Canine Chronic Inflammatory Rhinitis

Rebecca C. Windsor, DVM*, and Lynelle R. Johnson, DVM, PhD, DACVIM†

Chronic inflammatory rhinitis is commonly found in dogs with chronic nasal disease and is characterized by lymphoplasmacytic infiltrates in the nasal mucosa in the absence of an obvious etiologic process. The pathogenesis of lymphoplasmacytic rhinitis remains unknown. Animals respond poorly to antibiotics, oral glucocorticoids, and antihistamines, making primary infectious, immune-mediated, or allergic etiologies unlikely. Aberrant immune response to inhaled organisms or allergens may induce inflammation in some animals. Common clinical signs include nasal discharge, sneezing, coughing, epistaxis, and stertor. Diagnosis is made by performing a thorough history, physical examination, radiography or advanced imaging (via computed tomography or magnetic resonance imaging), rhinoscopy, and nasal mucosal biopsy to rule out primary etiologies of nasal discharge. Treatment strategies have included various antibiotics, antihistamines, oral and inhalant steroids, nonsteroidal antiinflammatories, and antifungal medications. Some dogs may respond partially to doxycycline or azithromycin, although it is unclear whether response is related to antimicrobial or antiinflammatory properties of these drugs. Hydration of the nasal cavity through nasal drops or aerosols may limit nasal discharge, and some animals may improve with inhalant (but rarely oral) glucocorticoids.

Keywords rhinitis, nasal, canine, inflammatory, lymphoplasmacytic

The most common causes of chronic nasal discharge in dogs include nasal neoplasia, fungal rhinitis, and lymphoplasmacytic rhinitis (LPR), also referred to as inflammatory rhinitis. Other causes of chronic nasal disease include nasal foreign body, rhinitis secondary to dental disease, parasitic rhinitis (Pneumonyssoides caninum), and primary ciliary dyskinesia. Idiopathic LPR is recognized with increasing frequency in the canine population and may be more common in certain geographic locations. Diagnosis is made via histopathologic identification of a lymphoplasmacytic infiltrate in the nasal mucosa with exclusion of specific causes of chronic inflammation. An effective therapeutic regimen for dogs with LPR has not been established, largely because the underlying pathogenesis is still unknown.

Etiology

The etiology of LPR has not been determined, although infectious, allergic, and immune-mediated mechanisms have been suggested. LPR may have a multifactorial etiology in some dogs and/or different etiologies in different dogs, making it difficult to develop general treatment guidelines.

Primary Infection

Primary bacterial infection of the nasal cavity is rare, and no single infectious organism has been identified in dogs with LPR. However some dogs respond anecdotally to certain antibiotics including doxycycline and azithromycin, leading to the speculation that certain bacterial organisms such as Chlamydophila, Mycoplasma, or Bartonella could be involved in the pathogenesis of LPR. Chlamydophila is a primary upper respiratory pathogen in humans, cats, and other species. Bartonella has been associated with nasal discharge, granulomatous rhinitis, and epistaxis in dogs. A recent study investigating the role of infectious organisms in LPR quantified DNA loads of Chlamydophila, Bartonella, Canine-adenovirus 2 (CAV-2), and Parainfluenza virus 3 (PI-3) in biopsy samples from dogs with LPR by the use of quantitative PCR, and a role for these organisms could not be established. In addition, endpoint PCR was used to examine nasal biopsy samples for evidence of Mycoplasma spp. and this also failed to identify a specific pathogen in DNA extracted from formalin-fixed nasal biopsy samples. The poor long-term response to multiple antibiotics in dogs with LPR suggests that a primary bacterial infectious etiology is unlikely, although ongoing studies investigating serologic evidence of Bartonella in dogs...
with LPR may provide valuable information on the role of this organism in the syndrome.

Secondary Infection
Secondary bacterial infection is common in dogs with chronic nasal disease, which may explain the transient response to antibiotics seen in some dogs with LPR. Nasal cultures from dogs with LPR yield mixed bacterial growth of normal nasal flora including *Staphylococcus*, *Streptococcus*, *Escherichia coli*, *Proteus*, *Pasteurella*, *Corynebacterium*, *Bordetella*, and *Pseudomonas*. A recent study demonstrated no significant difference in bacterial DNA loads among dogs with LPR, fungal rhinitis, and nasal neoplasia; however, all three disease groups had significantly higher bacterial loads than did healthy control dogs. Accumulation of bacterial organisms in dogs with chronic nasal disease could result from mucus trapping and decreased nasal mucosal defense mechanisms.

