the dog and is characterized by compact masses of mycelia (“fungal balls”) filling larger airspaces or frontal sinuses.

Diagnosis of nasal aspergillosis is confirmed by visualization of fungal plaques on nasal mucosa and demonstration of branching septate hyphae on cytologic or histologic samples from affected regions within the nose. There is high accuracy of cytology samples in the diagnosis of nasal aspergillosis or penicilliosis when collection is done under direct endoscopic visualization; whereas, there is poor value of samples collected by blind swabs or preparations from samples of nasal discharge. Serologic tests positive for aspergillosis also support the diagnosis although negative results may occur even with extensive disease. Cultures of nasal discharge may be misleading in that 30-40% of cultures from normal dogs and those with nasal neoplasia can yield Aspergillus or Penicillium species. Despite properly obtained samples there are some cases that fail to demonstrate fungal organisms. Repeated sampling or a trial of antifungal drugs may well be indicated in dogs with a high index of suspicion for nasal aspergillosis.

The prognosis for treatment of nasal aspergillosis is fair to good, but relapses are possible necessitating re-treatment. Treatment of nasal aspergillosis has classically been approached with topical infusion of either clotrimazole or enilconazole, providing the cribriform plate is intact. Topical therapy is more effective than orally administered antifungal agents. Clotrimazole (Lotrimin solution®, Schering Plough Corp.) is available over the counter as a 1% solution and enilconazole (Clinifarm-EC®, Sterwin Labs, Inc.) is provided as 13.8% concentrate which is diluted to a 1, 2, or 5% solution prior to instillation in the nasal cavity. Debridement and removal of diseased turbinate structures through the rostral nares prior to topical therapy will greatly improve response to treatment. Topical therapy with either drug alone is not effective in dogs in which the organism has invaded soft tissue structures adjacent to the nose. In these cases, topical therapy is recommended to be combined with systemic antifungal agents. Exploratory rhinotomy and turbinectomy prior to topical treatment or oral antifungal therapy is often detrimental and not recommended.

The topical application of enilconazole through surgically placed catheters into the frontal sinuses and nasal chambers has a success rate up to 90%. This procedure is quite distressing to most patients, however. Catheters are implanted surgically into both nasal chambers and frontal sinuses via trephine holes in the sinuses. Enilconazole is flushed through the catheters twice daily at a dosage of 10 mg/kg for a total of 7-10 days. Complications include

premature removal of the catheters, subcutaneous emphysema, inappetence, and ptyalism. Some patients may become aggressive and intolerant of the procedure necessitating premature abandonment of therapy. Because of these serious and frequent side-effects, topical therapy with clotrimazole is the treatment of choice. Clotrimazole is applied as a soak with the solution maintained in the nasal cavities for 1 hour with the patient under anesthesia. A total volume of 60 ml of a 1% solution of clotrimazole is slowly infused through catheters placed into the right and left nares. A nasopharyngeal Foley catheter and sponges placed in the caudal pharyngeal region are positioned prior to the procedure to minimize leakage of the infusate caudally. The head is rotated every 15 minutes to ensure contact with all nasal surfaces. Up to 90% of patients may be cured with a single procedure, although some dogs will require a second procedure 3 weeks later. Side effects of clotrimazole therapy include severe pharyngitis and pharyngeal edema.

