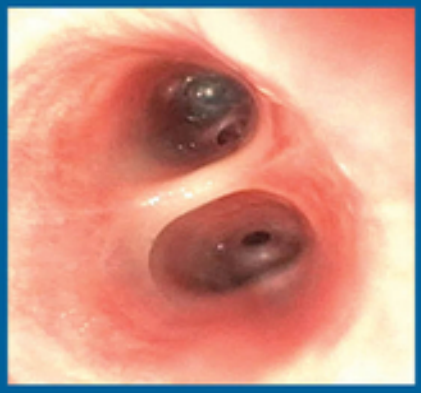
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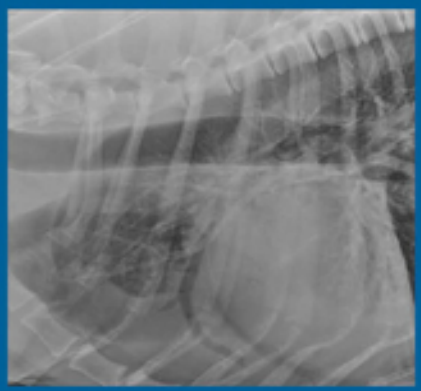
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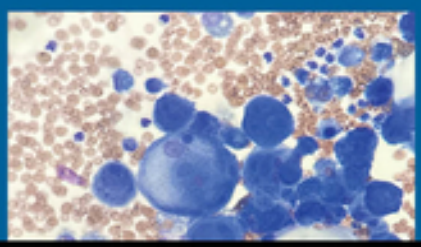






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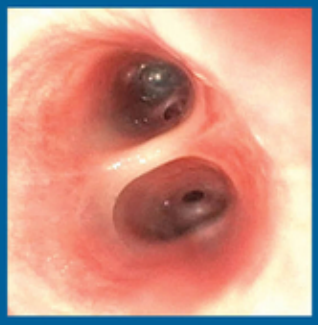


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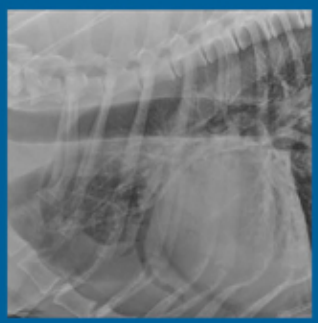
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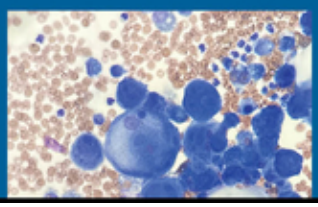
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Table of Contents

- Cover
- Table of Contents
- Title Page
- Copyright Page
- Dedication Page
- Preface
- Acknowledgments
- 1 Localization of Disease
  - Nasal Discharge
  - Loud Breathing
  - Cough
  - Tachypnea versus Panting
  - Exercise Intolerance
  - Differentiating Cardiac from Respiratory Disease
  - Additional Considerations
  - References
- 2 Respiratory Diagnostics
  - General
  - Diagnostic Imaging
  - Airway Sampling
  - Respiratory Endoscopy
  - Sample Analysis
  - References
- 3 Respiratory Therapeutics
  - Considerations in Drug Therapy
  - Routes of Administration
  - Adjunct Therapy

References
4 Nasal Disorders
Structural Diseases
Infectious Diseases
Inflammatory Diseases
Other Nasal Diseases
References
5 Diseases of Airways
Structural Disorders
Infectious Diseases
Inflammatory Disorders
Neoplastic Disorders
References
6 Parenchymal Disease
Structural Diseases
Infectious Diseases
Inflammatory Disorders
References
7 Pleural and Mediastinal Disease
Structural Disorders
Infectious Disorders
Other Pleural Disorders
References
8 Vascular Disorders
Structural Disorders
Infectious Disorders
Miscellaneous Disorders
References
Glossary
Index

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List of Tables

Chapter 1

Table 1.1 Causes of nasal discharge in dogs and cats.

Table 1.2 Respiratory causes of cough in dogs and cats.

Chapter 2

Table 2.1 Normal coagulation parameters for dogs and cats (University of Ca...

Table 2.2 Normal blood gas values for dogs and cats.

Table 2.3 Respiratory causes of hypoxemia.

Table 2.4 Airway sampling techniques for various lung patterns.

Table 2.5 Select anesthetic agents that can be considered to facilitate res...

Table 2.6 General guidelines for performing bronchoalveolar lavage (BAL).

Table 2.7 Lower respiratory tract flora found in healthy dogs and cats.

Table 2.8 Characteristics of pleural fluid.

Chapter 3

Table 3.1 Gram-stain characteristics and antibiotic susceptibility for comm...

Table 3.2 Drug dosages of antibiotics commonly used for respiratory tract i...

Table 3.3 Side effects of commonly used antibiotics.

Table 3.4 Antifungal drug therapy.

Chapter 5

Table 5.1 Congenital forms of laryngeal paralysis.

Table 5.2 List of pathogens currently identified as involved in canine infe...

Table 5.3 Clinical characteristics, diagnostic methods, and treatment for p...

Chapter 6

Table 6.1 Bacterial organisms commonly found in dogs with lower respiratory...

Table 6.2 Bacterial organisms commonly found in cats with lower respiratory ...

Table 6.3 Characteristics of common fungal organisms.

Chapter 7

Table 7.1 Organisms commonly identified in animals with pyothorax.

List of Illustrations

Chapter 1

Figure 1.1 Nasal airflow can be assessed by occluding one nostril and assess...

Figure 1.2 Palpation during ocular retropulsion can suggest the presence of ...

Figure 1.3 In the normal animal, palpation of the soft palate will readily d...

Figure 1.4 Prior to thoracic auscultation, the laryngeal and cervical trache...

Figure 1.5 Each region of the thorax should be percussed to detect regional ...

Chapter 2

Figure 2.1 Coagulation cascade. FDPs, fibrin degradation products.

Figure 2.2 Pulse oximetry measures hemoglobin saturation with oxygen, which ...

Figure 2.3 (a and b) The urinary catheter used to collect an airway sample d...

Figure 2.4 During instillation of fluid to the airways, the three-way stopco...

Figure 2.5 A sterile suction trap can be secured below the patient during th...

Figure 2.6 An over-the-needle catheter (lower half of the slide) can be used...

Figure 2.7 (a) To initiate a transtracheal wash, the over-the-needle cathete...

Figure 2.8 The short catheter has been seated between the tracheal rings and...

Figure 2.9 Visualization of the choanae is obtained by inserting a flexible ...

Figure 2.10 Image of the normal nasopharynx in (a) a dog and (b) a cat. The ...

Figure 2.11 The sheath (~5 mm outer diameter) for the telescope portion of t...

Figure 2.12 Normal nasal turbinates in (a) the dog and (b) the cat.

Figure 2.13 Prior to entering the nasal cavity, the cytology brush should be...

Figure 2.14 Diagnostic yield of a nasal biopsy sample is improved when the s...

Figure 2.15 Nasal flush can be performed in a cat by inserting a syringe tip...

Figure 2.16 (a) Right-angle forceps can be used to place a Foley catheter ab...

Figure 2.17 A periodontal probe is inserted along the gum lines surrounding ...

Figure 2.18 Endoscopic image of the larynx showing the palate (P), cornicula...

Figure 2.19 A bronchoscopy adapter allows passage of a ~5.0 mm endoscope thr...

Figure 2.20 Endoscopic view of the normal canine trachea.

Figure 2.21 Endoscopic view of the carina illustrating the openings into the...

Figure 2.22 Distal airways in the dog exhibit relatively sharp bifurcations ...

Figure 2.23 Bronchoalveolar lavage (BAL) is performed by gently wedging the ...

Figure 2.24 (a) To initiate thoracocentesis, the skin is tented and the cath...

Figure 2.25 Ultrasound guidance is used to obtain a lung biopsy using a Temn...

Figure 2.26 Cytocentrifuge of a normal BAL sample (40×) reveals primarily ma...

Chapter 3

Figure 3.1 Nebulization is administered in a cat carrier covered in plastic ...

Figure 3.2 Chest coupage is performed after nebulization by using cupped han...

Figure 3.3 Transected skull shows placement of a nasal oxygen catheter throu...

Figure 3.4 For removal of viscid pleural fluid associated with pyothorax, ad...

Figure 3.5 This cat is in left lateral recumbency with the head to the right...

Figure 3.6 (a) The red rubber catheter and stabilizing catheter are assemble...

Figure 3.7 A purse-string suture and finger cot pattern are used to close th...

Figure 3.8 Mila small-bore chest tube kit contains (from top to bottom) 14 a...

Figure 3.9 The plastic sheath used to deploy the J wire contains a groove to...

Figure 3.10 (a) Right lateral and (b) dorsoventral radiographs in a dog, sho...

Chapter 4

Figure 4.1 Retroflex view of the choanae in a Pug shows hyperemic and swolle...

Figure 4.2 Stenotic nares in a brachycephalic cat.

Figure 4.3 Position of the soft palate in a brachycephalic dog. E represents...

Figure 4.4 Everted laryngeal ventricles (S) are evident at the ventral-most ...

Figure 4.5 Laryngeal collapse in a 2-year-old Norwich Terrier. Cuneiform pro...

Figure 4.6 Rhinoscopic view of the left nasal cavity of a dog that had acute...

Figure 4.7 An adult cat evaluated for chronic nasal discharge was placed und...

Figure 4.8 An adult DMH cat has obvious facial swelling on the left side of ...

Figure 4.9 Retroflex view of the choanae in a 17-year-old spayed female dome...

Figure 4.10 Computed tomography images from a young dog with nasopharyngeal ...

Figure 4.11 (a) The dorsal portion of the nose is distorted by a mass lesion...

Figure 4.12 Cytology of an impression smear from a nasal mass in a cat. Wrig...

Figure 4.13 Depigmentation at the entrance to the right nasal cavity.

Figure 4.14 Open mouth radiographic view (a) of the nasal cavity in a 2-year...

Figure 4.15 Computed tomography (CT) images from two dogs with confirmed sin...

Figure 4.16 Fungal plaques identified during endoscopy in a dog with sino-na...

Figure 4.17 New methylene blue staining of an impression smear from the samp...

Figure 4.18 Placement of nasal catheters for treatment of sino-nasal aspergi...

Figure 4.19 CT image of the rostral nasal cavity from a cat presented for a ...

Figure 4.20 Retroflex view of the choanae in a 10-year-old spayed female (FS...

Figure 4.21 Cervical radiograph from a 4-year-old spayed female domestic sho...

Figure 4.22 Endoscopic view of the choanae reveals a nasopharyngeal polyp.

Figure 4.23 Open mouth views of the nasal cavity of a cat taken under genera...

Figure 4.24 Computed tomography image of the nasal cavity in a cat with righ...

Figure 4.25 Computed tomography image through the frontal sinus and nasophar...

Figure 4.26 Rhinoscopic image in a cat with chronic rhinosinusitis reveals m...

Figure 4.27 Computed tomography findings in a dog with lymphoplasmacytic rhi...

Figure 4.28 Rhinoscopic image from a dog with idiopathic LPR reveals mucosal...

Figure 4.29 Facial asymmetry is evident in this 9-year-old male castrated do...

Figure 4.30 Computed tomography image from a 9-year-old spayed female (FS) D...

Figure 4.31 Rhinoscopic image from a dog with nasal neoplasia reveals a soft...

Figure 4.32 Nasal mite found in the nose of a dog presented for reverse snee...

Case Figure 1 Computed tomography.

Case Figure 2 Rhinoscopy.

Chapter 5

Figure 5.1 Right lateral cervical radiograph of a 9-year-old male castrated ...

Figure 5.2 Endoscopic image of an 11-year-old male castrated (MC) Labrador R...

Figure 5.3 Laryngoscopic image from a 1-year-old Norwich Terrier with inspir...

Figure 5.4 Laryngoscopic image from an 11-year-old Maltese with intermittent...

Figure 5.5 The airways are exposed to atmospheric pressure in the cervical r...

Figure 5.6 Inspiratory (a) and expiratory (b) fluoroscopic images from a 13-...

Figure 5.7 Fluoroscopic image from a 15-year-old spayed female (FS) Pug demo...

Figure 5.8 (a) Grade I: The cartilage ring structure of the trachea remains ...

Figure 5.9 Bronchoscopic image demonstrating 70–100% collapse of lobar bronc...

Figure 5.10 Prosthetic rings used for external support in dogs with cervical...

Figure 5.11 Catheter delivery system and close-up of a distal deployment ste...

Figure 5.12 (a) Right lateral and (b) ventrodorsal radiographs from an 8-yea...

Figure 5.13 Sagittal reconstruction of a computed tomography (CT) image from...

Figure 5.14 Bronchoscopic image of the lungs from a cat with bronchiectasis....

Figure 5.15 Right lateral (a), left lateral (b), and ventrodorsal (c) radiog...

Figure 5.16 Bronchoscopic visualization of the distal airways in a 1 year ol...

Figure 5.17 Bronchoscopy in a 6 year old Golden-Doodle with a 1 month histor...

Figure 5.18 (a) Right lateral and (b) dorsoventral radiographs from a 12-yea...

Figure 5.19 Bronchoscopic images from two dogs with chronic bronchitis. (a) ...

Figure 5.20 Neutrophilic airway cytology from a dog with chronic bronchitis ...

Figure 5.21 (a) Right lateral and (b) dorsoventral radiographs from a 2-year...

Figure 5.22 Right lateral radiograph from a 4-year-old male castrated (MC) R...

Figure 5.23 (a) Left lateral and (b) ventrodorsal radiographs from a 9-year-...

Figure 5.24 Bronchoalveolar lavage cytology from two cats with feline bronch...

Figure 5.25 Right lateral radiographs from (a) an 11-year-old cat with a lar...

Figure 5.26 Bronchoscopic image from a 10-year-old cat with an adenocarcinom...

Case Figure 1 Cervical radiograph (a). Thoracic radiographs (b–d).

Case Figure 2 Bronchial collapse at the left cranial and caudal lobar bronch...

Chapter 6

Figure 6.1 Electron microscopy image showing two abnormal cilia in cross-sec...

Figure 6.2 (a) Right lateral and (b) dorsoventral radiographs from a dog wit...

Figure 6.3 Bronchoscopic image demonstrating torsion of the right middle lun...

Figure 6.4 Fluoroscopic image demonstrates barium being coughed or regurgita...

Figure 6.5 (a) Right lateral, (b) left lateral, and (c) dorsoventral radiogr...

Figure 6.6 Bronchoscopy image from a dog with *Mycoplasma* pneumonia reveals a...

Figure 6.7 Airway cytology from bronchoalveolar lavage (BAL) fluid confirms ...

Figure 6.8 Right lateral thoracic radiographs from a dog with (a) coccidioid...

Figure 6.9 (a) Right lateral and (b) dorsoventral radiographs from a 2-year-...

Figure 6.10 (a) Right lateral and (b) dorsoventral radiographs from a 3-year...

Figure 6.11 BAL cytology from a dog with *Pneumocystis* pneumonia reveals clas...

Figure 6.12 Gross necropsy findings from a dog with pyogranulomatous pneumon...

Figure 6.13 (a) Right lateral and (b) dorsoventral radiographs from a 1-year...

Figure 6.14 (a) Dorsoventral radiograph and (b) cross-sectional computed tom...

Figure 6.15 Bronchoscopic images from dogs with eosinophilic lung disease ca...

Figure 6.16 Airway cytology from a dog with eosinophilic lung disease confir...

Figure 6.17 (a) Left lateral and (b) dorsoventral radiographs from a 12-year...

Figure 6.18 (a) Right lateral and (b) dorsoventral radiographs of a 2-year-o...

Figure 6.19 (a) Right lateral and (b) dorsoventral radiographs from a 12-yea...

Figure 6.20 (a) Right lateral and (b) dorsoventral radiographs from a 17-yea...

Figure 6.21 (a) Right lateral and (b) dorsoventral radiographs from a 10-yea...

Figure 6.22 Pulmonary metastasis of a thyroid carcinoma in a 13-year-old spa...

Figure 6.23 (a) Right lateral radiograph and (b) gross necropsy findings in ...

Figure 6.24 Bronchoscopic image from a 10-year-old male castrated domestic s...

Figure 6.25 Cytology from a BAL sample in a 13-year-old castrated male (MC) ...

Case Figure 1 Lateral (a and b) and dorsoventral (c) thoracic radiographs.

Case Figure 2 Bronchoscopy.

Case Figure 3 BAL fluid was hypercellular.

Chapter 7

Figure 7.1 (a) Right lateral and (b) dorsoventral radiographs from a 7-year-...

Figure 7.2 Computed tomographic slice through the caudal thorax of a 6-year-...

Figure 7.3 Thoracic radiographs with red markings outlining the boundaries o...

Figure 7.4 Right lateral radiograph from an 18-month-old spayed female domes...

Figure 7.5 (a) Right lateral and (b) dorsoventral radiographs of a 2-year-ol...

Figure 7.6 (a) Right lateral and (b) ventrodorsal radiographs from a 6-year-...

Figure 7.7 Pleural fluid cytology from a cat with pleural effusion reveals d...

Figure 7.8 (a) Lateral scout image from computed tomography and (b) a cross-...

Figure 7.9 This 9-year-old spayed female (FS) Mix breed dog demonstrates pto...

Figure 7.10 Dorsoventral radiograph from a Bulldog demonstrates widening of ...

Figure 7.11 Right lateral radiograph from an 11-year-old Labrador reveals a ...

Figure 7.12 (a) Right lateral and (b) dorsoventral radiographs from a 7-year...

Figure 7.13 (a) Right and (b) left lateral radiographs show rounding of the ...

Figure 7.14 Chylous effusion is typically opaque due to the presence of chyl...

Figure 7.15 (a) Right and (b) left lateral radiographs from a cat with chylo...

Figure 7.16 Necropsy image from a 5-year-old spayed female domestic short ha...

Case Figure 1 Thoracic radiographs.

Case Figure 2 Lymphoscintigraphy.

Chapter 8

Figure 8.1 Dorsoventral film radiograph from a dog documented to have a pulm...

Figure 8.2 Perfusion scan from the dog depicted in Figure 8.1 indicates a la...

Figure 8.3 (a) Right lateral and (b) dorsoventral radiographs from a 4-year-...

Figure 8.4 Echocardiographic image from the dog depicted in Figure 8.3 demon...

Figure 8.5 (a) Right lateral and (b) dorsoventral radiographs from a 5-year-...

Figure 8.6 (a) Right lateral and (b) dorsoventral radiographs from a 13-year...

Figure 8.7 Doppler echocardiography reveals tricuspid regurgitation with an ...

Figure 8.8 Two-dimensional Doppler image from the right parasternal short-ax...

Figure 8.9 Type I (normal), type II, and type III pulmonary velocity profile...

Figure 8.10 This right parasternal short-axis view through the left (L) and ...

Figure 8.11 (a) Right lateral and (b) dorsoventral radiographs from a 10-yea...

Case Figure 1 Dorsoventral (a) and lateral (b and c) thoracic radiographs.

Case Figure 2 Echocardiography demonstrating the right pulmonary artery inde...

Canine and Feline Respiratory Medicine

Third Edition

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This book would not have been possible without the support of my husband and life partner, David Maggs, who will forever be my inspiration in teaching, in research, and in writing.

Preface



Patients with respiratory disease often represent a diagnostic challenge because clinical signs are so similar among different disease processes that affect the respiratory system. Nasal discharge is typical with many upper respiratory conditions, cough encompasses infectious, inflammatory, and neoplastic diseases, and difficulty breathing can result from a disorder anywhere along the respiratory tract. In addition, animals with cardiac and systemic diseases often present with respiratory signs, which means that all cases require thought and introspection on appropriate localization of disease as well as the underlying pathophysiology. The most critical piece of the puzzle is a comprehensive respiratory examination, which provides the key to a rational diagnostic work-up. This book has been designed to provide easily understood pathways to a clinical diagnosis in an expeditious fashion. It is my hope that this contribution to the veterinary literature conveys highly specific details on respiratory examination, diagnostics, and diseases in a clinically relevant, logical, and easy-to-read fashion. This extensively updated edition includes new knowledge that has been generated on respiratory diseases and diagnostic testing and provides case examples to illustrate diagnostic pathways.