Role of Fungal Organisms
*Aspergillus* and *Penicillium* spp. are common inhabitants of the canine nasal cavity, and a positive fungal culture can be found in the absence of primary fungal rhinitis. *Candida*, *Trichosporum*, and *Cladosporium* have also been cultured from dogs with LPR. In the study assessing molecular content of paraffin-embedded nasal tissue from dogs, higher fungal DNA loads were reported in dogs with LPR than in healthy control dogs and dogs with nasal neoplasia. Mucus trapping and decreased nasal defense mechanisms alone cannot explain this difference because dogs with nasal neoplasia would be expected to have similar mucosal compromise to dogs with LPR. Further research is required to determine the significance of increased fungal DNA in dogs with LPR. Fungal hypersensitivity characterized by an aberrant immune response has been identified in human chronic rhinosinusitis (CRS) patients. Humans with CRS exhibit a humoral and cellular (Th1 and Th2) response to airborne fungi. T-cell sensitization to fungus leads to production of T-helper 2 cytokine release, namely Interleukin-5. Fungal hypersensitivity in humans appears to be characterized by IgG3 rather than IgE production, suggesting that the hypersensitivity is not a true allergic response. Although humans with CRS do exhibit a predominantly eosinophilic infiltration. In humans, the quantity of fungal DNA does not correlate with disease severity. Further research is needed to assess the immune response of affected dogs to resident fungal organisms.

Allergy
There is some speculation that respiratory allergy may manifest with signs of chronic rhinitis as is seen in humans, although evidence of allergic rhinitis as a recognized disease entity in dogs has yet to be established. It is possible that dogs with LPR exhibit a heightened immune response to inhaled environmental allergens; however, no published studies to date have demonstrated an allergic inflammatory pattern in dogs with naturally occurring LPR. Experimentally, nasal congestion has been induced using ragweed pollen in Beagle colonies, and evidence of allergic response to house dust mite antigen characterized by increased IL-4 expression and Th2 immune response was identified in the peripheral blood mononuclear cells of three dogs with rhinitis. Nasal mucosal biopsies were not collected from dogs in these studies so it is not known whether lymphoplasmacytic infiltration characterized the disease. Dogs with LPR generally respond poorly to antihistamines and glucocorticoids, making an allergic etiology unlikely.

Immune-Mediated
The initial report describing LPR suggested that the disease was likely immune-mediated because three of five dogs in that study demonstrated a favorable response to glucocorticoids. Historically, in our experience, most dogs with LPR have exhibited a poor response to oral glucocorticoid treatment, suggesting that a primary immune-mediated etiology is unlikely. Cats with nasal inflammation exhibit a heightened Th1 immune response that is more pronounced as inflammation becomes more severe; however, information is not available in dogs. Further studies evaluating the immune-regulatory patterns in the nasal mucosa of dogs with LPR are required to determine the role of immune dysregulation in disease.

<table>
<thead>
<tr>
<th>Table 1 Common Clinical Signs in 37 Dogs with Idiopathic Rhinitis</th>
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<tbody>
<tr>
<td><strong>Mucopurulent, mucoid, or serosanguineous nasal discharge</strong></td>
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<tr>
<td><strong>Sneezing</strong></td>
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<tr>
<td><strong>Coughing</strong></td>
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<tr>
<td><strong>Epistaxis</strong></td>
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<tr>
<td><strong>Reverse sneezing</strong></td>
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<td><strong>Stertor</strong></td>
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<td><strong>Ocular discharge</strong></td>
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<td><strong>Pawing at the muzzle</strong></td>
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Important historical features in dogs with chronic rhinitis include duration and progression of clinical signs, character and laterality of nasal discharge, and response to previous medical therapies. LPR can be seen in any breed but occurs most commonly in large-breed dogs. There is no apparent age or sex predilection. Duration of clinical signs may range from weeks to years at the time of diagnostic evaluation. The most common clinical signs include nasal discharge, sneezing, coughing (likely secondary to pharyngitis caused by swallowing irritant nasal secretions), and episodes of epistaxis (Table 1). Although signs related to LPR are often bilateral, many dogs with LPR have unilateral or lateralizing signs on presentation. Laterality of clinical signs based on history and physical examination correlates poorly with computed tomography, rhinoscopy, and biopsy findings. Therefore, while unilateral nasal discharge is classically considered more typical of nasal neoplasia, fungal rhinitis, foreign body rhinitis, or an oronasal fistula, LPR remains a consideration, and all dogs with unilateral nasal discharge historically or on physical examination should be evaluated for bilateral nasal disease. Other clinical signs of LPR may include reverse sneezing, stertor, ocular discharge, and pawing/rubbing at the muzzle.
Dogs with LPR typically have a history of poor or transient response to medical treatment. Many animals demonstrate little improvement with antibiotics, antihistamines, and glucocorticoids alone or in combination, while some demonstrate a transient response with return of clinical signs when medications are discontinued.