Recently another approach with excellent success rate, shorter treatment time, and low patient morbidity has been reported using a combination of clotrimazole irrigation and depot therapy. Frontal sinus trephination is followed by a short, five-minute flushing of 1% topical clotrimazole solution followed by a 1% clotrimazole cream instilled as a depot agent into the frontal sinuses. The dog is positioned in sternal recumbency with the pharynx packed with cotton gauze to prevent aspiration of fluid debris and the head is tilted downwards to allow fluid from the nasal sinuses to drain rostrally. The frontal bone is trephined to permit passage of a 10 French gauge Jacques urethral catheter into each sinus. The sinuses are first irrigated with 500 ml of warm saline over 5 minutes to establish appropriate catheter placement and patency of the nasofrontal ostium. The sinus are then irrigated with 1% clotrimazole solution. For dogs weighing more than 10 kg, a total of 1 g of clotrimazole solution is used (50 ml per side) and for dogs weighing less than 10 kg, a total of 500 mg is used (25 ml per side). Clotrimazole 1% cream is then introduced into the frontal sinuses. For dogs weight more than 10 kg, a total of 40 g (20 g per side) is used and for dogs weighing less than 10 kg a total of 20 g (10 g per side) is used. The catheters are then removed, the skin incisions are closed, and excess fluid is allowed to drain from the sinuses before the pharyngeal gauze is removed. With this treatment protocol, 86% of dogs with nasal aspergillosis or penicilliosis established a cure from infection. This author suspects that cure rate would be greater if debridement of diseased nasal turbinates through the rostral nares is done prior to the combination clotrimazole irrigation and depot therapy is performed.

Oral antifungal agents have relatively poor efficacy against Aspergillus infection, but are recommended if the cribriform plate is penetrated. Oral antifungal agents are used in combination with topical agents if invasion of local bone and soft tissue structures is present. The newer azole derivatives have the best results. Side effects of the azole antifungal agents include anorexia, vomiting, lethargy, elevated BUN, skin ulcerations, fever, and hepatotoxicity. Itraconazole (Sporanox®, Janssen) is recommended due to its low toxicity. Itraconazole 5 mg/kg q12h, PO given for 3-6 months may cure up to 60-70% of dogs with aspergillosis, although some studies have shown marginal effects of this drug on this disease. Terbinafine (Lamisil®, Novartis) is another option and well tolerated. Terbinafine 5-10 mg/kg q12h, PO appears to have similar efficacy to itraconazole when given for 3-6 months. Fluconazole (Diflucan®, Pfizer) is an additional alternative with a cure rate up to 60% when given at a dose of 2.5-5 mg/kg q12h, PO for 3-6 moths. Voriconazole (Vfend®, Pfizer) is a new generation broad-spectrum antifungal agent that shows activity against a wide range of yeasts and filamentous fungi. Voriconazole demonstrates both fungicidal and fungistatic activities in vitro against Aspergillus sp. superior to that of fluconazole. Voriconazole may prove to be an effective antifungal drug for treatment, however clinical experience with this drug is currently lacking in veterinary medicine.

Idiopathic Lymphoplasmacytic (Chronic) Rhinitis

Idiopathic lymphoplasmacytic rhinitis is a relatively common cause of chronic nasal disease in the dog. The definitive etiology of lymphoplasmacytic rhinitis remains undetermined; however, it is likely a stereotyped chronic inflammatory response to multiple precipitating factors. Inhaled aeroallergens and irritants likely play a primary role in development of this disease. Hypersensitivity to native commensal fungal organisms within the nose also may play a role in some patients. Young to middle-aged dolichocephalic and mesaticephalic large breed dogs and Dachshunds are typically affected. Chronic unilateral to bilateral mucoid to mucopurulent nasal discharge is often present, although some dogs may have mucohemorrhagic discharge or epistaxis. Obstruction to airflow through the nose may result from excessive mucous within nasal passages and turbinate mucosal edema. Lymphoplasmacytic inflammation may be present with nasal neoplasia, fungal rhinitis or foreign body rhinitis, therefore it is imperative that these diseases be thoroughly excluded before a diagnosis of idiopathic lymphoplasmacytic (chronic) rhinitis is entertained.

Nasal radiography is not sufficient to differentiate chronic inflammatory rhinitis from neoplasia or fungal rhinitis because similar changes such as turbinate destruction and soft tissue opacification of the nasal passages and frontal sinus may be seen in each of these diseases. Nasal CT is recommended because it greatly enhances the ability

to differentiate inflammatory from neoplastic diseases. Nasal CT lesions with idiopathic chronic rhinitis may be completely unremarkable or disclose unilateral or bilateral mild to moderate turbinate destruction with mucous accumulation within air passages and sinuses. Occasionally the turbinate destruction may be severe mimicking that seen with fungal rhinitis. Destruction of the nasal septum, frontal sinuses or cribriform plate, or extension of soft tissue density into the nasopharynx or periorbital region is not expected with idiopathic chronic rhinitis and should prompt investigation into fungal rhinitis or neoplastic disease.