My goal with this text was to integrate relevant anatomy, physiology, and pathophysiology in a rational and readable manner that is immediately clinically applicable for the busy practitioner and inquiring student. I approached this task recognizing that the major comprehensive textbooks in veterinary medicine contain excellent chapters on respiratory disorders. My book aims to provide a cohesive and complete discussion in a user-friendly, single-author volume. The first section deals with the common presenting signs demonstrated by patients with respiratory disease (nasal discharge, loud breathing, cough, tachypnea versus panting, and exercise intolerance) as well as a section on differentiating cardiac from respiratory disease. The next chapter contains detailed how-to descriptions of the most important diagnostic methods needed to confirm a respiratory disease as well as interpretation of the results. I then devote an extensive chapter to therapeutic options, addressing concerns about appropriate antibiotic stewardship with recognition of knowledge gaps in the field. The remainder of the book has thorough explanations of individual diseases, divided into chapters

dealing with disorders of the nose, airways, lung parenchyma, pleura, and pulmonary vasculature. Each chapter follows the same easy-to-read order, with diseases subdivided by etiology into structural, infectious, inflammatory, and neoplastic disorders.

I hope that this third edition of my textbook will instill confidence in students and practitioners as they identify and manage respiratory conditions of dogs and cats.

Acknowledgments

I am indebted to my clients and patients at the University of California, Davis, Veterinary Medical Teaching Hospital, who taught me so much about respiratory medicine and continually challenged me to find answers to their problems.

This work was completed with the support of my colleagues at UC Davis, who have afforded me the opportunity and freedom to pursue respiratory medicine as my passion for the past 24 years. Clinicians and house officers in all services have supported my clinical efforts as well as my research, and my departmental colleagues and the School's leadership have been both encouraging and accommodating. In particular, I am grateful for assistance from Drs. Alessia Cenani, Philipp Mayhew, and Lance Visser in completion of this edition.

This book is the result of years of discovery and clinical effort, and it would not have been possible without the inspiration from colleagues and collaborators in the USA and worldwide, who share a fascination with and great knowledge of respiratory medicine. The veterinarians I have met through the American and European Colleges of Veterinary Internal Medicine and the Veterinary Comparative Respiratory Society have motivated me to continue my search for knowledge and to share what I have learned.

1
Localization of Disease

Nasal Discharge

History

Nasal discharge is almost always a sign of local disease within the nasal cavity, however there are some instances when nasal discharge can occur with lower respiratory, gastrointestinal, or systemic disease. One exception to a purely nasal localization of nasal discharge is eosinophilic bronchopneumopathy, an inflammatory condition of the epithelial lining of the airways and lungs that can also involve the nasal epithelium. Affected animals can have nasal signs that last longer or are more noticeable to owners than are lower respiratory signs. Interestingly, cats with eosinophilic lower airway disease do not display this clinical finding. Nasal discharge can also accompany infectious lower respiratory tract disease in the dog that coughs airway material into the nasopharynx, which subsequently drains from the nose. This happens less commonly in the cat. Thirdly, some animals with vomiting or regurgitation will display nasal discharge because of nasopharyngeal regurgitation of gastrointestinal contents. This might be more common in brachycephalic breeds, which frequently develop pharyngeal collapse associated with increased inspiratory respiratory effort (Pollard et al. 2018). Brachycephalic animals also are prone to oral mishandling of food due to excessive pharyngeal folds and because of multiple gastrointestinal diseases, including hiatal hernia, gastroesophageal reflux, and mild inflammatory intestinal disease that leads to vomiting or regurgitation. All of these features contribute to nasal discharge in brachycephalic animals, with brachycephalic dogs affected more often than cats. Finally, nasal discharge, particularly sanguinous nasal discharge, can be encountered in systemic diseases associated with coagulopathies (thrombocytopenia, thrombocytopathy, coagulation factor defects), hypertension, or

hyperviscosity syndrome, such as encountered with leishmaniasis and chronic ehrlichiosis.

The most common respiratory causes of nasal discharge include infectious, inflammatory, and neoplastic disorders as well as dental-related nasal disease and foreign bodies (Table 1.1). Additional clinical signs that can be seen in animals with nasal disease include sneezing or reverse sneezing, pawing or rubbing at the face, noisy breathing or mouth breathing, facial pain, or an unexplained odor near the head.

When evaluating the animal with nasal discharge, important considerations include the duration of signs, the type of discharge as well as changes in its character over time, and the presence of unilateral, bilateral, or progressive signs. Acute onset of nasal discharge is often accompanied by sneezing, is frequently paroxysmal in nature, and is most commonly associated with infectious upper respiratory tract disease or a foreign body. Affected animals can have signs that resolve within a week without treatment, however some dogs or cats are so severely affected that they are rapidly taken to the veterinarian to determine a plan for intervention. Occasionally, dogs with nasal foreign bodies will have resolution of signs despite continued presence of organic matter within the nose. This represents a diagnostic and therapeutic dilemma, particularly in the dog that has an appropriate signalment and exposure history for a nasal foreign body. Failure to investigate signs and potentially retrieve a foreign body can have long-term consequences due to migration of the foreign body into the central nervous system or development of a secondary fungal infection. The most frustrating cases are those with chronic, slowly progressive nasal discharge and sneezing over weeks to months to years before the severity of disease prompts veterinary care. Prioritizing various empiric therapies requires an assessment of the top differential diagnoses likely in each case and determining what treatment is least likely to worsen signs, to interfere with further diagnostic testing, or to hamper the owner from pursuing specific work-up.

Table 1.1 Causes of nasal discharge in dogs and cats.

	Dog	**Cat**
Infectious	Canine infectious respiratory disease complex[a]	Acute upper respiratory tract disease complex[b]
	Aspergillus	*Cryptococcus*
	Cryptococococcus	*Aspergillus*
	Penicillium	
	Rhinosporidium	
	Leishmania	
	Ehrlichia	
Inflammatory	Lymphoplasmacytic rhinitis	Feline chronic rhinosinusitis
Neoplastic	Adenocarcinoma	Lymphoma
	Sarcoma	Adenocarcinoma
	Lymphoma	Sarcoma
Local	Tooth root abscess	Nasal or nasopharyngeal polyp
	Oronasal fistula	Tooth root abscess
	Trauma	Oronasal fistula
	Foreign body	Foreign body
	Nasal or nasopharyngeal polyp	Trauma
Other	Primary ciliary dyskinesia	Primary ciliary dyskinesia
	Nasal mites	
	Xeromycteria (dry nose syndrome)	

[a] Reported causes include canine adenovirus-2, canine parainfluenza-3 virus, canine respiratory coronavirus, canine herpesvirus, canine distemper virus, canine influenza viruses (H3N8, H3N2, H1N1), pneumovirus, *Bordetella*, *Mycoplasma cynos, Mycoplasma*

canis, and *Streptococcus equi* subsp. *zooepidemicus*. Novel viral organisms are continually being identified.

[b] Reported causes include feline herpesvirus-1, feline calicivirus, *Chlamydia*, *Bordetella,* and *Mycoplasma*.

With many causes of nasal signs, including viral disease or foreign body, discharge is serous initially and then progresses to a mucoid character when inflammation induces mucus production or when secondary bacterial infection develops. Yellow-green nasal discharge can be an indicator of eosinophilic disease, but is also encountered in other infectious or inflammatory conditions, while brown-tinged discharge suggests the presence of blood within the mucus. Bright red blood can be found in combination with nasal discharge because of trauma to blood vessels associated with the primary disease process or due to the severity of sneezing. Epistaxis with or without nasal discharge has been associated with local causes of disease, including inflammatory rhinitis, canine aspergillosis, and neoplasia; however, in animals with pure epistaxis, systemic disorders must be considered, including coagulopathies, hyperviscosity syndrome, and systemic hypertension.

Nasal discharge that is strictly unilateral is most suspicious for local disease caused by a foreign body, trauma, tooth root abscess or oronasal fistula, or for an early fungal infection or neoplasm. However, arterial hypertension or a coagulopathy can also result in unilateral nasal bleeding despite being a systemic disease. Interestingly, inflammatory diseases such as lymphoplasmacytic rhinitis in the dog and feline chronic rhinosinusitis can present with lateralizing clinical signs, although in most of these cases, imaging and histology reveal that both sides of the nasal cavity are affected.

Non-respiratory history that should be collected includes environmental exposure to foreign bodies, previous trauma, and evidence of vomiting or regurgitation. For animals with epistaxis, potential exposure to rodenticides or vector-borne diseases that can result in thrombocytopenia, thrombocytopathy, or vasculitis (such as *Ehrlichia* or Rocky Mountain Spotted Fever) should be identified. In addition, history should be scrutinized for signs consistent with systemic diseases such as hyperthyroidism, renal disease, or adrenal disease, which can result in arterial hypertension.

Signalment

Young animals with nasal discharge are most often affected by infectious upper respiratory tract diseases. A nasopharyngeal polyp should be considered when discharge is accompanied by obstructed breathing, stertorous respirations, gagging, or retching. Primary ciliary dyskinesia is a defect of innate immunity inherited in an autosomal recessive fashion that causes ineffectual mucociliary clearance, trapping of secretions, and recurrent infection. Therefore, this condition is frequently recognized in a younger animal. Affected dogs are often purebred, with an increased prevalence in the Bichon Frise, Old English Sheepdog (Merveille et al. 2014), and Newfoundland (Watson et al. 1999); genetic mutations have also been reported in the Alaskan Malamute (Anderegg et al. 2019), and Rough Collie (Hug et al. 2019) although any breed of dog or cat can be affected. While neoplastic disease most typically affects older animals, it also occurs in young to middle-aged animals (2–5 years of age) and can be particularly aggressive in these younger animals, especially in the canine population. Nasal aspergillosis is most often encountered in younger dogs and older cats. Cryptococcosis and inflammatory rhinitis can affect dogs or cats of any age.

Nasal disease of most types (fungal, neoplastic, and inflammatory, as well as dental-related and foreign body disease) is most commonly encountered in dolichocephalic dog breeds, likely because of the large surface area available for foreign body entrapment, for metabolism of inhaled toxicants, or for neoplastic transformation. An unusual combination of rhinitis and bronchopneumonia has been reported in the Irish wolfhound, where a genetic defect in respiratory immunity is suspected but has not been confirmed (Clercx et al. 2003).

Physical Examination

A complete physical examination is essential in every animal presented for evaluation of respiratory disease. In animals with nasal discharge, important features to focus on include the presence or absence of nasal airflow, changes in ocular retropulsion, ability to depress the soft palate easily into the dorsal nasopharyngeal wall, regional local lymph node enlargement, and facial asymmetry or

pain. These parts of the physical examination are most important because they can help identify the space-occupying nature of some causes of nasal disease, particularly nasal neoplasia, feline cryptococcosis, feline aspergillosis, and nasopharyngeal polyps, and because these physical examination findings can indicate local extension or metastasis.

Nasal airflow can be assessed by holding a chilled microscope slide in front of each nostril to show fogging of the glass or by using a wisp of cotton (from a cotton ball or swab) to watch for air movement. The mouth should be held closed during this maneuver, and occlusion of the alternate nostril can be helpful for enhancing airflow through the side of the nasal cavity to be examined (Figure 1.1). Cats create minimal airflow and a very thin wisp of cotton should be used and held in front of the nostril from above and below to check for flow. Alternatively, a stethoscope can be used to listen for airflow from each nostril. An animal with a mass effect in the nasal cavity or nasopharynx will fail to fog the glass, to move the cotton wisp, or to generate a sound at the stethoscope, and will often object to having the nose partly obstructed because it inhibits airflow. Conversely, even animals with heavy mucus accumulation in the nasal cavity will typically retain nasal airflow.

Facial palpation is performed to assess for a pain response, to locate swellings and depressions in bony structures, and to check for symmetry of the skull. Neoplastic processes and fungal infections are most likely to result in abnormal findings. Ocular retropulsion is a part of the facial examination and is performed by placing each thumb over the closed lids and pressing gently backward, upward, medially, and laterally (Figure 1.2). Nasal lesions that are producing a mass effect behind the globe (primarily a neoplasm, fungal granuloma, or retrobulbar abscess) will cause a lateralizing difference in the resistance to depression. Altered retropulsion is difficult to assess in a brachycephalic animal because the eyes are naturally more protruberant than in other dogs or cats. Palpation within the oral cavity can reveal bony abnormalities in the hard palate or might suggest a mass lesion above the soft palate. To perform this examination, the mouth is held open, and the roof of the mouth is palpated from the front of the hard palate through to the end of the soft palate. In the normal animal, the soft palate is

readily depressed upward into the dorsal nasopharyngeal wall (Figure 1.3). A mass in this area (most commonly a neoplasm, fungal granuloma, or polyp) will resist depression. The dental arcade should also be evaluated during the oral examination, although it is important to remember that tooth root disease can be present in the absence of external signs and dental probing requires anesthesia.



Figure 1.1 Nasal airflow can be assessed by occluding one nostril and assessing flow from the alternate nostril with a cotton wisp or chilled microscope slide.



Figure 1.2 Palpation during ocular retropulsion can suggest the presence of a mass lesion in the optic canal or retrobulbar space.

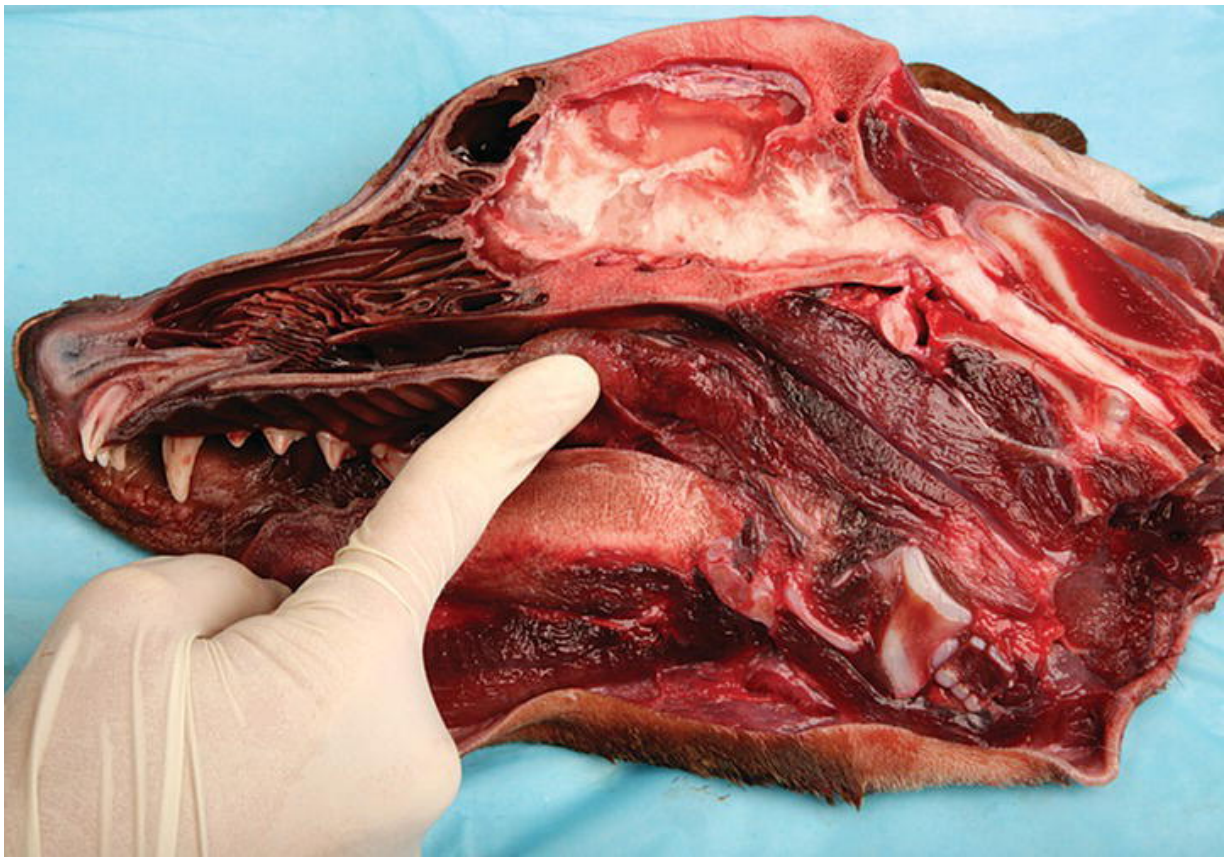


Figure 1.3 In the normal animal, palpation of the soft palate will readily depress tissue into the dorsal nasopharyngeal wall. The presence of a mass lesion in the nasopharynx will result in resistance to depression.

Neoplastic disease or cryptococcosis within the nasal cavity leads to ipsilateral mandibular lymph node involvement and the disease process can sometimes be identified by cytology of a lymph node aspirate, even when there is no palpable enlargement. Nasal aspergillosis can result in reactive lymphadenopathy, although no fungal elements will be found on aspiration cytology. Nasal depigmentation along the drainage path of nasal discharge is a relatively specific feature of canine nasal aspergillosis found in up to 40% of cases and is thought to result from elaboration of a dermonecrotic toxin by the fungus (see Chapter 4).

Loud Breathing

Definition

Loud breathing most commonly results from a disorder affecting the nasal cavity or upper airway (larynx, pharynx, or cervical trachea), although occasionally animals with lower airway disease will present for evaluation of breathing that is loud or audible to an owner. Stertor and stridor are loud sounds resulting from narrowing of upper or large airways and are often audible without a stethoscope, although subtle stridor can be missed without specific auscultation over the larynx. Importantly, some animals will suffer from both stertor and stridor, which can have important ramifications for documenting the extent and severity of the obstructive disease, as well as for defining optimal treatment.

Stertor is a discontinuous gurgling or snoring sound that is produced as air flows past a soft tissue obstruction in the upper airway. It can be caused by narrowing within the nasal cavity or nasopharynx (from a polyp, mass, caudal aberrant turbinates, or stenosis), by elongation or thickening of the soft palate, or by edema or eversion of laryngeal ventricles (saccules). Tonsillar enlargement or mass lesions in the oral cavity can also lead to stertor. In brachycephalic dogs and cats, it is not possible to localize the source of stertor on physical examination alone and stertor is often multi-factorial. Stertor varies in tone and pitch, and it can be audible on inspiration, expiration, or both.

In contrast, stridor is classically an inspiratory noise of a single, high pitch that results from rapid flow of air past a rigid obstruction, such as a paralyzed or collapsed larynx. Stridor can also be heard in an animal with a laryngeal mass or occasionally in an animal with nasopharyngeal narrowing due to stenosis or a mass. It can also be ausculted in an animal with a fixed large airway obstruction due to stenosis, hypoplasia, compression, or a mass effect. The airway obstruction can be anywhere from the larynx to the cervical or intrathoracic trachea. In severe cases where a large mass is obstructing airflow, stridor can be present on both inspiration and expiration. Finally, cervical tracheal collapse can also result in stridor, typically on inspiration.

Epiglottic retroversion is a cause of intermittent airway obstruction in dogs in which sporadic respiratory distress is present in

conjunction with stridor or stertor. Although rarely reported, it is increasingly recognized as a cause of serious clinical disease (see Chapter 5).

Signalment

Stertor is commonly encountered in brachycephalic dog breeds such as Bulldogs (English and French), Pugs, and Boston Terriers, and is also heard in Himalayan and Persian cats. Loud breathing is often present early in life and becomes worse with the development of additional respiratory disease or with weight gain. Some animals are not presented for evaluation of stertor and respiratory difficulty until late in life because of the perception that noisy respiration is "normal" for the breed.