Physical Examination
The most common physical examination findings in dogs with LPR include fresh or dry nasal discharge or crusting around the nares. Most animals have mucoid or mucopurulent discharge, but hemorrhagic or serous discharge may be seen. Nasal airflow should be assessed using a microscope slide or cotton ball wisp. When assessing the patency of airflow, each nostril should be manually occluded to watch for a stress response, indicating occluded nasal airflow in the contralateral nostril. Nasal airflow is normally preserved in dogs with LPR, since obstruction would be more typical of a mass lesion.

Facial palpation is often unremarkable in patients with LPR, which may be helpful in differentiating it from fungal rhinitis and nasal neoplasia, where facial pain is more common. Dogs with nasal neoplasia may also exhibit facial or skull deformity, which is not seen in dogs with LPR. Ocular retropropulsion should be performed to detect retrobulbar masses or abscesses as a cause for nasal discharge. Nasal planar depigmentation may rarely be noted in dogs with severe and long-standing discharge associated with LPR but is more commonly exhibited in dogs with fungal rhinitis or immune-mediated dermatologic diseases such as discoid lupus erythematosus. Assessment of regional lymph nodes is important in animals with nasal discharge due to the tendency for neoplastic processes to metastasize locally. Lymph nodes are often enlarged in dogs with LPR or fungal rhinitis, but aspiration cytology reveals a reactive inflammatory process rather than neoplasia.

Diagnostic Evaluation
Laboratory Evaluation
Complete blood count, chemistry panel, and urinalysis are often unremarkable in patients with chronic rhinitis. Dogs with epistaxis should be evaluated for clotting abnormalities by performing a platelet count OSPT, APTT, and BMBT to rule out coagulopathies, thrombocytopenias, and/or thrombocytopenias. Dogs presenting primarily for epistaxis should also have blood pressure measured for detection of systemic hypertension.

Imaging Techniques
Radiography has been used in some cases to help differentiate LPR from nasal neoplasia but has become less popular due to the availability of superior imaging techniques. Some dogs with LPR have radiographic evidence of lucent foci and multifocal lesions, which are not typically seen in dogs with nasal neoplasia. Neoplastic lesions are more likely to invade surrounding bone; however, neoplastic lesions without obvious osteolysis may be difficult to differentiate from chronic rhinitis cases as both diseases cause soft-tissue opacification. Although one study identified the absence of frontal sinus involvement on radiographs as a positive predictive indicator for LPR compared with neoplasia, a recent study showed that a high percentage of dogs with LPR have frontal sinus fluid accumulation. LPR is difficult to differentiate from fungal rhinitis via radiography as both can cause turbinate destruction and frontal sinus accumulation.

Recent studies have demonstrated that computed tomography (CT) is more sensitive and specific than radiography in differentiating LPR, nasal neoplasia, and fungal rhinitis. The most common CT findings in dogs with LPR include fluid accumulation within the nasal passages, soft-tissue opacification, turbinate destruction, frontal sinus accumulation, and gas pocketing (Figs. 1 and 2 and Table 2) Imaging abnormalities noted on CT are often diffusely distributed throughout the nasal cavity, but rostral or caudal localization may be observed. Turbinate destruction tends to be less severe in dogs with LPR compared with dogs with nasal neoplasia or fungal rhinitis. Dogs with nasal neoplasia commonly exhibit a soft-tissue density with extensive turbinate destruction, while those with fungal rhinitis exhibit extensive turbinate destruction and hyperfluency of the nasal passages.

Magnetic resonance imaging (MRI) is another excellent imaging modality for the nasal cavity, providing superior soft-tissue detail compared with CT. However, no studies to date have compared the sensitivity and specificity of CT and MRI for differentiating causes of chronic nasal disease, and CT is currently the most popular imaging technique due to its lower cost compared with MRI.