The most common rhinoscopic abnormalities seen are unilateral or bilateral erythema or hyperemia and edema of the nasal mucosa with the presence of mucopus with air passages. Turbinate atrophy or loss is occasionally appreciated. Nasal samples for microbial culture are not informative and not recommended. Histologic changes include mild to severe lymphoplasmacytic inflammation with occasional infiltration of neutrophils or eosinophils[3]. Turbinate remodeling or destruction may be absent or vary from mild to severe. The severity of histologic changes may show discordance between the right and left sides of the nasal cavity.

Treatment for idiopathic lymphoplasmacytic rhinitis is extremely frustrating with cure rarely achieved. Although this is not a life-threatening disease, owners of dogs so affected are often distraught by their pets nasal obstruction or the need to frequently clean up nasal discharge or nasal hemorrhage within the house. Allergen avoidance is rarely helpful; however, avoidance of secondhand smoke can substantially reduce signs in some dogs. Despite earlier reports in the literature, systemic corticosteroids are seldom effective in controlling clinical signs, and actually may worsen clinical signs. The use of oral glucocorticoid medications should be avoided. Topical glucocorticoid therapy with nasal steroid drops or aerosolized steroids administered using metered dose inhalers attached to a spacer and tightly fitting face mask has been shown anecdotal promise in some dogs with chronic rhinitis. Antihistamine medications are rarely effective, but they occasionally slightly reduce the severity of nasal discharge. Long-term administration of antibiotics having immunomodulatory effects combined with nonsteroidal antiinflammatory agents can be helpful in some dogs. Doxycycline 3-5 mg/kg q12h, PO or azithromycin 5 mg/kg q24h, PO in combination with piroxicam 0.3 mg/kg q24h, PO is recommended. If distinct clinical improvement is observed within 2 weeks, daily piroxicam therapy is continued but the frequency of administration of doxycycline is reduced to once daily or azithromycin reduced to twice weekly. Therapy will likely be required for a minimum of 6 months if not indefinitely.

This author is currently investigating the use of oral itraconazole therapy in dogs refractory to other therapeutic modalities out of reasoning that chronic fungal hypersensitivity to ubiquitous fungi may play a role in this disease. Chronic rhinosinusitis in humans is an inflammatory disease with numerous predisposing factors, including genetics, pollution, anatomic abnormalities, bacteria, and fungus. Hypersensitivity to ubiquitous fungi is currently thought to play a role in some people with chronic rhinosinusitis. Immune sensitization to ubiquitous fungi with subsequent production of various cytokines has been proposed as initiating and later perpetuating factors for chronic rhinosinusitis in humans. Topical antifungal therapy has been shown to benefit some human patients with chronic rhinosinusitis, but not others. Nasal biopsies from dogs with lymphoplasmacytic rhinitis have been reported to display an elevated transcription of fungal genes as compared to dogs with nasal neoplasia using PCR techniques. Whether hypersensitivity to ubiquitous commensal nasal fungal organisms is involved or molecular techniques are detecting entrapment of fungal organisms is unclear. Preliminary experience with the administration of itraconazole 5 mg/kg q12h, PO for a minimum of 3-6 months has shown a dramatic beneficial improvement of clinical signs in some dogs with this disease. Although eosinophilic inflammation is characteristic for humans with chronic rhinosinusitis and lymphoplasmacytic inflammation is characteristic for dogs with idiopathic chronic rhinitis, there may be a species-dependent difference in cytokine response and subsequent inflammatory response to fungal organisms. At this time it is unclear, but fungal hypersensitivity may be a significant underlying cause for lymphoplasmacytic rhinitis in some dogs.