Animals with stridor due to congenital laryngeal paralysis are usually young (6–12 weeks) when clinical signs are first apparent, although some breeds show signs at 4–6 months and others at 1–2 years of age. Affected breeds include the Dalmatian, Rottweiler, Great Pyrenees, Bouvier des Flandres, Siberian Husky, White German Shepherd, and some cats (see Chapter 5). Certain breeds have concurrent polyneuropathy (Table 5.1). Acquired laryngeal paralysis is most commonly found in older, large breed dogs such as Labrador and Golden Retrievers as part of a generalized polyneuropathy that affects primarily long nerves in the body such as the recurrent laryngeal nerve and spinal nerves to the limbs. Because the larynx is responsible for phonation and breathing, dysfunction of that nerve is often the first abnormality noticed by owners. Brachycephalic breed dogs that develop laryngeal collapse are usually older at the time of diagnosis; however, because this is an end-stage manifestation of airway obstruction, the age at which the condition is recognized varies depending on the severity of the obstruction. Atypical breeds such as the Norwich terrier, can manifest signs at a young age.

Physical Examination

In a normal animal, breathing is quiet at rest. Stertor and stridor can often be heard without the use of a stethoscope; however, in some instances, careful auscultation over the neck region is needed to confirm stridor. Increasing respiratory flow rate by gentle exercise

can improve detection of stridor; however, panting must be discouraged. In the normal animal, auscultation over the larynx and trachea will reveal loud, hollow sounds that are heard equally on inspiration and expiration. Because upper respiratory noises are typically loud and can obscure lung sounds, auscultation of the larynx and tracheal region is recommended in all patients prior to thoracic auscultation to improve differentiation of upper from lower respiratory sounds. Listening specifically to upper airway noises through the stethoscope can also train the mind to filter out those sounds while ausculting the heart; this will facilitate detection of heart sounds and murmurs. Simultaneous palpation of femoral pulses is also helpful in this situation to provide a tactile sensation in timing of heart sounds and murmurs. This is particularly helpful in brachycephalic breeds (Figure 1.4).

Brachycephalic breeds commonly have visible stenotic nares as part of the disease complex, and excessive oropharyngeal folds can be evident on oral examination, although it is difficult to assess palate length in the awake animal due to breed conformation and presence of excessive froth in the back of the throat. Confirming an appropriate gag reflex is important in evaluating the patient with stridor, because swallowing abnormalities can potentiate aspiration. Finally, detecting the presence of bilateral nasal airflow assists in ruling out the nasopharynx or both nasal cavities as the site for generation of stridor or stertor.



Figure 1.4 Prior to thoracic auscultation, the laryngeal and cervical tracheal regions are ausculted to define upper airway sounds.

Cough

History

Cough occurs because of activation of irritant receptors that lie between epithelial cells lining the airways, and it can be triggered by

inflammatory products of neutrophils or eosinophils, by the presence of excess secretions, and by airway compression or collapse (Table 1.2). Important historical features to determine include the onset and duration of cough, the character of the cough, exposure to foreign material or potential infectious diseases, and environmental features that appear to trigger cough. For example, dogs that cough after drinking or in the middle of the night might be suffering from aspiration injury.

The character of the cough described by the owner is occasionally helpful when prioritizing a list of differential diagnoses, although substantial overlap exists among the causes of cough. Animals with a wet- or moist-sounding cough can have excessive airway secretions due to infectious or inflammatory airway disease or as a result of parenchymal disease such as pneumonia. Observant owners of the animal with a productive cough might note that the animal swallows after coughing or retches to remove secretions from the upper airway. However, diseases of the airway can also result in a dry cough when secretions are minimal or early in the course of disease. Infectious respiratory disease in young puppies typically results in a hoarse, seal-bark cough and this is often ascribed to bordetellosis, although any of the organisms associated with canine infectious respiratory disease could be responsible. Cough in animals affected only by airway collapse is often harsh and can be chronic, intermittent, or paroxysmal in nature. A honking cough is frequently described in dogs with tracheal or airway collapse and a brisk, snapping sound on expiration is suggestive of large airway (bronchial) collapse. Animals with pneumonia tend to have a softer cough along with a vague history of illness characterized by anorexia and lethargy. Dogs with heart disease also can have a soft cough associated with signs of tachypnea, exercise intolerance, or lethargy. With severe or fulminant pulmonary edema, a dog might expectorate pink foam because edema fluid has flooded the alveolar space and entered the airways. However, the common association of cough with congestive heart failure has been called into question (Ferasin et al. 2013), and it can be challenging to differentiate cardiac from respiratory disease (see later).

Table 1.2 Respiratory causes of cough in dogs and cats.

	Dog	Cat
Infectious tracheobronchitis	Canine infectious respiratory disease complex[a]	*Mycoplasma* *Bordetella*
Pneumonia	Bacterial	Bacterial
	Aspiration	Aspiration
	Foreign body	Foreign body
	Fungal	Fungal[b]
	Interstitial[b]	Interstitial[b]
Inflammatory disease	Chronic bronchitis	Asthma/chronic bronchitis
	Eosinophilic bronchopneumopathy	
Neoplasia	Primary	Primary
	Metastatic	Metastatic
Structural disorders	Bronchiectasis	Bronchiectasis
	Airway collapse	

[a] Reported causes include canine adenovirus-2, canine parainfluenza-3 virus, canine respiratory coronavirus, canine herpesvirus, influenza viruses, and canine distemper virus along with *Bordetella*, *Mycoplasma*, and *Streptococcus equi* subsp. *zooepidemicus*.

[b] More commonly a cause of tachypnea than cough.

Determining environmental and travel history is important for animals with cough. Exposure to a high-density dog population should raise concern for disease associated with canine infectious respiratory disease complex. If the cough is harsh and dry, *Bordetella* should be considered, while a soft, chronic cough could be suggestive of canine influenza virus infection. Sporting dogs that develop an acute onset of cough or have a chronic, antibiotic-responsive cough could have foreign body pneumonia. Fungal pneumonia should be suspected in coughing animals have traveled to endemic regions. In those dogs or cats, cough is usually

accompanied by tachypnea and systemic signs of illness. Finally, environmental history is important, because exposure to pollutants and airway irritants can exacerbate upper or lower airway diseases in both dogs and cats, although it remains unclear whether or not exposure to second-hand smoke is an important factor in worsening cough in animals (Hawkins et al. 2010).

Signalment

In general, younger animals might be more likely to develop infectious or foreign body pneumonia, while older animals develop bronchitis, neoplasia, airway collapse, and perhaps aspiration pneumonia. Dogs with eosinophilic or fungal pneumonia also tend to be young to middle-aged. Asthma/bronchitis seems to affect cats of all ages, although perhaps the eosinophilic form is more common in younger animals. Cervical tracheal collapse might be noted more commonly in younger dogs, while older dogs get both tracheal collapse and bronchomalacia.

The breeds affected depend on the underlying case of cough. For example, an older Retriever-type dog is likely to develop laryngeal paralysis and subsequent aspiration pneumonia, while brachycephalic breeds can aspirate at a young or older age, developing either pneumonia or pneumonitis. Ciliary dyskinesia can result in antibiotic responsive cough and nasal discharge in breeds described earlier under nasal discharge. Tracheal collapse affects toy and small breed dogs, while chronic bronchitis and bronchomalacia can affect any size or breed of dog. Irish Wolfhounds seem to be predisposed to pneumonia and also develop a rhinitis/bronchopneumonia syndrome, while Standard Poodles and Cocker Spaniels appear to be prone to bronchiectasis.

Physical Examination

One of the more difficult challenges in assessing animals with respiratory disease is the development of good auscultation skills. Practice and patience are required because audible sounds are altered by age, body condition score, conformation, respiratory pattern, and the presence of disease. As mentioned earlier, careful auscultation should include the larynx and trachea, followed by

listening to all lung fields (left, right, caudal, cranial, dorsal, and ventral). The anatomic origin for lung sounds has not been fully established; however, normal lung sounds are usually designated as bronchial, vesicular, or bronchovesicular. Bronchial sounds are loud and are heard best over the large airways near the hilus. Typically, they are louder and longer during expiration than inspiration and have a tubular character. Vesicular lung sounds are soft, heard best and longer on inspiration, and can be detected over the periphery of the chest in normal animals. The sound resembles a breeze passing through leaves on a tree. Bronchovesicular sounds (a mixture of bronchial and vesicular qualities) are typically louder on inspiration than expiration.

Lung sounds in animals with airway or parenchymal disease are often increased in loudness or harshness, and harsh bronchovesicular sounds can be the only physical examination finding in some animals with lower respiratory disease despite the presence of marked radiographic changes. Adventitious (abnormal) lung sounds (crackles and wheezes) are discontinuous noises and are not always present in respiratory patients, but should always be taken as an indicator of disease when ausculted. Adventitious lung sounds can be enhanced by inducing a cough or a deep breath, or by exercising the patient. In normal animals, it is difficult to induce a cough by palpating the trachea; however, animals with airway or parenchymal disease usually have increased tracheal sensitivity due to activation of irritant receptors by infection or inflammation.

Crackles are thought to result from rapid opening or closure of airways, but could also arise from equalization in pressure as air passes through fluid or mucus-filled airways. They can be heard at any point during inspiration or expiration. Fine or soft crackles are suggestive of pulmonary edema, particularly if ausculted in the hilar region of a dog, whereas coarse crackles are more suggestive of airway or parenchymal disease. Dogs or cats with pulmonary fibrosis can display either fine or coarse crackles that are ausculted diffusely across the chest. Auscultation in dogs with airway collapse can reveal diffuse crackles, perhaps because of the presence of concurrent bronchitis or because of opening and closure of smaller airways during the phases of respiration. In the latter case, crackles are often present during both inspiration and expiration. A loud snapping

sound over the hilar region at end expiration is suggestive of collapse of the intrathoracic trachea, carina, or mainstem bronchi. Wheezes are believed to arise from air passing through airways narrowed by intraluminal mucus, extraluminal compression, or by collapse or constriction, and are usually heard on expiration.

Tachypnea versus Panting

History

Tachypnea is most often associated with parenchymal or pleural disease, although in the cat tachypnea can also be encountered with inflammatory airway disease, particularly an asthma attack of bronchoconstriction. Parenchymal diseases that lead to tachypnea are primarily pneumonia and pulmonary edema. Pneumonia (infectious, aspiration, fungal, or interstitial) can be fulminant and acute, or it can be chronic and insidious in onset. Both pneumonia and pulmonary edema are typically associated with systemic signs of illness such as lethargy, anorexia, and weight loss. Tachypnea is also a characteristic of pulmonary vascular disease, particularly pulmonary embolic disease. This can be a reflection of vascular obstruction or alterations in central control of respiration.

Tachypnea due to pneumothorax is usually acute; however, pleural effusive disorders can result in either an acute presentation with respiratory distress or a more chronic development of signs due to slow accumulation of fluid. Usually, the degree of respiratory distress is associated with the rapidity of fluid or air accumulation rather than with the specific volume present. Cats seem to be particularly sensitive to addition of a final, critical volume of fluid that overcomes their ability to compensate.

Tachypnea must be differentiated from panting, which is typically characterized by rapid, open-mouth breathing that does not result in abnormalities in gas exchange. Also, panting is not typically associated with a change in respiratory pattern or effort. Panting can be related to an upper airway or laryngeal disorder, but more often will reflect systemic illnesses such as cortisol or norepinephrine excess, or metabolic acidosis due to diabetic ketosis, diarrhea,

uremia, or renal tubular acidosis. Central nervous system disorders that affect the respiratory center can result in panting as can abdominal distention due to organomegaly, neoplasia, pregnancy, obesity, ascites, gastric dilatation, or torsion. Finally, anxiety, pain, and hyperthermia can result in incessant panting.

Physical Examination

Cervical and thoracic auscultation, as described for evaluation of animals with cough, is important for animals that present with tachypnea, because many respiratory diseases will result in both cough and tachypnea. In addition to listening for increased sounds, it is important to determine if there is an absence of lung sounds, which might indicate the presence of fluid or air in the pleural space.

A notable clinical finding associated with parenchymal or pleural disease is a rapid, shallow breathing pattern, although with pleural disease, exaggerated chest wall motion or hyperpnea can sometimes be present in conjunction with a rapid respiratory rate. In animals with severe respiratory distress, elbows are abducted and the neck is extended to facilitate movement of air into the alveoli. Parenchymal diseases are characterized by increased or harsh lung sounds or by detection of adventitious sounds, particularly crackles. When pleural effusion is present, lung sounds are ausculted in the dorsal fields only and muffled sounds are heard ventrally; heart sounds are also muffled. Pneumothorax leads to an absence of lung sounds dorsally due to compression by air, and lung sounds are present in the ventral fields only. In some cases, a line of demarcation can be ausculted between normal and abnormal lung sounds, indicating a fluid line or the boundaries of air accumulation.

In addition to auscultation, thoracic percussion aids in determining if pleural disease is present. Percussion can be performed using a pleximeter and mallet or by placing the fingers of one hand on the chest and firmly striking them with fingers of the opposite hand (Figure 1.5). The sound that develops will vary depending on whether an air or fluid density is present within the thoracic cavity. Percussion of the chest in a region filled with fluid reveals a dull sound, while in an animal with pneumothorax or air trapping, percussion results in increased resonance. This technique is

somewhat limited in a cat or small dog because of the small size of the thoracic cavity.

A general physical examination would include assessment of mucus membranes for pallor suggestive of anemia, tachycardia which could accompany stress or anxiety, and abdominal distention that would support organomegaly or neoplasia as causes for panting instead of tachypnea.



Figure 1.5 Each region of the thorax should be percussed to detect regional differences in the air/soft tissue sounds that are created. One hand is placed against the thorax and is rapped quickly and sharply with the curved fingers of the alternate hand.

Exercise Intolerance

History

Exercise intolerance can result from respiratory, cardiac, musculoskeletal, neurologic, or metabolic diseases. Respiratory

disorders that result in exercise intolerance usually do so through airway obstruction in diseases such as laryngeal paralysis or bronchomalacia in the dog, asthma in the cat, or chronic bronchitis in either species, or through hypoxemia associated with parenchymal disease. Historical features in animals with airway obstruction can include loud breathing noises as well as progressive tiring and a reduced level of activity. Upper airway obstruction due to laryngeal disease can be accompanied by reports of dysphonia, decreased vocalization, gagging, or retching, while lower airway obstruction due to bronchoconstriction or inflammation is usually associated with cough.

Physical Examination

In the older, large breed dog presented for evaluation of exercise intolerance, careful attention should be paid to laryngeal auscultation for stridor suggestive of laryngeal paralysis. Increased tracheal sensitivity and loud or adventitious lung sounds in cats or dogs with exercise intolerance but no systemic signs of illness suggest that bronchial narrowing, collapse, or inflammation could be responsible for exercise intolerance. Animals that display tachypnea on physical examination, abnormal lung sounds, and systemic signs of illness likely suffer from some form of pneumonia, and if absence of lung sounds is detected, a pleural effusive disorder should be considered.

Differentiating Cardiac from Respiratory Disease

It can be difficult to distinguish animals with congestive heart failure from those with respiratory disease because of the similarity in clinical signs, physical examination findings, and sometimes even radiographic changes. In addition, some animals suffer from heart and lung or airway diseases concurrently, although in most situations one clinical syndrome predominates as the cause for presenting signs. Disorders of the respiratory tract that cause clinical complaints similar to those found in cardiac disease include asthma in cats and bronchitis in dogs, and pneumonia, pulmonary edema,

and interstitial diseases in both species. In addition, respiratory or systemic causes of pleural effusion must be distinguished from hydrothorax due to biventricular heart failure. It is also important to understand that the presence of disease in one organ can lead to secondary disease in the other thoracic organ. For example, a number of respiratory disorders such as tracheobronchomalacia and pulmonary fibrosis can result in pulmonary hypertension and even right heart failure.

History

As suggested earlier, the presence and character of cough can sometimes be helpful in distinguishing cardiac from lung or airway disease. Typically, the cough in dogs with airway disease is chronic, harsh, and paroxysmal, but can be dry or productive. In contrast, dogs in congestive heart failure will have a soft, moist cough, as do some dogs with pneumonia. Cats with bronchial disease virtually always have a history of cough, while only 5–25% of cats with congestive heart failure might have cough in the history (Dickson et al. 2018). Cats with airway disease can present with rapid breathing, although in a study of cats presented to the veterinarian for respiratory distress, severe tachypnea was more common in cats with cardiac disease (Dickson et al. 2018). Pulmonary edema is often associated with an acute onset of clinical signs referable to the respiratory tract in association with constitutional signs of lethargy, inappetence, and depression. Animals with pneumonia frequently have a vague history of illness that can be acute or chronic but is also characterized by anorexia, malaise, and weight loss. Dogs with cardiac disease are often cachectic and lethargic, while dogs with chronic bronchitis are typically robust or obese and have a healthy appetite. Dogs or cats with pulmonary fibrosis generally display a gradual deterioration in exercise tolerance, and tachypnea or difficulty breathing is noted later during the course of disease.

Signalment

Signalment can be an important clue to determining whether cardiac or respiratory disease is more likely in a given case. A young animal with a heart murmur and clinical signs of cardiopulmonary disease is

a likely candidate for congenital heart disease. Young to middle-aged cats can be affected by hypertrophic cardiomyopathy or feline bronchial disease. It is more difficult to identify the primary cause of clinical signs in middle-aged to older small breed dogs, because they can be affected by airway collapse, chronic bronchitis, and degenerative valvular disease concurrently. Exacerbation of any of these disease processes could be the cause for clinical presentation to the veterinarian.

Dobermans, Golden Retrievers, and giant breed dogs are commonly affected by cardiac disease, while primary respiratory conditions are less common in these dogs, with the exception of aspiration pneumonia associated with laryngeal paralysis, which is common in Retriever breeds. It is also important to recall that large breed dogs can be affected by airway collapse, chronic bronchitis, and pneumonia. Idiopathic pulmonary fibrosis is most commonly reported in older West Highland White Terriers, but other terrier breeds can be affected as well as cats, and younger dogs can also occasionally develop interstitial lung disease. A Maine Coon or Ragdoll cat is more often affected by hypertrophic cardiomyopathy, while a Siamese cat might be more likely to develop airway disease.

Physical Examination

Assessment of the respiratory pattern can be helpful in differentiating airway disease from cardiac disorders. In general, bronchomalacia and bronchitis in the dog or cat will be associated with increased effort on expiration or prolongation of the expiratory phase of respiration, while dogs or cats with pneumonia, pulmonary edema, or pleural effusion will more often display tachypnea.

Body temperature can be somewhat helpful in distinguishing cardiac from respiratory disease at least in cats, as a low body temperature in a cat is more typical with cardiac disease (Dickson et al. 2018), although substantial overlap can be found. Heart rate is helpful in differentiating cardiac from respiratory disease in the dog, because dogs with respiratory disease often have elevated vagal tone, which leads to a slower heart rate and an exaggerated respiratory arrhythmia. In congestive heart failure, activation of the sympathetic nervous system leads to an increased heart rate, and the presence of

a tachyarrhythmia would make cardiac disease more likely in a dog. One exception to this rule might be the Miniature Schnauzer, which can have a low heart rate in heart failure because of concurrent sinus node disease. Heart rate is less helpful in differentiating cardiac from respiratory disease in cats, because they rarely develop a respiratory arrhythmia (except with upper airway, particularly nasopharyngeal obstruction) and are more likely to be tachycardic due to stress, but there is a general trend toward higher heart rates in cats with cardiac causes of respiratory distress (Dickson et al. 2018).

Murmurs in dogs are not highly sensitive or specific for confirming congestive failure as a cause for clinical signs, although murmur intensity as well as progressive increase in intensity appears to be an important indicator of clinically significant cardiac disease in dogs with myxomatous mitral valve disease (Lord et al. 2010, 2011). Heart murmurs in cats are also neither sensitive nor specific for cardiac disease, because a substantial proportion of cats with hypertrophic cardiomyopathy lack a heart murmur and the physiologic murmur of right ventricular outflow tract obstruction is very common in cats.