Rhinoscopy
Rhinoscopic evaluation of patients with chronic nasal disease is essential. For complete assessment of the nasal mucosa and turbinates, a rigid or flexible endoscope is required. The most common rhinoscopic features in dogs with inflammatory rhinitis include mucoid or mucopurulent discharge, hyperemic, edematous, and/or friable nasal mucosa, and mild turbinate atrophy or destruction (Fig. 3 and Table 3). Indistinct soft-tissue opacities noted on CT can be visualized rhinoscopically, allowing differentiation among nasal masses, nasal polyps, and mucus plugs. Fungal plaques or nasal mites may also be observed rhinoscopically, thus providing a primary etiology for nasal discharge. Representative biopsy specimens are best obtained by rhinoscopic identification of areas of
significant nasal mucosal pathology and visualization of the area sampled for histopathology.

Other diagnostic techniques to perform after rhinoscopy are examination of the nasopharyngeal region using a dental mirror or retroflexed endoscope to look for nasopharyngeal polyps and dental probing to rule out oronasal fistula or dental disease as a cause for unilateral nasal discharge.

**Histopathology**

Nasal biopsy samples of dogs with chronic, idiopathic, inflammatory rhinitis are characterized by a primarily lymphoplasmacytic infiltrate, but concurrent neutrophilic or less commonly eosinophilic infiltrate may also be seen. Epithelial changes are usually mild but may include epithelial hyperplasia and erosion. Turbinate remodeling or destruction can also be evident. The majority of dogs with unilateral clinical signs have bilateral nasal mucosal pathology, and severity of inflammation between the two sides of the nasal cavity often varies.

**Culture and Cytology**

Obtaining a positive culture of bacterial and/or fungal organisms in dogs with inflammatory rhinitis is not uncommon and likely reflects normal nasal mucosal flora or secondary infection rather than primary infectious rhinitis. Culture results from the rostral nasal cavity may differ from the caudal nasal cavity. Similarly, brush or lavage samples from superficial epithelium may not adequately reflect bacterial and fungal infiltration into the nasal mucosa. When culture is desired, collection of a deep nasal lavage using a protected catheter brush or submission of a nasal biopsy sample for culture should be considered.

Nasal mucosal cytology may be used to identify fungal or neoplastic lesions in some cases; however, cytology has poor sensitivity and specificity compared with histology in nasal mucosal samples and is often unreliable for detecting chronic changes.

### Table 2: Computed Tomography in 33 Dogs with Idiopathic Rhinitis

<table>
<thead>
<tr>
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<th>Cases (%)</th>
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<tbody>
<tr>
<td>Normal</td>
<td>4/33 (12%)</td>
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<tr>
<td>Unilateral lesions</td>
<td>8/33 (24%)</td>
</tr>
<tr>
<td>Bilateral lesions</td>
<td>21/33 (64%)</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>27/33 (82%)</td>
</tr>
<tr>
<td>Soft-tissue opacification</td>
<td>25/33 (78%)</td>
</tr>
<tr>
<td>Plaque-like lesions</td>
<td>24/33 (73%)</td>
</tr>
<tr>
<td>Turbinate destruction</td>
<td>23/33 (70%)</td>
</tr>
<tr>
<td>Gas pocketing</td>
<td>23/33 (70%)</td>
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<tr>
<td>Frontal sinus opacification</td>
<td>14/33 (42%)</td>
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</table>

### Table 3: Rhinoscopic Findings in 37 Dogs with Idiopathic Rhinitis

<table>
<thead>
<tr>
<th></th>
<th>Cases (%)</th>
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<tbody>
<tr>
<td>Normal</td>
<td>1/37 (3%)</td>
</tr>
<tr>
<td>Unilateral lesions</td>
<td>7/37 (19%)</td>
</tr>
<tr>
<td>Bilateral lesions</td>
<td>21/37 (57%)</td>
</tr>
<tr>
<td>Mucoid or mucopurulent discharge</td>
<td>29/37 (78%)</td>
</tr>
<tr>
<td>Hyperemic, or inflamed mucosa</td>
<td>26/37 (70%)</td>
</tr>
<tr>
<td>Mucosal edema</td>
<td>8/37 (22%)</td>
</tr>
<tr>
<td>Turbinate atrophy, destruction, or loss</td>
<td>8/37 (22%)</td>
</tr>
<tr>
<td>Hemorrhage or blood clots</td>
<td>5/37 (14%)</td>
</tr>
<tr>
<td>Mucosal friability</td>
<td>4/37 (11%)</td>
</tr>
</tbody>
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Treatment

No effective treatment regimen for LPR has been established; therefore, animals are commonly treated with a variety of medications including antibiotics, antiinflammatory drugs (glucocorticoids: oral or topical, or nonsteroidal antiinflammatory drugs), antihistamines, and antifungal medications.