Nasal Neoplasia and Nasal Polyps

Nasal neoplasia is an important cause of chronic nasal disease in middle aged to older dolichocephalic and mesaticephalic dogs. Nasal neoplasia accounts for approximately one third of all dogs with chronic nasal disease. Tumors of epithelial origin account for approximately two thirds of canine nasal neoplasms. The majority of nasal tumors are malignant and primarily arise within the nasal cavity, although they occasionally may arise in the paranasal sinuses. Nasal tumors are primarily locally invasive with local to widespread destruction of nasal turbinates seen initially and invasion of septal, cribriform, or facial bones later in the course of disease. Metastasis to regional lymph nodes or lung may occur, but this is rare and generally occurring in the very late stage of disease. Clinical signs are primarily related to obstruction of air flow through the nasal cavities, mucopurulent nasal discharge, epistaxis, sneezing, and reverse sneeze. Facial deformity or swelling, exophthalmia, or neurological signs may be seen as a result of tumor destruction of facial bones or cribriform plate. Facial pain and head shyness is

rarely seen (unlike that with fungal rhinitis). In some patients, initial clinical signs may be very subtile with unexplained onset of snoring and occasional reverse sneeze reported.

For dogs presenting primarily for epistaxis, a coagulation profile, CBC with platelet count, blood pressure, and serum proteins should minimally be evaluated in order to rule out coagulation disorders, hypertension, and hyperviscosity syndromes as possible causes for epistaxis prior to nasal diagnostic imaging studies and nasal biopsy. Nasal radiographs are frequently limited in their ability to distinguish subtile lesions or changes seen with nasal tumors that overlap with chronic and fungal rhinitis. Nasal CT is a vastly superior imaging modality for differentiating neoplastic from nonneoplastic disease and detection of bone destruction and neoplastic extension into surrounding structures. Nasal CT also is needed for staging, to delineate tumor boundaries, and to plan for radiation therapy. Three-dimensional reconstructions of the CT study may clarify the extent of bone destruction in situations where very subtile boney lesions are present. Retroflex nasopharyngoscopy is recommended to evaluate the nasopharyngeal region and identification of tumor extension through the caudal nares. Anterior rhinoscopy in dogs with nasal neoplasia may reveal a mass lesion protruding within and occluding nasal air passages. Multiple biopsies of masses should be obtained to increase the likelihood of diagnosis as severe inflammation often surrounds nasal tumors. Frequently nasal tumors cannot be visualized due to hemorrhage or because their origin is in an inaccessible region of the nose. In these situations, nasal CT studies facilitate direction and location for blind biopsy of the affected region of the nose.

Radiation therapy is the treatment of choice for most nasal tumors. Thoracic radiographs are recommended when nasal neoplasia is identified prior to radiation therapy to rule out metastatic lung disease. Surgery alone is ineffective with survival times similar to that observed in untreated dogs. Results with cryosurgery, either alone or in combination with radiation therapy, have been disappointing and is not recommended. There is limited information on the response of nasal tumors to chemotherapy alone. The median survival in a very small group of dogs with nasal adenocarcinoma given cisplatin alone was 20 weeks, which is comparable to no treatment. However, cisplatin is occasionally used as a radiation sensitizer in radiotherapy protocols. Cytoreductive surgery is recommended prior to orthovoltage radiation therapy. Depending on the mode of radiation therapy available, approximate median survival times are between 16.5-23 months and approximate 1 year survival rates are between 54-60% in dogs with nasal neoplasia. Exenteration of the nasal cavity following accelerated radiotherapy significantly prolongs survival time in dogs with intranasal neoplasia over radiotherapy alone.

Polyps within the nasal cavity are very rare in dogs. These are usually unilateral and rhinotomy is required for removal of the polypous tissue and surrounding conchae. Recurrence 1-2 years later is possible. To date, in all dogs I have seen with an initial diagnosis of a polyp, careful review of nasal CT has demonstrated localized turbinate destruction and the subsequent histologic diagnosis following surgical resection of the polypous tissue has been low-grade fibrosarcoma associated with moderate to severe chronic inflammation.