Dogs with pulmonary hypertension as a consequence of primary lung disease can also display a prominent heart murmur. While a right-sided murmur of tricuspid regurgitation might be anticipated in these dogs, many have a left-sided murmur and can be demonstrated to have both mitral and tricuspid regurgitation. Rarely, a split second heart sound can be ausculted with severe pulmonary hypertension.

Detection of a gallop sound is highly suggestive of substantial cardiac disease, particularly hypertrophic cardiomyopathy in the cat and dilated cardiomyopathy in the dog. Arrhythmias, and especially tachyarrhythmias, with pulse deficits would be much more commonly encountered in an animal with heart disease than in an animal with a respiratory cause of signs.

Tachypnea or hyperpnea can be found in animals with disease of cardiac or respiratory origin. In some dogs and cats with chronic bronchitis and in dogs with tracheobronchomalacia, increased expiratory effort, prolonged expiratory time, and abdominal effort on expiration can be seen. Pneumonia, pulmonary edema, and interstitial fibrosis result in restrictive lung disease due to stiffening of the pulmonary parenchyma that leads to rapid, shallow breathing.

Pleural effusion of cardiac, respiratory, or systemic origin will also result in an elevated respiratory rate and either shallow respirations or an exaggerated respiratory effort.

Wheezes might be ausculted on expiration in animals with bronchial disease or inspiratory and expiratory crackles can be heard in dogs. The crackles detected in animals with bronchial disease are generally harsher than those heard in dogs or cats with pulmonary edema. In many animals with heart failure, lung sounds are relatively normal or only very fine, soft crackles can be ausculted. Crackles on inspiration can be prominent in dogs with pulmonary fibrosis, and these adventitious lung sounds can be ausculted over the entire thorax in animals with pulmonary fibrosis. Crackles in animals with pneumonia are sometimes localized to certain lung regions. For example, in an animal with aspiration pneumonia, abnormal lung sounds may be localized to the cranioventral lung regions or the middle lung lobes.

If pleural effusion is present due to pulmonary, cardiac, or systemic causes, heart and lung sounds will be dampened ventrally, while lung sounds are heard in the dorsal lung regions. Pleural effusion due to right heart disease is generally associated with distention of the jugular veins due to increased venous pressure. A hepatojugular reflux, enlarged liver, or ascites can also be detected. In cats, pleural and pericardial effusion can occur due to left-sided heart disease. Pleural effusion associated with infectious etiologies (pyothorax in the dog and cat or feline infectious peritonitis in the cat) is more likely to result in fever than non-infectious causes but is not always present. Pleural effusion can be unilateral when a high protein exudate is the cause, particularly pyothorax or chylothorax. In those cases, lung and heart sounds will be dampened only on the side of the effusion.

Additional Considerations

A complete physical exam is warranted in all patients presenting with signs of respiratory disease such as cough, tachypnea, or difficulty breathing. Abdominal palpation might reveal the presence of ascites or an abdominal mass. A dilated fundic exam is important

for investigating infectious diseases as the cause for respiratory signs, including feline infectious peritonitis, canine distemper virus, and fungal infections.

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2
Respiratory Diagnostics

General

Laboratory Testing

Basic laboratory work – complete blood count (CBC) and biochemical panel – in combination with a urinalysis is often performed during the work-up of a respiratory patient and can help support the presence of an underlying respiratory tract disease. With local infectious or inflammatory disease processes such as rhinitis and tracheobronchitis, hematologic changes are typically absent. In contrast, in animals with nasal neoplasia and those with parenchymal diseases such as bacterial or aspiration pneumonia or pyothorax, a neutrophilic leukocytosis is often found, and a left shift on the leukogram supports an infectious bacterial process. Peripheral neutrophilia or eosinophilia is reported in eosinophilic pneumonia/bronchopneumopathy and in feline bronchial disease. Fungal pneumonia is anticipated to result in neutrophilia and monocytosis, reflecting the chronic nature of the disease. It is unusual for chronic hypoxemia to result in polycythemia (hematocrit >65%), with one study reporting no correlation between hypoxemia and any red blood cell parameters (Holopainen et al. 2022). Polycythemia should be considered more suggestive of a right to left cardiac shunt than with a respiratory cause of hypoxemia.

Biochemical abnormalities in respiratory diseases are usually non-specific. Hyperglobulinemia can result from chronic antigenic stimulation in cases of feline bronchial disease, fungal pneumonia, chronic foreign body or aspiration pneumonia, or bronchiectasis, and concurrent mild hypoalbuminemia is occasionally present as a negative acute phase response.

Molecular diagnostics are increasingly used to document the presence of nucleic acids from an infectious organism, such as feline

herpesvirus-1, *Bordetella*, or *Mycoplasma*, in either upper or lower respiratory tract disease; however, there are important limitations to the interpretation of these results (see the sections on specific diseases). It is critical to understand that a positive molecular assay indicates only the presence of nucleic acids of the organism and does not confirm that the organism is responsible for the clinical disease identified. While culture techniques can be similarly misleading because many organisms are part of the normal flora of the respiratory tract, positive culture results reflect the presence of a multiplying, viable organism within the sample. Culture also allows assessment of susceptibility to antimicrobials.

Various studies have investigated the utility of biomarkers for differentiating cardiac from respiratory disease in animals presenting for cough or respiratory difficulty. The most common biomarker evaluated is plasma N-terminal pro-brain natriuretic peptide (NT-BNP), which is produced in response to ventricular strain or stretch. A commercially available enzyme-linked immunosorbent assay (ELISA) test is available for dogs and cats that provides a quantitative measure of NT-BNP. This biomarker is reliably elevated in dogs with congestive heart failure in comparison to dogs with respiratory disease; however, there is overlap between groups and in some studies, the non-cardiac causes of respiratory distress are poorly defined. It is unclear whether NT-BNP is of added benefit when compared to combined assessment of history, physical examination, thoracic radiographs, and cardiac ultrasound in dogs. Also, the utility of measurement has not been assessed in dogs that have concurent cardiac and respiratory disease.

A point-of-care test is available for assessing feline NT-BNP, and this can be applied to serum or pleural effusion fluid. Positive BNP tests in combination with appropriate cardiac and lung ultrasound examination could reliably establish congestive heart failure as the cause of respiratory distress, although the plasma BNP test was elevated in over 25% of cats with respiratory distress that was not due to cardiac disease (Ward et al. 2018). Renal disease can also increase BNP levels, therefore caution is warranted in relying on BNP alone for a diagnosis.

Testing for Hemorrhage

Animals presented for epistaxis, hemoptysis, and hemothorax require additional considerations when completing a diagnostic work-up because of the concern for worsening the animal's clinical presentation with invasive procedures in the presence of a bleeding disorder. Therefore, prior to performing diagnostic testing for local causes of bleeding, systemic causes of bleeding should be ruled out. Disorders of primary hemostasis (deficits in platelet number or function and vasculitis), secondary coagulopathic disorders (defects in clotting factors), and hypertension should all be considered. Epistaxis is most commonly seen with defects of primary hemostasis, and especially in animals with severe thrombocytopenia, although occasionally it will be seen in animals with hypertension. Vasculitic disorders or hyperviscosity can also result in nasal bleeding or in pulmonary hemorrhage, as is believed to occur in leptospirosis and leishmaniasis. Disorders of secondary hemostasis, and rodenticide intoxications in particular, lead to respiratory distress in association with parenchymal bleeding and can also cause mild to moderate pleural effusion.

A CBC will provide accurate assessment of platelet numbers, although determination of platelet function requires additional tests. A von Willebrand factor antigen assay is commercially available, but more specific tests of platelet function are typically only available at academic or research institutions. However, a buccal mucosal bleeding time (BMBT) can be performed in hospital practices to estimate *in vivo* platelet and vascular function. This test requires a compliant dog or a heavily sedated cat, because of the need for gentle restraint and for working in the region of the mouth.

To perform a BMBT, the animal is restrained in lateral recumbency and the lip is gently restrained upward with a strip of gauze to expose the buccal mucosa. Multiple squares of paper towel or filter paper should be available to gently blot the region below the incision into the mucosa. A spring-loaded device containing a retractable blade (Surgicutt®, Accriva Diagnostics or JorVet®, Jorgensen Laboratories, Loveland, CO, USA) is used to make a standardized incision on the mucosa opposite the premolars. Blood can be blotted from below the incision line, but the clot should not be disturbed in

order to obtain an accurate bleeding time. In normal cats, a clot will develop in 1–2 minutes and in dogs, a clot will be observed in 2–4 minutes.

For animals with hemoptysis or hemothorax, a disorder of secondary hemostasis should be investigated by performing a coagulation panel (Figure 2.1). The one-stage prothrombin time (OSPT) provides an assessment of the extrinsic coagulation pathway and vitamin K-dependent factors (II, VII, IX, X), while the activated partial thromboplastin time (APTT) evaluates the intrinsic and common pathway. In an emergency room, the activated clotting time (ACT) is often used to assess the intrinsic and common pathway (Table 2.1).

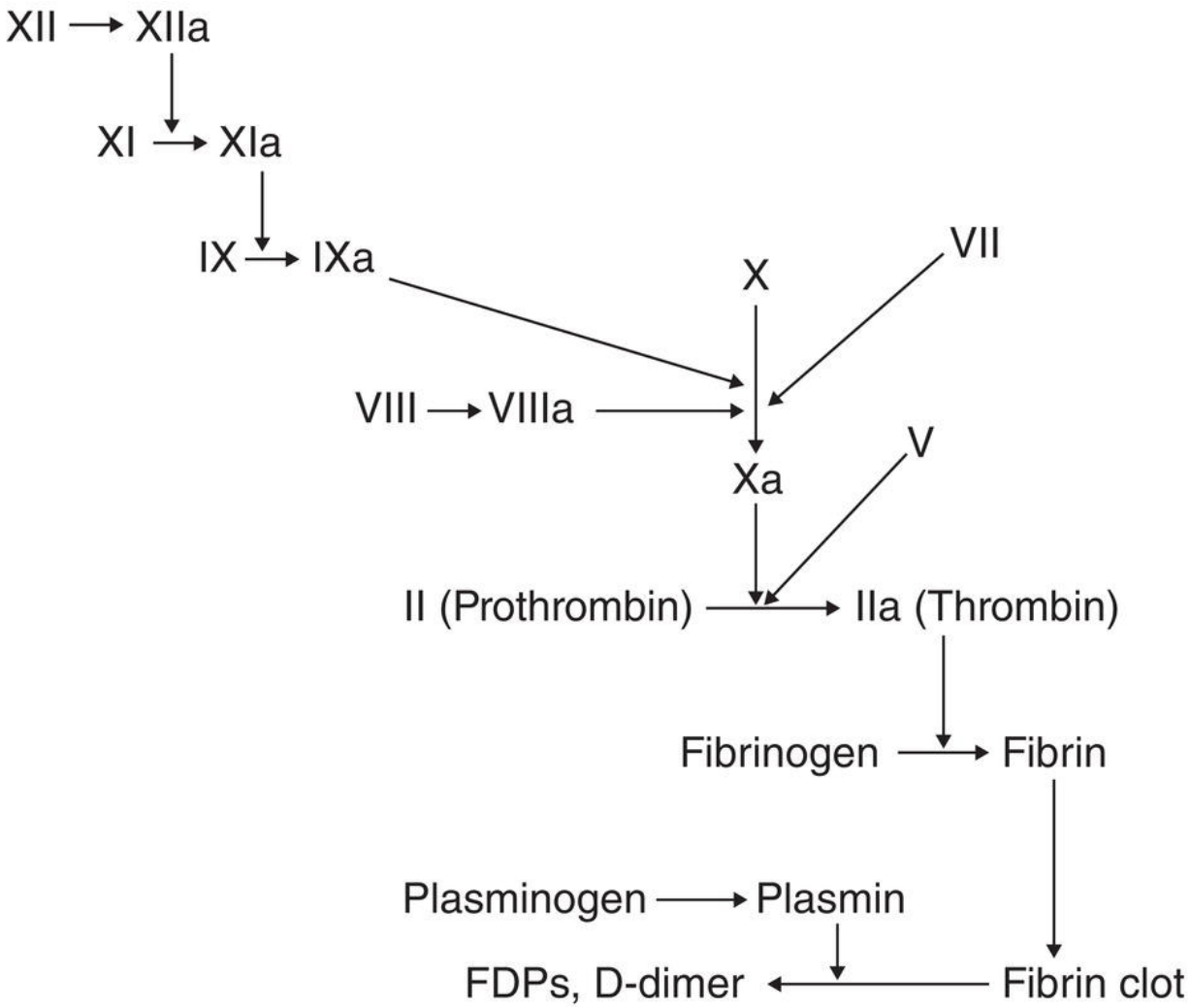


Figure 2.1 Coagulation cascade. FDPs, fibrin degradation products.

Table 2.1 Normal coagulation parameters for dogs and cats (University of California, Davis).

Coagulation test	Canine reference interval	Feline reference interval
OSPT (seconds)	7.0–9.3	10.0–15.3
APTT (seconds)	10.4–12.9	11.2–16.0
ACT (seconds)	80–120	
D-dimer (ng/ml)	0–186	
Fibrinogen (mg/dl)	109–311	73–356

Coagulation test	Canine reference interval	Feline reference interval
Von Willebrand factor (%)	90–229	
Anti-thrombin III (%)	65–145	75–110 (Cornell University)

Additional tests of coagulation include D-dimer and thromboelastography. D-dimer measures the breakdown product of cross-linked fibrin and is a reliable indicator that clotting and fibrinolysis have occurred. While this is a highly useful test in assessing the likelihood of pulmonary embolism in human patients, the test is commonly elevated in dogs with a variety of disease processes. Thromboelastography evaluates the kinetics of clot formation and breakdown, and thus can identify both hyper- and hypocoagulable states that could require intervention (Kol and Borjesson 2010). This test can be used to assess the need for anti-thrombotics and for monitoring use of anticoagulants (see Chapter 8).

Testing for Allergy

An allergic etiology is often presumed when airway eosinophilia is documented, such as with eosinophilic airway disease/asthma in cats and eosinophilic lung disease in dogs, or with nasal signs in dogs or cats because of the tendency to correlate animal diseases with human diseases. Owners can ascribe seasonality to clinical signs based on their own diseases and fail to take into account the role that irritants in the environment might play. For example, animals that develop clinical signs as the weather warms might be responding to dusts or molds dispersed by air conditioning units rather than to environmental allergens.

Much remains unknown about the immune systems of veterinary species, and wide exposure to endo- and ecto-parasitism that can cause eosinophilia hampers investigations into the role of potential hypersensitivity in naturally occurring respiratory diseases. Options for testing include total serum IgE, allergen specific IgE levels, and intradermal testing (IDT), but few tests have been fully validated in

cats and dogs. Serologic tests can provide conflicting results depending on the methodology used, and IDT is notoriously difficult to interpret in cats. The effect of age on the immune response also has to be taken into consideration with well-designed clinical investigations. Thus, the role of allergy in naturally occurring respiratory diseases remains controversial and routine allergy testing is not currently recommended for respiratory diseases.

Pulse Oximetry

Pulse oximetry provides an estimate of hemoglobin saturation with oxygen and is inexpensive, non-invasive, and easy to perform. However, one problem with the technique is that it has low sensitivity and specificity for identifying normal versus abnormal arterial oxygenation in awake patients (Farrell et al. 2019). Methodology relies on detection of differential light transmission through oxygenated and deoxygenated hemoglobin, which have different absorption spectra, as blood passes through the circulatory system. Therefore, measurement is impacted by the pigment of overlying tissue and potentially by the amount of light in the area where the test is being performed. The sensor subtracts the signal between pulses from the height of the pulse wave to determine oxygenation of inflowing blood only. Because of this feature, pulse oximetry can provide a falsely low measurement in a hypotensive patient with weak pulses or in an animal with anemia. Patient movement can hamper detection of the impulse. Finally, this technique cannot differentiate between methemoglobin and oxyhemoglobin and will be inaccurate in any animal with a dyshemoglobinemia.

A pulse oximeter reading below 95% correlates with a partial pressure of oxygen (P_aO_2) of less than 80 mmHg (Figure 2.2). When such a reading is obtained, an arterial blood gas analysis should be performed, if available, to confirm the presence and degree of hypoxemia. Sites that can be used to obtain a pulse oximetry measurement include the lip, tongue, between the toes, on the ear pinna, on the vulva or penis, and sometimes on the flank fold. The probe can be applied to various sites several times to obtain a signal, and detection of a strong pulse rate suggests that the reading is likely

accurate. It is important to remember that the pulse oximeter measures only oxygenation, not ventilation, which is assessed by measuring P_aCO_2. A venous blood gas analysis can be used as an approximation of this parameter.

Because of limitations in technology and various patient factors, direct measurement of P_aO_2 indicates that hypoxemia is absent in up to 7% of dogs with abnormal pulse oximeter readings and can be present in a similar proportion of dogs with pulse oximetry readings above 95% (Farrell et al. 2019). Therefore, an arterial blood gas would be advised whenever possible to ensure an accurate assessment of the patient, although in a practice setting this is rarely possible.

Despite its limitations, pulse oximetry can be useful prior to anesthetizing the patient for a respiratory procedure, as it provides a baseline for comparison during recovery. Pulse oximetry could also be considered somewhat helpful in determining response to therapy in hypoxemic patients, because improvements in oxygenation occur prior to radiographic changes. However, because of the sigmoidal relationship between hemoglobin saturation and arterial oxygen, oximetry remains a crude estimate of lung function. Also, this curve is shifted to the right (reducing the affinity of hemoglobin for oxygen and enhancing tissue delivery) by conditions associated with exercise and disease, such as increased temperature, decreased blood pH, increased P_aCO_2, and increased 2,3-diphosphoglycerate (DPG) produced in red blood cells during glycolysis. Thus, changes in disease status can hamper the interpretation of results.

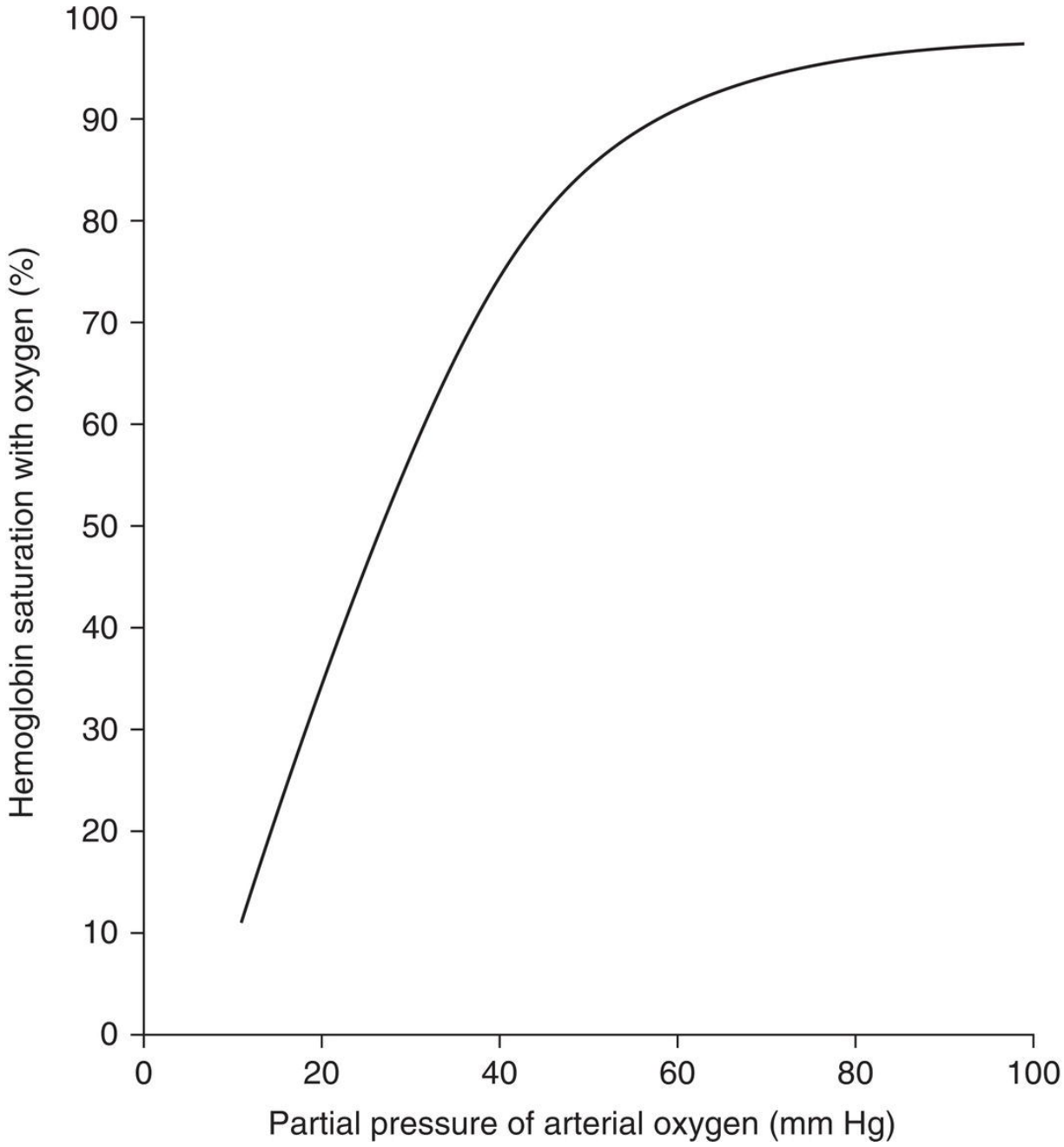


Figure 2.2 Pulse oximetry measures hemoglobin saturation with oxygen, which has a sigmoidal relationship with the partial pressure of arterial oxygen (P_aO_2). A hemoglobin saturation <95% equates to a P_aO_2 <80 mmHg and suggests hypoxemia.