Antibiotics

Dogs with mucopurulent nasal discharge likely have some degree of secondary bacterial contamination. Antibiotic treatment in these animals may help to reduce the severity of the nasal discharge and alter the character of discharge from mucopurulent to serous, but complete sustained resolution of nasal discharge is rarely achieved. Most nasal bacterial infections are susceptible to multiple antibiotics. Some dogs respond well to doxycycline (3 to 5 mg/kg PO twice per day), which may be attributed partially to its antiinflammatory effects. Macrolides such as azithromycin (5 mg/kg daily for 5 days, then twice weekly) have also been effective in some dogs.

Although the long-term response to antibiotics has not been reported, it is unlikely that such treatment results in cure of disease. Extended courses of suppressive antibiotic therapy or intermittent treatment with such drugs may be required for control of signs. If the severity of the nasal discharge worsens when antibiotics are discontinued, it is advisable to reinstitute therapy with the same antibiotic to avoid development of antibiotic resistance by use of multiple antibiotics.

Anti-Inflammatory Agents

Oral glucocorticoids have not proven effective in treating most dogs with LPR; therefore, long-term use of oral steroids should be avoided because of systemic side effects. Topical glucocorticoid sprays such as fluticasone can be applied if the dog will tolerate them. Topical nasal steroid drops may be applied if the dog will tolerate them; however, these sprays may be more efficacious in reducing nasal inflammation in certain cases. These drugs are also sometimes used in feline nonspecific rhinitis, when it is unclear whether an infectious etiology might be present. The most commonly used drug is likely piroxicam. Like all nonsteroidal agents, this drug can be associated with gastrointestinal effects associated with GI ulceration and with renal dysfunction. When used at 0.3 mg/kg PO daily in healthy animals, it is unlikely to have untoward side effects, although owners should be instructed to watch for anorexia, vomiting, or abdominal pain.

Antihistamines

Antihistamines are occasionally used in LPR dogs, although response is typically poor, and the sedative effects of some antihistamines may outweigh any therapeutic benefit. Also, antihistamines may have the undesirable side effect of drying nasal secretions and worsening mucus accumulation. However, if sneezing and nasal discharge worsen seasonally and an inhaled environmental allergen is suspected, an antihistamine trial may be employed.

Antifungal Therapy

A few dogs with LPR have been treated empirically with topical antifungal medications ( clotrimazole, enilconazole) to treat a possible undiagnosed fungal rhinitis; however, improvement in clinical signs was not noted.3 Response to oral antifungals has not been reported. Variable results have been reported in human chronic sinusitis patients with suspected fungal hypersensitivity. Nasal amphotericin B resulted in deterioration of symptoms in one study,33 while proving safe and effective in another.34

Other Therapies

Some dogs with LPR may present with signs of reverse sneezing. Reverse sneezing occurs in response to irritation of the nasal mucosa, which may be caused by inhaled irritants or occasionally by the nasal mite, P. caninum. Dogs that exhibit reverse sneezing should be treated empirically with ivermectin (or milbemycin in Collie breeds) to rule out parasitic infestation as a cause of rhinitis before pursuing aggressive diagnostics.

Increasing nasal hydration through the use of topical saline drops or with saline inhalation or nebulization can aid in evacuation of the nasal cavity. Dogs are variably tolerant of saline nasal drops administered to the nasal cavity, but this is the least expensive alternative for liquefying nasal secretions and encouraging removal from the nasal cavity.

Conclusion

Inflammatory rhinitis is commonly found in dogs with chronic nasal disease. The etiology of this disorder remains unknown and may involve different pathogenic mechanisms in different dogs with chronic nasal disease. Some dogs may exhibit an aberrant immune response to commensal fungal organisms or other inhaled pathogens or irritants. The diagnosis of LPR requires a thorough history and physical examination, advanced imaging (CT or MRI), rhinoscopic evaluation, and biopsy. Culture and cytology may occasionally prove useful in differentiating LPR from other causes of rhinitis (ie, fungal rhinitis and neoplasia). The poor response to treatment with antibiotics, glucocorticoids, and antihistamines makes LPR a frustrating condition to treat. Current recommendations to be considered include the use of doxycycline or azithromycin for their antiinflammatory as well as...
antibacterial effects, and trial therapy with piroxicam. Owners should be advised that antibiotics only treat secondary bacterial infections and nasal discharge will likely return once antibiotics are discontinued. Use of multiple antibiotics should be avoided. Oral corticosteroids have shown little therapeutic benefit and should be avoided due to unwanted systemic effects. However, inhalant corticosteroids may be effective in some patients. Further research is required to identify the pathogenesis of LPR with the aim of developing an effective treatment regimen.

References