Other clinical features can impact interpretation of the oxyhemoglobin saturation curve. Stored red blood cells have lower concentrations of 2,3-DPG, and transfusion with this product

increases the affinity of hemoglobin for oxygen and reduces oxygen delivery to the tissues. It appears that this is primarily a concern during the first 4–12 hours after transfusion, until 2,3-DPG concentrations rebound. Finally, hypophosphatemia also decreases 2,3-DPG which would impact interpretation of pulse oximetry readings.

Arterial Blood Gas Analysis

Arterial samples are obtained by direct puncture of the dorsal metatarsal artery in dogs and the femoral artery in cats and small dogs, using a small gauge (25 gauge) heparinized syringe. In anesthetized animals, the lingual artery can yield a sufficient sample for analysis. It is easiest to use a self-filling, pre-heparinized syringe to obtain an arterial blood gas. The artery is palpated and stabilized with two fingers of one hand while the syringe is firmly placed through the wall of the artery. Typically, the syringe will fill quite rapidly when the artery is entered (versus the vein), although low pulse pressures in sick animals can make this difficult to interpret. When there is uncertainty about whether or not an arterial sample has been obtained, a venous sample can be submitted for comparison. Approximately 0.5 ml blood is needed for analysis and the sample must be tightly stoppered to prevent entrance of air into the sample and stored on ice until evaluated. After withdrawal of the needle from the artery, firm pressure is applied to the vessel for 3–5 minutes to prevent hemorrhage. An arterial blood gas analysis measures P_aO_2, pH, total carbon dioxide (CO_2), and hemoglobin saturation with oxygen, and allows calculation of bicarbonate, base excess and deficit, and oxygen content (Table 2.2). A $P_aO_2 < 80$ mmHg indicates hypoxemia and a $P_aCO_2 > 45$ mmHg is consistent with hypoventilation.

Table 2.2 Normal blood gas values for dogs and cats.

	Dog	Cat
P_aO_2 (mmHg)	90 (80–105)	100 (95–105)
P_aCO_2 (mmHg)	37 (32–43)	31 (26–36)
pH	7.35–7.45	7.35–7.45
HCO_3 (mmol/l)	22 (18–26)	18 (14–22)

HCO_3, bicarbonate; P_aCO_2, partial pressure of carbon dioxide; P_aO_2, partial pressure of oxygen.

Alveolar–Arterial Oxygen Gradient and PF Ratio

The alveolar–arterial (A–a) oxygen gradient calculates the difference between the calculated alveolar oxygen level expected for the animal given its ventilatory status and the measured arterial oxygen level. Thus, the A–a gradient corrects for the level of ventilation performed by the animal and allows comparison of blood gas data throughout the course of disease that is not impacted by the effect of an increase or a decrease in P_aCO_2 on P_aO_2. The A–a oxygen gradient is calculated as:

$$A - a = F_iO_2\left(PB - PH_2O\right) - \left(P_aCO_2 \div 0.9\right) - P_aO_2$$

where F_iO_2 is the fraction of inspired oxygen (0.21 on room air), PB is the barometric pressure (in mmHg), PH_2O is the water vapor pressure (47 mmHg at 37°C), and R is the respiratory quotient (ratio of CO_2 production to O_2 consumption, usually assigned a value between 0.8 and 1.0). P_aO_2 and P_aCO_2 are obtained from blood gas analysis. The normal value for the A–a oxygen gradient is <15.

The PaO_2/FiO_2 ratio (PF or oxygenation ratio) provides a measure of the ability of the lung to oxygenate as the fraction of inspired oxygen changes from room air to 100% oxygen. This is calculated by dividing arterial oxygen by FiO_2 (ranging from 0.21 to 1.0). Normal animals have a PF ratio of ~500 at sea level. Values between 300 and 500 indicate mild impairment of oxygenation, while values <200 indicate serious decrements in oxygenation. This ratio can be followed during

treatment of a hypoxemic patient to determine therapeutic response, although the FiO is typically approximated by a ventilator setting rather than being measured directly. A PF ratio <200–300 is one of the criteria for a diagnosis of acute respiratory distress syndrome.

Causes of Hypoxemia

Obtaining an arterial blood gas, calculating the A–a gradient, and assessing response of hemoglobin saturation or P_aO_2 to exogenous oxygen supplementation allow assumptions to be made about the most likely physiologic mechanism responsible for hypoxemia (Table 2.3). While this can help determine the most likely cause of hypoxemia, ventilation/perfusion mismatch underlies the pathophysiology of hypoxemia in almost all lung diseases, and many clinical disorders have multiple contributors to hypoxemia.

Diagnostic Imaging

Radiography

Radiography is often the key to creating an appropriate list of differential diagnoses for the respiratory case and for determining the type of sampling method that is most likely to achieve a final diagnosis, such as endoscopy, fine-needle aspiration (FNA), or an airway wash (Table 2.4). It will also help determine the need for advanced imaging, including fluoroscopy, ultrasound, nuclear scintigraphy, or computed tomography (CT). The widespread use of digital radiography has enhanced the evaluation of pulmonary patterns. Diagnostic imaging features for each disease are presented in the relevant sections.

Table 2.3 Respiratory causes of hypoxemia.

Mechanism	Clinical attributes	Causes
Hypoventilation	High P_aCO_2	Anesthesia
	Normal A–a gradient	Upper airway obstruction
	Improved by oxygen supplementation	Neuromuscular weakness
	Improved by increasing alveolar ventilation	CNS disease
V/Q mismatch	Increased A–a gradient	Virtually any lung disease
	Mildly increased P_aCO_2	
	Markedly improved by oxygen supplementation	
Shunt	Increased A–a gradient Not improved by oxygen supplementationNot improved by increasing alveolar ventilation	Congenital right to left cardiac shunts
	Acute respiratory distress syndrome	
Diffusion impairment	Increased A–a gradient Seldom a major cause of hypoxemia at rest Causes hypoxemia during exercise or with low inspired oxygen Improved by oxygen supplementation	Interstitial lung diseasePulmonary edema
Reduced inspired oxygen	Improved by oxygen supplementationCauses hypoxemia during exercise or when diffusion is impaired	High altitude

A–a, alveolar–arterial; CNS, central nervous system; P_aO_2, partial pressure of oxygen, P_aCO_2, partial pressure of carbon dioxide.

Table 2.4 Airway sampling techniques for various lung patterns.

Radiographic pattern	Differential diagnoses	Sampling technique
Interstitial	Viral pneumonia	
	Rickettsial pneumonia	Lung biopsy
	Protozoal pneumonia	Bronchoscopy with BAL
	Hemorrhage	Tracheal wash
	Vasculitis	Fine-needle aspirate
	Pulmonary fibrosis	
	Neoplasia	
	Early pulmonary edema	
	Aspiration pneumonia	
Bronchial	Chronic bronchitis	Tracheal wash
	Feline bronchitis/asthma	Bronchoscopy with BAL
	Bronchiectasis	
	Parasitic bronchitis	
	Early bronchopneumonia	
Alveolar	Bronchopneumonia	Tracheal wash
	Aspiration pneumonia	Bronchoscopy with BAL
	Fungal pneumonia	Fine needle aspirate
	Hemorrhage	
	Pulmonary edema	
	Neoplasia	
	Non-cardiogenic pulmonary edema	
Consolidation	Neoplasia	Bronchoscopy with BAL

Radiographic pattern	Differential diagnoses	Sampling technique
	Lung lobe torsion	Fine-needle aspirate
	Consolidating pneumonia	Tracheal wash
	Granuloma	
	Bronchial obstruction	
	Feline bronchitis	
	Foreign body inhalation	
Vascular	Congenital heart disease	Echocardiography
	Congestive heart failure	
	Heartworm disease	
	Pulmonary hypertension	
	Pulmonary thromboembolism	
Effusion	Hydrothorax	Thoracocentesis
	Pyothorax	
	Hemothorax	
	Chylothorax	
	Neoplasia	
	Diaphragmatic hernia	

BAL: Bronchoalveolar lavage.

Orthogonal views are always recommended for evaluation of thoracic contents, and assessment of the thorax is improved by obtaining both left and right lateral views, as well as a dorsoventral or ventrodorsal image. Lateral images provide an optimized view of the lung closest to the radiographic unit, therefore a left lateral projection would be more likely to identify infiltrates in the right middle lung lobe in a patient with aspiration pneumonia. A right lateral projection might be preferred to investigate airway collapse at the left cranial lobar bronchus (cranial and caudal segments). The dorsoventral view provides better imaging of the cardiac silhouette and pulmonary vessels, although the ventrodorsal view allows better

detection of small volumes of pleural effusion, as well as infiltrates in the ventral or lateral portions of the lung. Importantly, attempts should be made to confirm the presence of pulmonary nodules on both a lateral and an orthogonal view.

In some patients, cervical radiographs can provide valuable information on the extrathoracic respiratory tract. Loss of the nasal air column from the nasal cavity into the nasopharynx, elongation or thickening of the soft palate, the suggestion of laryngeal edema or mass, air in the laryngeal ventricles, or caudal retraction of the larynx are features to investigate. These could reflect the presence of an upper airway obstructive lesion that might contribute to nasal discharge through nasopharyngeal regurgitation, disordered breathing associated with obstruction, or a lower respiratory tract process caused by mishandling of food and aspiration injury. Obtaining a lateral cervical view in addition to both lateral thoracic images can also enhance detection of tracheal collapse as well as intrathoracic airway or bronchial collapse.

Ultrasound

Ultrasound of the larynx can be used to evaluate patients for laryngeal paralysis or mass lesions, and cervical tracheal collapse can also be identified with ultrasound, although these studies can be technically challenging because soft tissues are adjacent to air-filled structures, which results in marked attenuation of the ultrasound beam. However, valuable information can be gained by an experienced ultrasonographer that is then confirmed by endoscopy.

Thoracic ultrasound is highly useful in detecting pleural fluid and evaluating parenchymal mass lesions, and has also proven effective in identifying pulmonary infiltrates, particularly in the emergency situation. Fluid or thickening in the alveolar–interstitial space results in the artifact of comet tails, referred to as B-lines. With alveolar–interstitial syndrome, the difference in echogenicity of fluid filled alveoli and surrounding gas generates hyperechoic wedges that extend to the pleura and move with respirations. In dogs and cats with pulmonary edema due to congestive heart failure, there is an increase in the number of detectable B-lines visible in multiple lung fields (Lisciandro et al. 2017; Ward et al. 2017), while the absence of

B lines can essentially rule out congestive heart failure. Because this technique relies on attenuation of the ultrasound beam by thickening of alveolar-interstitial junctions, other diseases that result in this process and extend to the lung periphery could lead to the generation of B-lines on ultrasound. Therefore, the use of lung ultrasound in large numbers of patients with respiratory conditions such as interstitial lung disease, pneumonia, and non-cardiogenic pulmonary edema requires additional study. Nonetheless, it appears that ultrasound of the lung could be used to evaluate patients for fluid overload or congestive heart failure and to assess response to therapy. This technique would likely be less stressful to the patient than recheck radiographs and would result in less radiation exposure for the health-care team.

Cardiac ultrasound can also be useful in providing preliminary assessment of cardiac structure and function in the emergency setting. Pericardial effusion is readily apparent as hypoechoic fluid constrained by a hyperechoic rim of pericardium that surrounds contracting myocardium. Decreased cardiac wall motion can be documented in dogs with dilated cardiomyopathy, although it is more challenging to make a diagnosis of hypertrophic cardiomyopathy in the cat. In dogs, the left atrial to aortic (LA-Ao) ratio can be assessed through a right parasternal short axis view to determine the likelihood of congestive heart failure. A LA-Ao ratio that exceeds 1.7 in this short axis view should be considered supportive of congestive heart failure in an animal with acute respiratory distress and pulmonary infiltrates. The LA-Ao ratio can be used similarly in cats.

Fluoroscopy

Airway fluoroscopy uses air as the contrast medium to evaluate dynamic changes in the luminal diameter of the airways during normal breathing and during cough. Fluoroscopy is typically performed in lateral recumbency. It most readily recognizes cervical tracheal collapse because of the large airway diameter but can also provide information on intrathoracic airway and lobar bronchial collapse. A fluoroscopic study performed in right lateral recumbency will highlight the left lung lobes, while a study in left lateral

recumbency will examine the right lobar bronchi. Right lateral recumbency appears to be used most commonly in the clinical situation. Dorsoventral positioning would likely be required to identify collapse of the accessory lobar bronchus. Fluoroscopy has poorer resolution than radiographs and the lower image quality can hamper interpretation of collapsing airways and pulmonary infiltrates. Extrathoracic airways will collapse on inspiration while intrathoracic collapse on expiration or cough.

Given the intricate relationship between neural pathways of the respiratory and digestive tracts as well as their close anatomic association, videofluoroscopic swallowing studies have a role in investigating the underlying etiology of some respiratory diseases as well as assessing the contribution of reflux to existing disease processes. Such specialized studies suggested occult aspiration injury as the sole cause of cough in some dogs and identified swallowing disorders contributing to cough in up to 75% of dogs with airway disease that lacked gastrointestinal signs (Grobman et al. 2019; Howard et al. 2023). Esophageal dysfunction and gastroesophageal reflux are common and can lead to chronic recurrent pneumonia or pneumonitis, particularly in dogs or cats with laryngeal dysfunction. Laryngeal paralysis in the geriatric Labrador is accompanied by esophageal dysmotility as part of a generalized neuropathy, and swallowing studies can help assess the risk for lower respiratory complications in affected dogs (see Chapter 5). Weak pharyngeal contractions occur in many different breeds of dogs and can predispose to aspiration events, although less is known in cats.

Interestingly, videofluoroscopy has revealed that brachycephalic breeds commonly display pharyngeal collapse (Pollard et al. 2018), likely due to anatomic issues and pressure fluctuations associated with respiratory effort. In addition to perpetuating aspiration injury to the lower respiratory tract, this can result in nasopharyngeal aspiration events that cause nasal discharge and upper respiratory tract inflammation.

Computed Tomography

Imaging the respiratory tract with CT provides superior detail in comparison to standard radiography because of the removal of

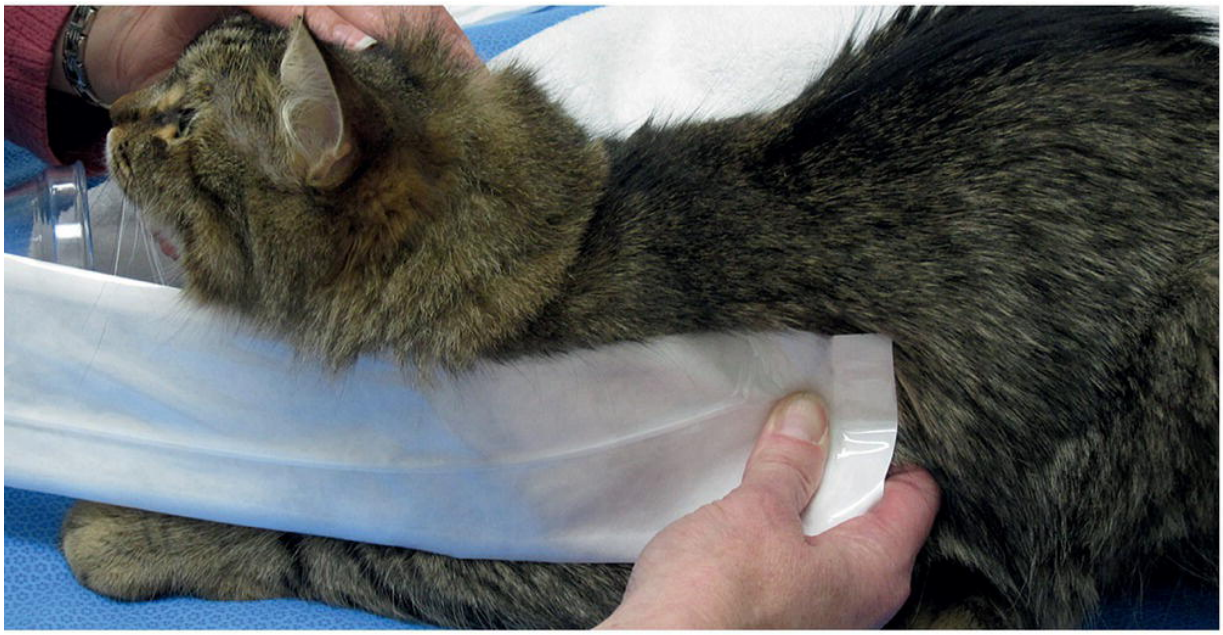
super-imposed structures and the ability to reformat images in three dimensions. Assessment of the extent of nasal conditions is improved when CT is performed because of the ability to assess cribriform plate involvement by various disease processes. When a helical CT is available, image acquisition is very fast; however, anesthesia is employed in most instances, particularly to obtain optimal images of the thorax under positive pressure ventilation. Some practices or university facilities perform CT in awake or sedated patients using a plexiglass holding chamber (VetMousetrap™; Oliveira et al. 2011). This might be most useful for nasal imaging as opposed to thoracic studies because respiratory motion artifact can obscure parenchymal details. It is a clinical decision whether the risks of anesthesia outweigh the value of images obtained, but often an intervention is planned after CT (e.g., endoscopy or surgery) which will also require anesthesia. For the thorax, the animal is typically ventilated several times and a breath hold at 15 cm water (H_2O) is employed to expand the chest during the 10–30 seconds of image acquisition. The combination of inspiratory and expiratory thoracic CT scanning can be used to assess airway dimensions and document airway collapse. Images can also be used to measure tracheal dimensions for management of tracheal collapse through placement of an intraluminal stent. CT improves detection of bronchiectasis and is valuable in assessment of interstitial lung diseases, as well as neoplasia.

Airway Sampling

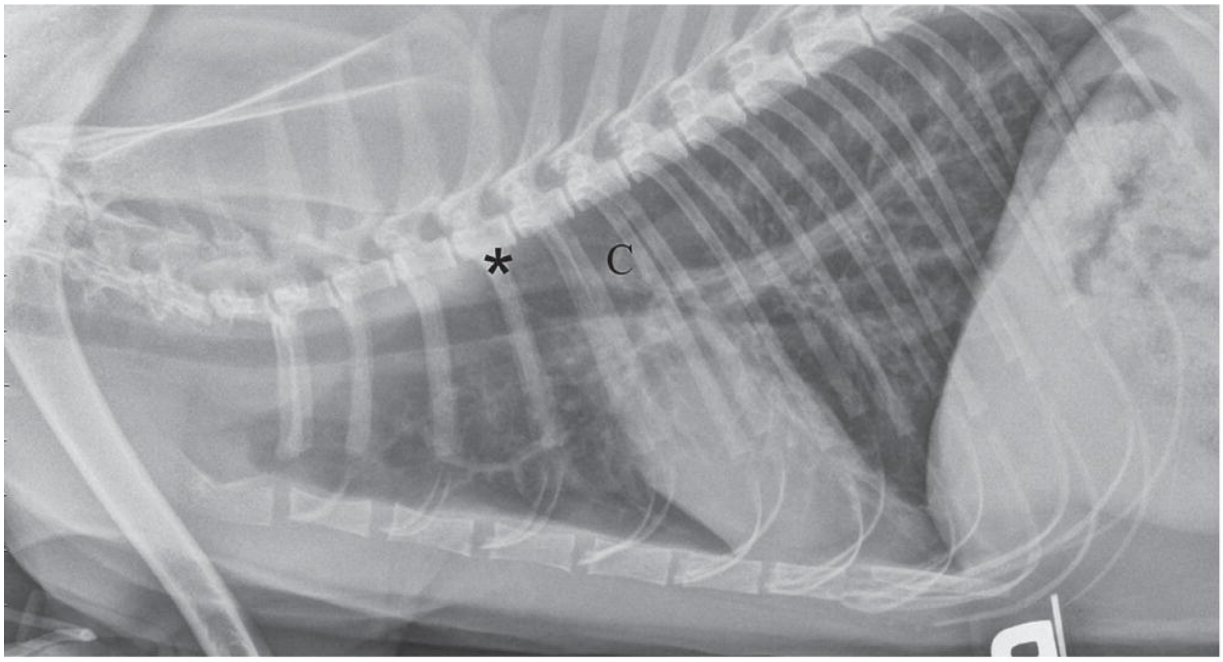
Transoral Tracheal Wash

A transoral tracheal wash is appropriate for use in the investigation of most causes of cough in large and small dogs or in cats. A sterile endotracheal tube and a sterile polypropylene or open-ended red rubber catheter (3.5–10 French) are needed. Prior to doing a tracheal wash, the catheter should be measured against the animal and marked at a position that estimates the location of the carina, which is approximately at the fourth intercostal space (Figure 2.3). Aggressive passage of the catheter too far distally can result in airway damage and is more likely to sample the bronchoalveolar

compartment rather than to obtain a global airway sample as is usually found at the carina. The animal is anesthetized with a short-acting anesthetic agent that allows intubation and approximately 10 minutes of anesthesia time. Options include propofol or alfaxalone combined with midazolam, or ketamine with midazolam to effect (Table 2.5). Lubricant should not be used on the endotracheal tube because it can adversely affect interpretation of cytology. Prior to intubation, the function of the larynx is assessed to ensure normal abduction on inspiration. In the cat, local lidocaine can be used to facilitate intubation and avoid contamination of the tube through contact with oropharyngeal or laryngeal mucosa, although providing an appropriate amount of time for drugs to take effect generally allows a clean intubation. The cuff of the endotracheal tube does not need to be inflated during the procedure, but an assistant should hold the endotracheal tube in place during sample collection.



(a)



(b)

Figure 2.3 (a and b) The urinary catheter used to collect an airway sample during a tracheal wash is measured to approximately the fourth rib (*) to avoid passing the catheter beyond the level of the carina (C).

Table 2.5 Select anesthetic agents that can be considered to facilitate respiratory procedures, to reduce anxiety, or for induction of anesthesia (Grimm et al. 2015) / with permission of John Wiley & Sons.

	Cat	**Dog**
Sedation for imaging or anxiety		
Acepromazine (IV, IM, SQ)	0.01–0.2 mg/kg	0.01–0.2 mg/kg
Butorphanol (IV, IM, SQ)	0.2–0.4 mg/kg	0.2–0.4 mg/kg
Dexmedetomidine (IV, IM)	0.002–0.010 mg/kg	0.002–0.010 mg/kg
Induction		
Propofol + midazolam (IV)	1–6 mg/kg + 0.2–0.3 mg/kg	1–5 mg/kg + 0.2–0.3 mg/kg
Ketamine + midazolam	1–5 (10) mg/kg + 0.2–0.3 mg/kg	1–5 (10) mg/kg + 0.2–0.5 mg/kg
Alfaxalone + midazolam	0.5–5 mg/kg + 0.1–0.3 mg/kg	0.5–3 mg/kg + 0.1–0.3 mg/kg
Constant rate infusion		
Propofol	0.1–0.4 mg/kg/min	0.2–0.6 mg/kg/min
Alfaxalone	0.1–0.4 mg/kg/min	0.1–0.3 mg/kg/min

With the endotracheal tube held in place, the polypropylene or red rubber catheter is passed sterilely through the tube to the fourth intercostal space, and the three-way stopcock with syringe is attached to the outer port. An aliquot of saline (4–6 ml or up to 10 ml in a larger dog) is slowly instilled into the airway followed by 2–3 ml of air to ensure that all fluid has exited the catheter (Figure 2.4). The stopcock is turned off to the syringe and either hand suction or house suction can be applied to aspirate fluid and cells from the lower airway via the third port on the stopcock. Use of a sterile suction trap (Figure 2.5) can be beneficial in collecting the sample when house suction is used. To accomplish this, an extension set is attached to

the third port of the stopcock, which is then attached to the suction trap, with the other tube from the suction trap connected to the house vacuum unit. If retrieval of fluid is less than desired, the cuff of the endotracheal tube can be inflated to improve suction. Retrieval of fluid can also be enhanced by having the assistant compress the chest, perform thoracic coupage, or stimulate a cough during suction. Instillation and aspiration of fluid can be repeated several times until an adequate sample has been retrieved. A sample that is visibly cloudy or contains mucus is apparently more likely to be diagnostic (Graham et al. 2021). Typically ~1.0 ml is sufficient for culture and cytology.



Figure 2.4 During instillation of fluid to the airways, the three-way stopcock is turned on to the catheter used to collect the airway wash and off to the suction catheter.

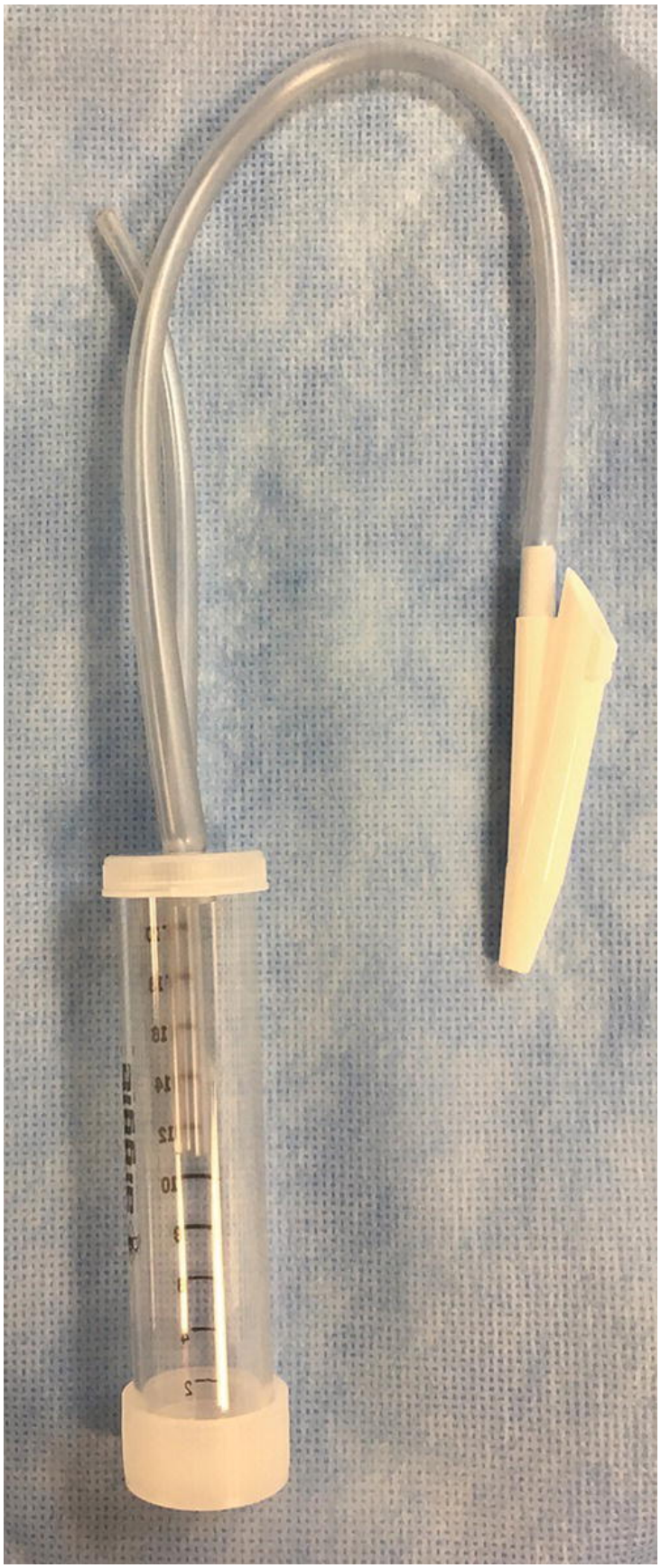


Figure 2.5 A sterile suction trap can be secured below the patient during the tracheal wash to use house suction for fluid retrieval. One tube is connected to the suction catheter and three-way stopcock used for the tracheal wash, while the other is connected to a suction device.

A modification of the transoral tracheal wash can be performed, which yields a sample more closely approximating that of a bronchoalveolar lavage (BAL). In the dog, this is achieved using a 16-French Argyle™ stomach tube (Sherwood Medical Co./Tyco Healthcare Kendall, Deland, FL; Hawkins and Berry 1999). The trachea of the dog must be large enough to accommodate an endotracheal tube that will not be fully occluded by the stomach tube. The stomach tube is shortened to remove any side holes on its distal end and to create a length that approximates the distance from the oral opening of the endotracheal tube to the last rib. The distal end of the tube can be tapered with a sterile pencil sharpener to improve the ability to wedge the tube within the airway, and the tube should be sterilized prior to use. Endotracheal intubation is carried out using a short-acting anesthetic agent (e.g. propofol or alfaxalone with midazolam) and a sterile endotracheal tube. The dog is placed in dorsal recumbency, and the modified stomach tube is passed slowly through the lumen of the endotracheal tube until it meets resistance. Gentle pressure should be used when passing and wedging this tube to avoid perforating the lung. As soon as slight resistance is encountered, the tube is withdrawn 1–2 cm and lavage is initiated with 20 ml of sterile saline followed by 5 ml of air. An adaptor might be needed to fit the syringe to the stomach tube. Gentle hand suction is applied to retrieve the fluid, and a second aliquot can be instilled as needed.

Non-bronchoscopic BAL has also been reported in the cat, and the cell distribution obtained on cytology matches that found with bronchoscopy and BAL (Hawkins et al. 1994). For this procedure, the cat is anesthetized and intubated with a sterile endotracheal tube similar to the method used for a transoral tracheal wash. The cuff is inflated and the cat is placed in lateral recumbency with the most affected side down. Aliquots of warmed sterile 0.9% saline (5 ml/kg, 1–3 aliquots) are instilled directly into the endotracheal tube using a

35 ml syringe with “Christmas tree” syringe adapter. Fluid is retrieved by hand aspiration. Elevating the hindquarters can facilitate collection, and approximately 65–70% fluid retrieval should be expected. A large volume of fluid is used in this technique, which is not always advisable in a cat with respiratory disease. Therefore, an alternative is to pass a urinary catheter (6–8 French) gently through a sterile endotracheal tube until resistance is met (Foster et al. 2004), in a manner similar to that employed when a modified stomach tube is used to perform blind BAL in a dog. Instillation and aspiration of 5–10 ml of sterile saline provides an adequate lavage sample for cultures and cytology. With either procedure, respiratory rate and pulse oximetry should be monitored to detect untoward reactions and oxygen supplied as needed. Importantly, whenever performing a respiratory procedure in a cat, pre-treatment with terbutaline (0.01 mg/kg subcutaneously) is recommended to avoid complications (especially hypoxemia) associated with bronchoconstriction.

Transtracheal Wash

A transtracheal wash is appropriate for larger dogs (>8 kg) or those that cannot be anesthetized for a transoral tracheal wash (e.g. an older dog with laryngeal paralysis). It should not be employed in small dogs, cats or kittens, or puppies and is more likely to be associated with worsened cough in a dog with marked tracheal sensitivity. Generally only local anesthesia is needed, although mild sedation with acepromazine and butorphanol or a similar short-acting combination can facilitate completion of the procedure. The animal is positioned in a sitting or standing position with the head held upward and the neck gently extended. Avoid over-extension of the neck, which is uncomfortable for the patient and could flatten the trachea, making it more difficult to penetrate between the rings.

The easiest way to perform a transtracheal wash is to use a 14 or 16 gauge over-the-needle catheter as a cannula to penetrate the trachea and a long, sterile 3.5 French urinary catheter to pass down into the airways for sample collection (Figure 2.6). Before entering the trachea with the short catheter, ensure that the long catheter will pass readily through that catheter or the procedure cannot be

completed. The trachea can be entered at the cricothyroid notch, but it is preferable to access the region lower on the neck between the tracheal rings to avoid potential damage to laryngeal structures (Figure 2.7a). This will also facilitate collection of a sample from closer to the carina in a larger dog. Choose a site on the neck where the trachea is easily palpated and can be stabilized against the neck muscles for insertion of the short catheter. The ventral portion of the neck is clipped and lightly scrubbed with antiseptic solution followed by alcohol wipes. Local anesthesia with lidocaine (0.25–0.5 ml) is applied at the skin and subcutaneous tissue down to the level of the tracheal rings. A more complete surgical preparation is performed after local anesthesia is instilled.

To begin catheter placement, the skin is tented at the site of lidocaine infusion and the catheter is passed through the skin at a perpendicular angle to the neck, with the bevel of the needle facing downward. If needed, prior to starting, a small stab incision can be made in the skin to facilitate passage of the catheter. When preparing to enter between the tracheal rings, the trachea is firmly stabilized against the neck muscles to prevent it from moving away from the needle. The tracheal rings and annular ligament can often be palpated with the tip of the needle, allowing entry of the short catheter directly between the cartilage rings. The trachea is almost immediately below the skin and only a minor amount of forward movement is required to enter the lumen. A distinct pop is usually felt when the needle enters the tracheal lumen, and the dog often coughs. With the needle and catheter in the airway, the hub of the needle is moved back towards the neck to a position more parallel with the trachea. This will facilitate passage of the catheter down the center of the airway (Figure 2.7b). The needle is withdrawn at this stage to pass the long, sampling catheter through the short catheter to the level of the carina (Figure 2.8).

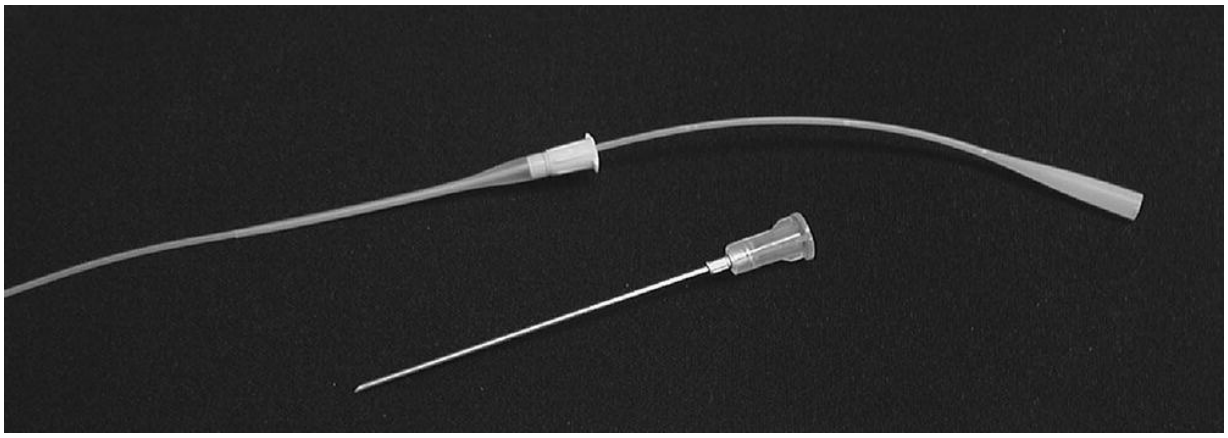
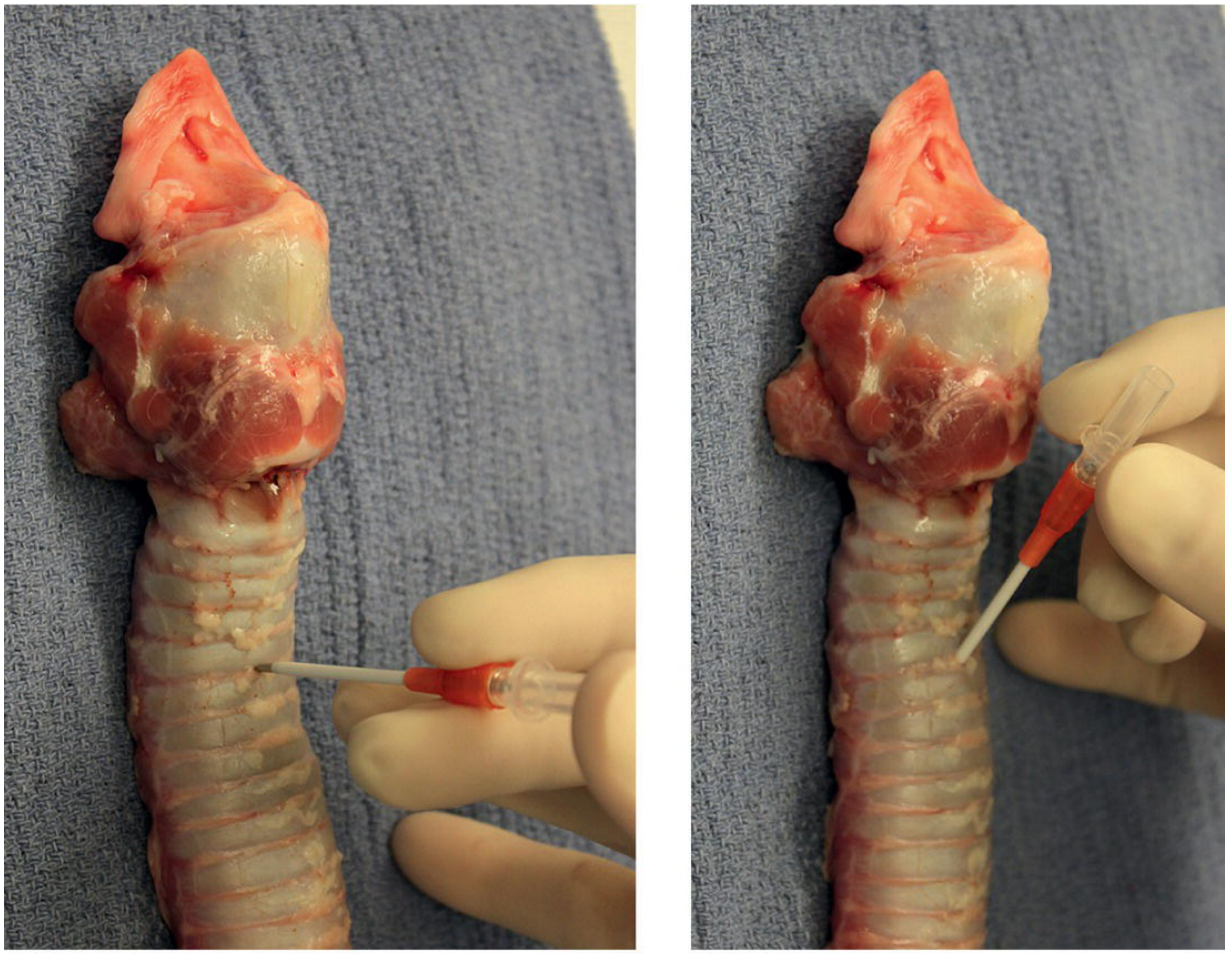


Figure 2.6 An over-the-needle catheter (lower half of the slide) can be used as a cannula to perform a transtracheal wash using a sterile urinary catheter.



(a) (b)

Figure 2.7 (a) To initiate a transtracheal wash, the over-the-needle catheter system is directed into the trachea at a perpendicular angle. (b) After penetrating between the tracheal rings, the hub of the catheter system is moved toward the neck to create a more parallel angle in order to feed the catheter off the needle in preparation for passing the urinary catheter.



Figure 2.8 The short catheter has been seated between the tracheal rings and is grasped firmly while the long catheter is passed down the trachea for collection of an airway sample.

The urinary catheter should move freely down the airway, and this usually stimulates coughing. If neither of these occurs, the sampling catheter could be traveling in subcutaneous tissue and both catheters should be removed (the long one first followed by the short one), and the procedure started over.

When the sampling catheter is fully deployed, the three-way stopcock and syringe can be attached to perform the airway wash as described for the transoral wash. Individual aliquots of saline (4–10 ml) followed by 2–3 ml of air are instilled into the airway, and suction is used to retrieve the fluid and cells from the lower airway, as detailed earlier.

Respiratory Endoscopy

Rhinoscopy

A full rhinoscopic examination includes evaluation of the caudal nasopharynx to visualize nasal openings at the choanae and inspection of the rostral nasal cavity. The best equipment to use in evaluating the caudal nasopharynx is an endoscope capable of 180° flexion that is ~5 mm in outer diameter (Figure 2.9). Smaller flexible endoscopes can be used but are at greater risk for damage if the animal gags during the procedure and the pharynx closes down on the scope. A rigid scope with a 120° viewing angle can also be used for this exam. If an endoscope is unavailable to complete the retroflexed exam, a bright light source and dental mirror can be used, along with a spay hook to retract the soft palate cranially, although this can be quite challenging in smaller animals. The dental mirror is placed in the back of the pharynx and angled above the soft palate while a light source is used to illuminate the view of the choanae in the mirror.

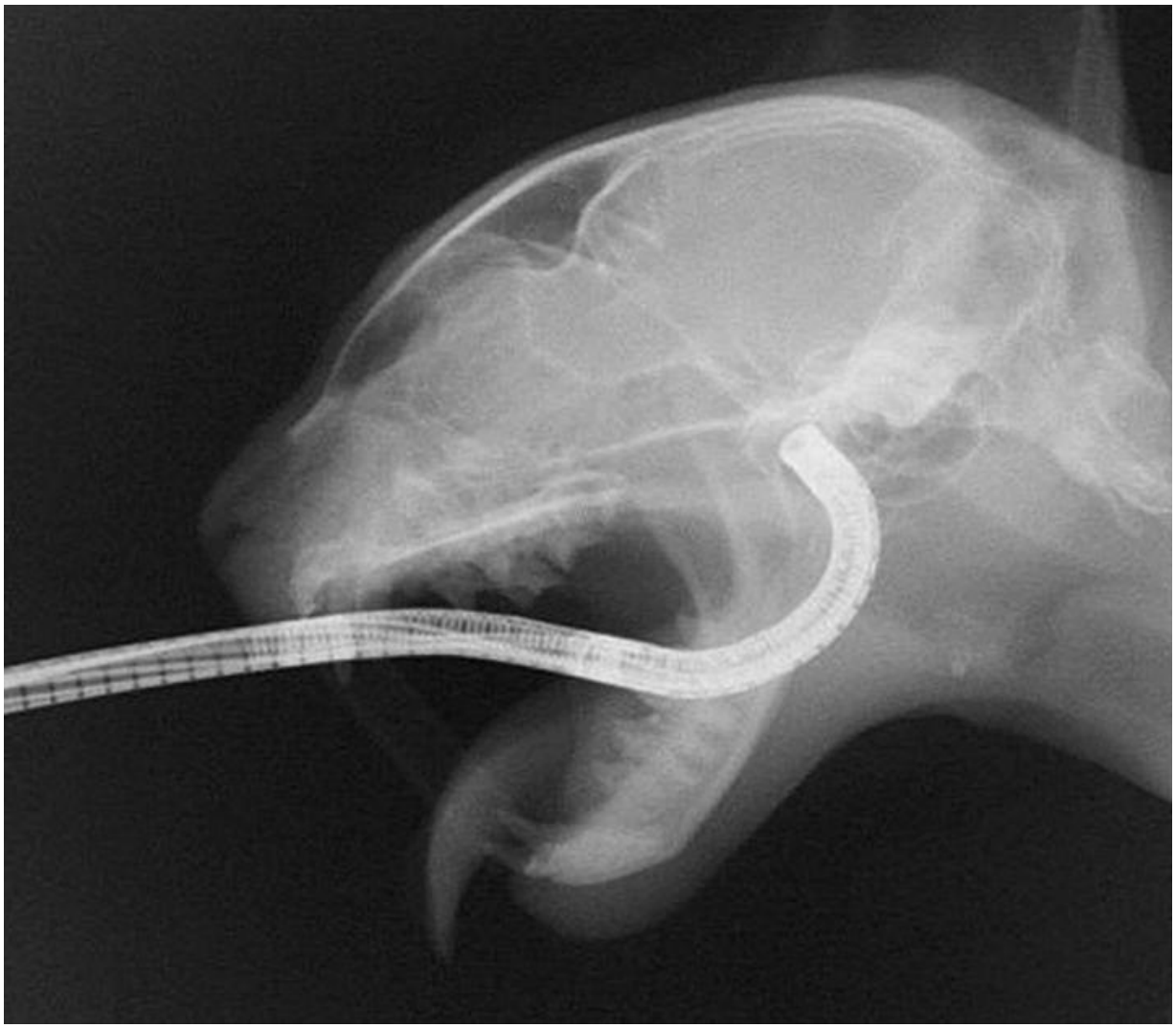


Figure 2.9 Visualization of the choanae is obtained by inserting a flexible endoscope into the oral cavity and flexing the scope maximally (180°) around the soft palate.

Examining the nasopharynx is a highly stimulatory procedure, and maxillary or infraorbital nerve blocks can improve acceptance of the procedure. Local anesthesia of the oropharynx with lidocaine gel on long cotton swabs also can facilitate placement of the endoscope around the soft palate. During a nasopharyngeal exam, two mouth gags are in place to hold the mouth wide open for placement of the endoscope or other equipment into position. Caution is warranted when using mouth gags in cats, because over-extension of the jaw can reduce retinal blood flow through the maxillary artery (the continuation of the external carotid as it crosses the mandible),

resulting in blindness (Barton-Lamb et al. 2013). Therefore, excess opening of the jaw should be avoided and time spent completing the examination kept to a minimum. Extending the neck and pulling the tongue forward will help place the instruments in the proper position in an expedient fashion. To achieve the appropriate view with an endoscope, the non-flexed scope is passed into the oral cavity beyond the soft palate and then flexed until the light can be seen above the soft palate. The scope is then pulled forward (with the flex in place) until the choanae are visualized. Note that the image is upside down and backward (Figure 2.10).

Foreign material can be removed from the nasopharynx or choanae using the endoscope and samples can be obtained for histopathology. To initiate this procedure, the endoscope is removed from the patient and forceps are passed through the biopsy channel with the tip of the scope in a non-flexed position until forceps are at the end of the scope. The scope is then inserted into the mouth and flexed about the soft palate, as previously described. Note that the degree of flexion the scope can achieve is reduced by the presence of forceps in the channel, making visualization of any lesion more challenging. Forceps are passed forward to grab a foreign body or mass lesion and firm traction is applied. It is most efficient and safest to unflex the scope, withdraw it from the patient, and extrude the forceps beyond the tip of the scope to remove the sample, rather than pulling the sample and instrument back through the scope.

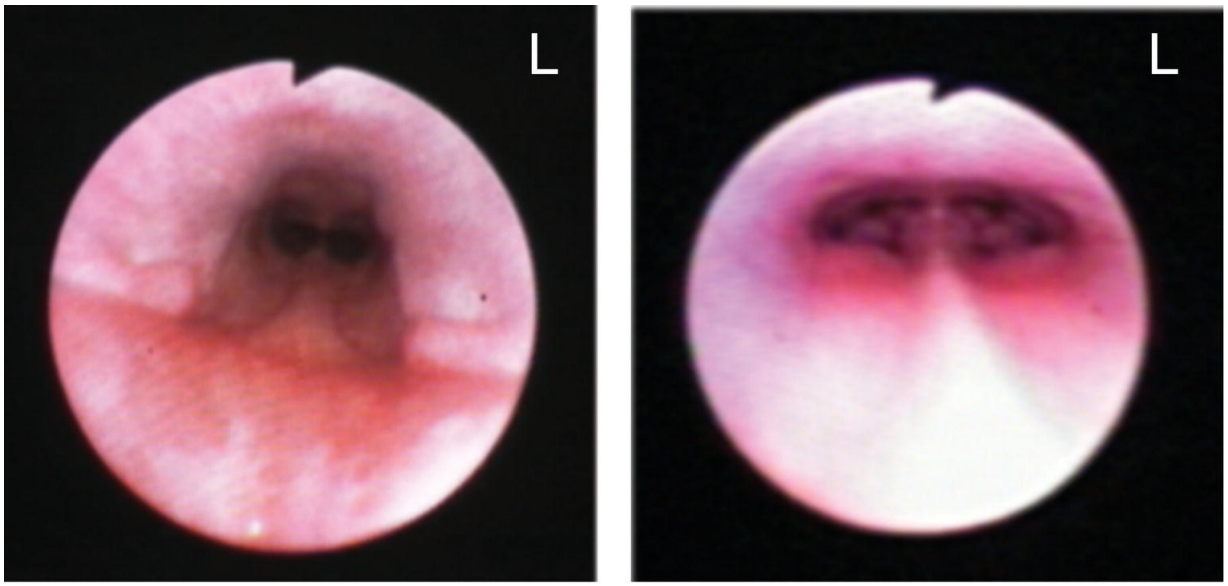


Figure 2.10 Image of the normal nasopharynx in (a) a dog and (b) a cat. The soft palate is dorsal in these images.

After the caudal nasopharynx has been examined and samples are obtained for histopathology as indicated, a moistened surgical laparotomy pad is used to pack the throat in order to prevent aspiration of fluid during rostral rhinoscopy. Inflation of the endotracheal tube cuff should be double checked at this time also. Equipment available for rostral rhinoscopy includes rigid endoscopes (with or without an external sheath), otoscopes, and small flexible endoscopes. Unfortunately, while otoscopes are routinely available in general veterinary practices, they provide very limited view within the nose of most animals and do not allow magnification while attempting to remove foreign material. Therefore, specialized endoscopes are most useful for performing rhinoscopic assessment. Rigid scopes have better optics, are easier to maneuver, and come in smaller sizes, while flexible scopes allow greater access to the nasal cavity and can permit examination of the frontal sinuses when there is marked turbinate destruction (such as in nasal aspergillosis). Rigid scopes are available with viewing angles from 0 to 30° and personal preference dictates which scope is most desirable. The 0° angle of view provides the most direct view of structures immediately rostral to the scope. Angled scopes require vertical manipulation of the instrument handle to visualize structures directly forward, but they can be beneficial in looking upwards or laterally in the nose.

Rhinoscopy can be performed using the telescope portion of the rigid scope alone (~2.8 mm outer diameter) or by using the sheathed scope (~5 mm outer diameter), which has flush and suction ports as well as a biopsy port available (Figure 2.11). The biopsy port of the sheath will accept standard endoscopic biopsy or foreign body retrieval instruments (1–1.8 mm).

Before entering the nasal cavity, the endoscope is placed against the skull and measured to the level of the medial canthus of the eye to approximate the position of the cribriform plate. A piece of tape is applied to the rigid telescope at this length (but not to a flexible endoscope), and the equipment should not be passed further than this point to avoid penetrating through the cribriform plate into the brain. The normal nasal cavity is made up of scrolls of turbinates comprising the dorsal, middle, and ventral concha. The mucosa is generally pink, with a pale sheen of serous secretions coating the smooth epithelial surface (Figure 2.12). The primary changes to look for during rhinoscopy are mucosal hyperemia, mucus accumulation, epithelial irregularities, turbinate destruction that is visualized as increased space between turbinates, or a mass effect that reduces space in the nasal cavity.

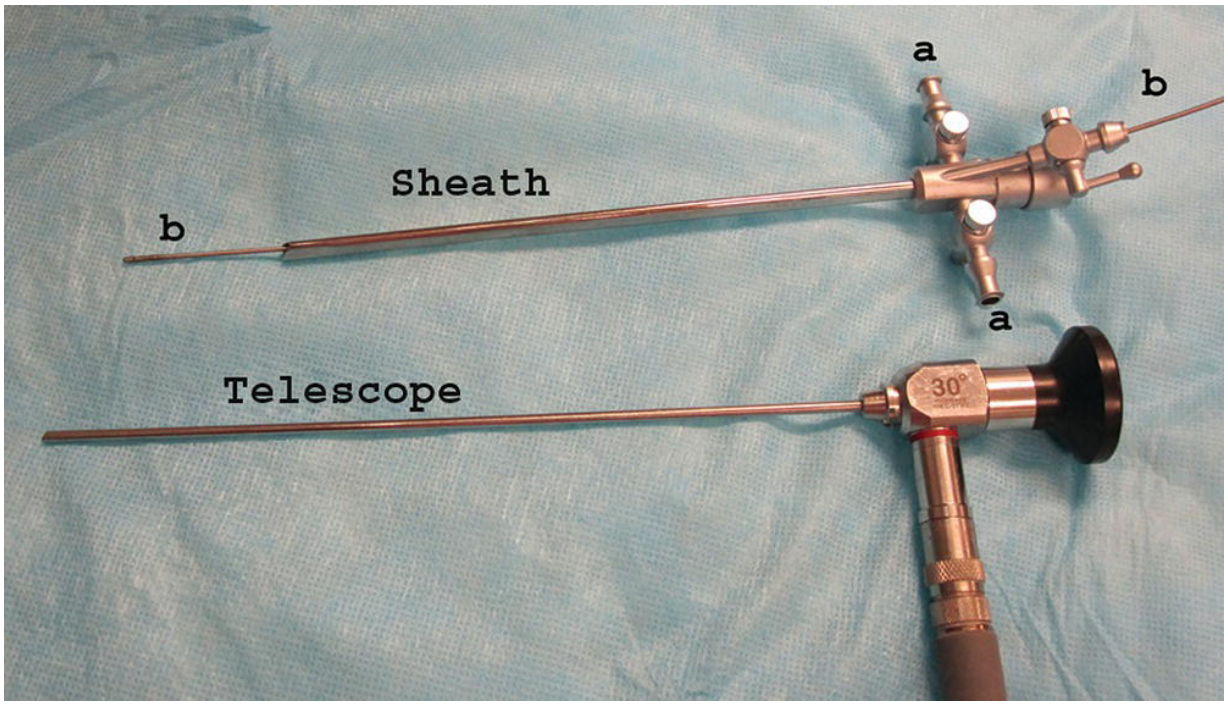


Figure 2.11 The sheath (~5 mm outer diameter) for the telescope portion of the rigid scope (~2.8 mm outer diameter) has flush and suction ports (a) as well as a biopsy port (b) available.

If indicated (usually only in a cat that has had repeated exposure to multiple antibiotics), an intranasal sample can be collected for bacterial culture. A sterile cytology brush (Cytosoft™, Medical Packaging Co., Panorama City, CA) is inserted into the ventral portion of the nasal cavity and gently twirled to collect cells and secretions (Figure 2.13).

After the initial visual inspection and when the cribriform plate is intact, nasal drops containing oxymetazoline or phenylephrine can be dropped or sprayed into the nasal cavity to create vasoconstriction. This will cause swollen and hyperemic mucosa to blanch and shrink, thus changing the overall appearance of the mucosa, but allowing improved access through the nasal meati. Topical anesthetic drops or a misted spray of tetracaine can also be used to help reduce the stimulation caused by rhinoscopy, although this is variably effective.

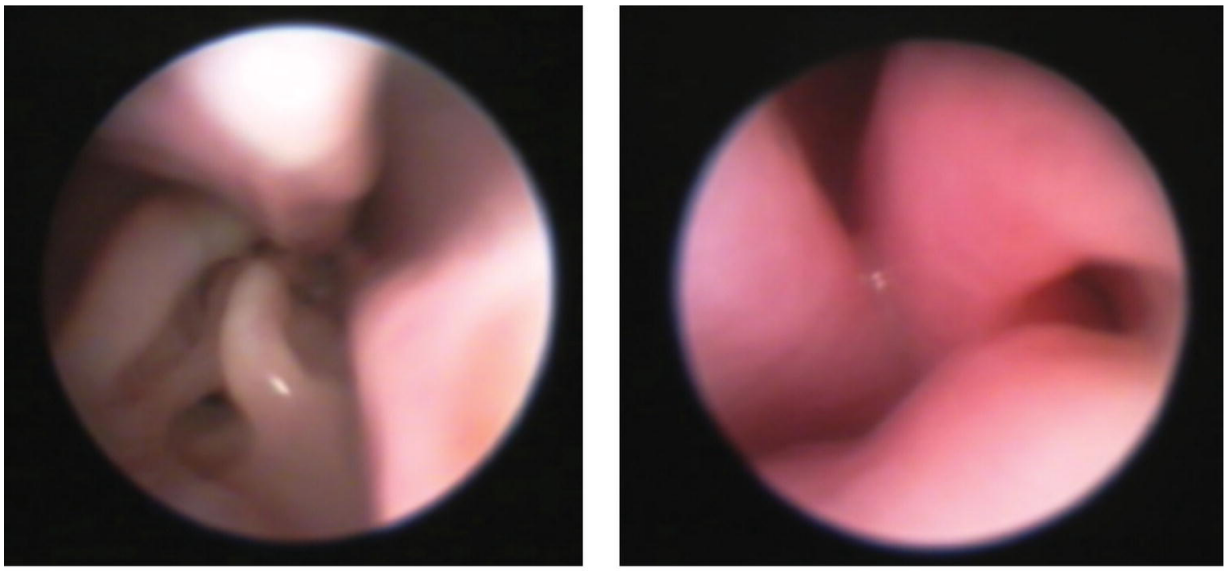


Figure 2.12 Normal nasal turbinates in (a) the dog and (b) the cat.



Figure 2.13 Prior to entering the nasal cavity, the cytology brush should be measured to the medial canthus of the eye to prevent placing the instrument too far distally, which could penetrate the brain. *Inset*: the brush contacts the nasal mucosa to collect cells and bacteria for culture.

Mass lesions, fungal plaques, and mucosal lesions should be biopsied

with visualization to improve the probability of achieving a diagnostic sample. With diffuse or generalized disease, an attempt should also be made to obtain at least the initial nasal biopsy with visualization of the area (Figure 2.14). This can be accomplished either by using a biopsy instrument that fits over the scope, by using a flexible biopsy instrument that passes through the sheathed scope, or by advancing a rigid biopsy instrument along the outside of the rigid scope. Once bleeding starts, the visual field is usually lost, although intermittent flush and suction can be used to clear the field. Nasal flush can be achieved by attaching a bag of chilled fluids to the biopsy port on the sheath of the scope, or by inserting a red rubber catheter into the nasal cavity and using syringes to obtain a pulsatile pressurized flush. In cats, a 20–60 ml syringe inserted into alternating nares can be used for nasal flush between episodes of visual scoping (Figure 2.15). Nasal flush should also be used if excessive mucus obscures visualization of the mucosa within the nasal cavity. If a foreign body is highly suspected but is not visualized or removed during the procedure, nasal flush will sometimes dislodge the material. The surgical laparatomy pad protecting the endotracheal tube should be removed periodically, examined for foreign material, and replaced with a new one. Also, if a foreign body is suspected, consider placing a Foley catheter in the caudal nasopharynx and using retrograde flush of the nasal cavities to dislodge items (Figure 2.16).

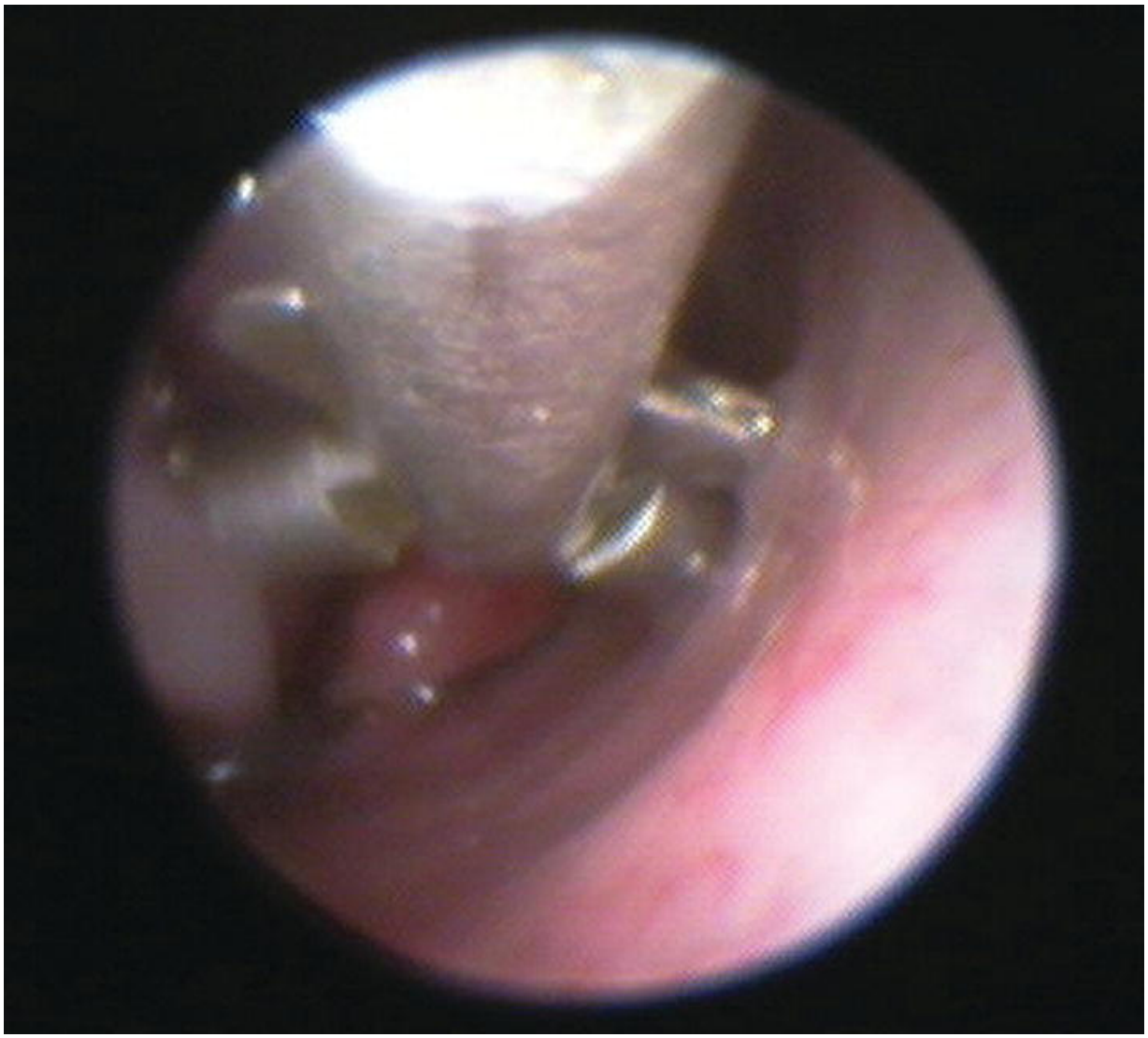


Figure 2.14 Diagnostic yield of a nasal biopsy sample is improved when the site to be sampled is visualized during the biopsy procedure.

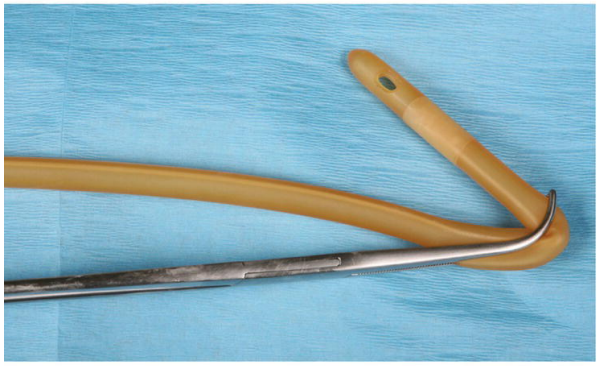

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Figure 2.15 Nasal flush can be performed in a cat by inserting a syringe tip into the nostril and injecting pulses of chilled saline through each nostril. The animal must be intubated and have a moistened laparatomy pad placed in the oral cavity to protect against tracheal aspiration.

After removing the moistened lap pad from the oral cavity, the airway above the endotracheal tube is suctioned to remove any additional fluid. Before recovery from anesthesia, a complete oral exam and dental probing are recommended to rule out dental disease as a cause for nasal discharge (Figure 2.17).

Laryngoscopy

Laryngoscopy can be performed as a stand-alone procedure to evaluate dysphonia or stridor, or during the preliminary assessment of the airways before a transoral tracheal wash or bronchoscopy. An accurate laryngeal examination is important because laryngeal dysfunction can be a contributing component to cough in up to 20% of dogs, even when signs of upper airway disease are lacking (Johnson 2016). An appropriate anesthetic protocol must be devised that provides a light plane of anesthesia, maintains respirations, and preserves laryngeal function (see Table 2.5). While multiple agents are appropriate for use, the key feature is to have spontaneous and vigorous respirations. An assistant is required to identify thoracic inspiratory efforts so that the examiner can insure coordination of laryngeal abduction with inspiration. If the plane of anesthesia is too deep, one to two boluses of doxapram (0.5–1.0 mg/kg) can be used to stimulate respirations (Miller et al. 2002).



(a)



(b)

Figure 2.16 (a) Right-angle forceps can be used to place a Foley catheter above the soft palate. (b) The forceps with Foley are inserted into the oral cavity and a spay hook can be used to retract the palate over the balloon portion of the Foley. The balloon is fully inflated and copious nasal flush is used to dislodge foreign material or exudate into a collection bowl.

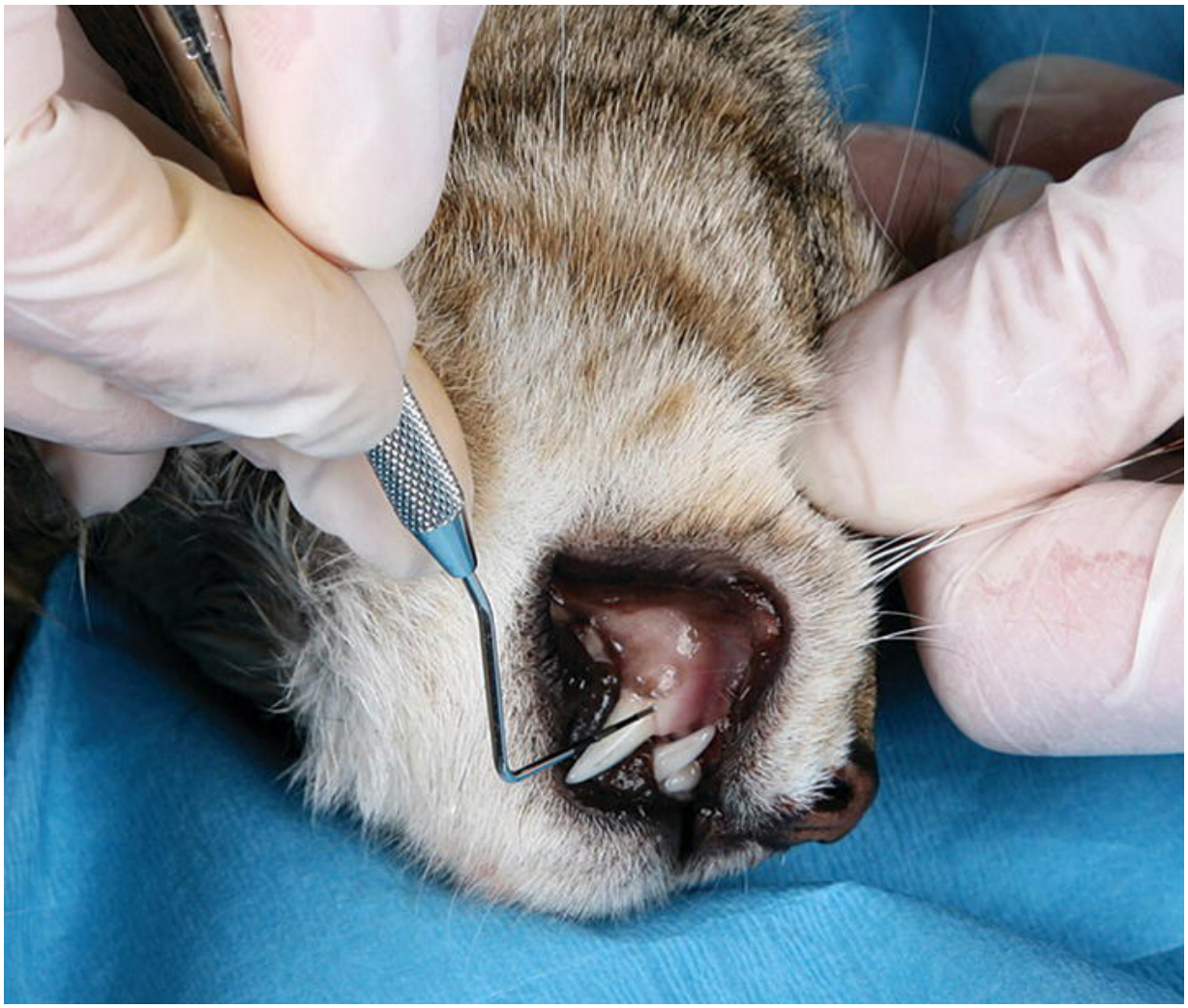


Figure 2.17 A periodontal probe is inserted along the gum lines surrounding each tooth after imaging and rhinoscopy have been completed. Periodontal pockets >1 mm depth in the cat and >2–3 mm depth in the dog could result in clinically significant nasal disease due to tracking of bacteria up the tooth root into the nasal cavity.

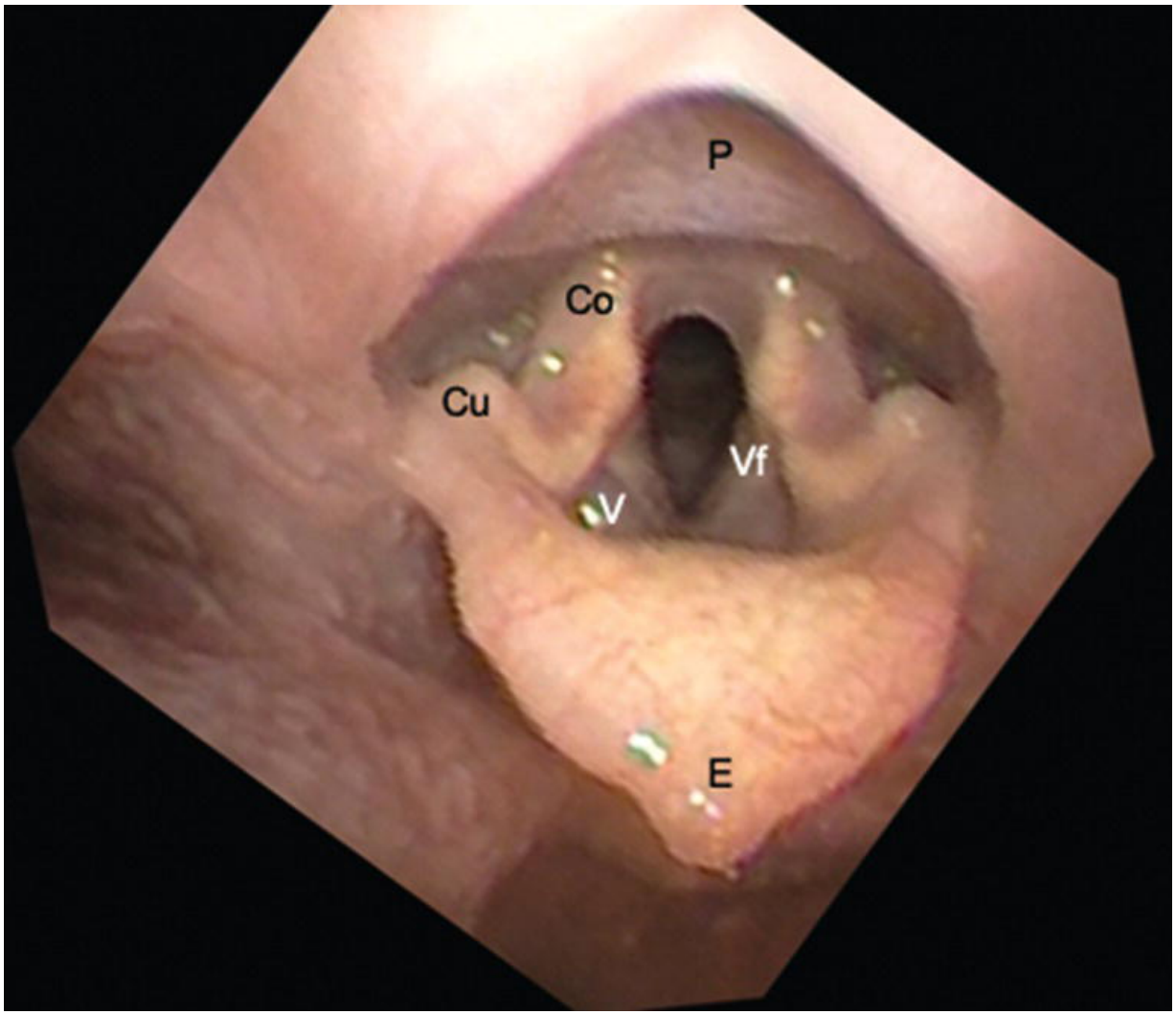


Figure 2.18 Endoscopic image of the larynx showing the palate (P), corniculate process of the arytenoids (Co), vocal folds (Vf), cuneiform process of the arytenoids (Cu), laryngeal ventricles (V), and epiglottis (E).

Laryngoscopy includes the assessment of function as well as examination of all structures in the area of the rima glottis, including the soft palate, tonsils, laryngeal aditus, and laryngeal ventricles/saccules (Figure 2.18). The larynx is inspected for edema, hyperemia, or accumulation of secretions, any of which could indicate injury due to turbulent airflow, acid reflux, or lower airway inflammation. Eversion of laryngeal ventricles is a common contributor to airflow obstruction in the upper airways (see Chapter 4), particularly in brachycephalic breeds. Because they are membranous tissues, laryngeal ventricles are very responsive to

manipulation and can become more swollen as the upper airway evaluation continues, so it is important not to over-interpret this finding. In the normal dog, the soft palate should not overlap with the epiglottis by more than a few millimeters. Tonsils should be within their crypts; enlargement or eversion is suggestive of inflammation or irritation.

Bronchoscopy

Bronchoscopy is one of the most useful techniques for obtaining a diagnosis in animals with airway or lung disease. It can define the location, grade, and extent of tracheal ring flattening for planning stabilization through surgery or stent implantation, will identify protrusion of the dorsal tracheal membrane into the tracheal lumen, can document tracheal inflammation or irritation, allows visualization of intrathoracic bronchial or airway collapse, and provides collection of a guided BAL fluid sample to determine the contribution of small airway disease to respiratory signs. It is also highly useful and successful in managing foreign body inhalation. However, it does require general anesthesia as well as familiarity with the anatomy of the airways to make it a viable diagnostic technique.

Flexible endoscopes used for bronchoscopy are typically ~4.9 mm outer diameter for canine bronchoscopy and either 55 cm in length or an extended length scope (85–110 cm). For bronchoscopy in smaller dogs and cats, 3.8 or 2.5 mm outer diameter endoscopes are preferred. The standard bronchoscope has 2-way flexion; some longer scopes have 4-way flexion depending on the manufacturer. The biopsy channel is used for BAL. Airway biopsy or Wang needle aspiration of mass lesions, cytology brushings of abnormal appearing epithelial lesions, and foreign body retrieval are performed via instruments inserted through the biopsy channel. Foreign bodies are generally withdrawn at the time they are first visualized, but biopsies or mucosal brushing should be performed after BAL to avoid blood contamination of the BAL fluid.

Complications that can be encountered after bronchoscopy are worsened cough or increased airway obstruction. These occur most commonly in dogs that have severe tracheal collapse or

bronchomalacia, because irritation of the airway potentiates a cough, and suppression of respiratory effort by anesthetic agents allows passive collapse of diseased large and small airways. Excessive stress and excitement during recovery that initiates cough or respiratory distress are particularly troublesome. This can be alleviated by a slow recovery from anesthesia with judicious use of sedatives that will not further suppress respiration. Coughing can be partly alleviated by administering dilute lidocaine (approximately 1 ml of 1% lidocaine for a small dog) through the bronchoscope into the trachea at the end of the procedure. Subcutaneous terbutaline (0.01 mg/kg) might improve respirations somewhat in dogs with collapsed airways (although it does not act as a bronchodilator in this situation), and recovery in an oxygen-enriched environment can lessen respiratory distress. Bronchospasm leading to hypoxemia can be a particular problem in the cat with inflammatory airway disease that has severe cough and respiratory distress. Terbutaline should be given subcutaneously immediately prior to the BAL at 0.01 mg/kg to produce airway smooth muscle relaxation and reduce complications. This can be repeated one to two times if complications of the procedure such as desaturation or wheezing arise. Aerosolized albuterol can be given through the endotracheal tube at the end of the procedure if injectable terbutaline is not available.

General anesthesia is required during bronchoscopy to suppress coughing and laryngospasm, to allow examination of the airways without inducing trauma, and to protect the endoscope. Bronchoscopy can be performed using gas anesthesia if the animal is large enough for a 7.5 mm endotracheal tube. A special T adapter is used to pass the scope through the endotracheal tube while administering anesthetic gas and venting expired gases (Figure 2.19). For cats and small dogs, endoscopes 2.5–3.8 mm in outer diameter, 55–70 cm in length are most advantageous. These scopes are very delicate and are typically not passed through the bronchoscopy adaptor and endotracheal tube due to possible damage to the insertion tube. Also, placement of the scope through a small endotracheal tube could lead to airway obstruction, accumulation of CO_2, and possible narcosis. In these small patients, anesthesia is maintained with a constant rate infusion of a drug such as propofol or alfaxolone (see Table 2.5). Jet ventilation can be used to provide

oxygenation through bulk flow, or oxygen can be supplied to the patient using a red rubber catheter attached to the oxygen supply. The catheter should terminate in the distal trachea to avoid the possibility of wedging it into a bronchus and causing airway rupture.



Figure 2.19 A bronchoscopy adapter allows passage of a ~5.0 mm endoscope through an endotracheal tube while oxygen and anesthetic gas are administered through the side port.

Virtually all animals undergoing bronchoscopy suffer respiratory embarrassment. Prior to bronchoscopy, patients are preoxygenated with a facemask, and an anesthetic protocol is chosen that avoids excessive cardiopulmonary depression. Animals are placed in sternal recumbency and two mouth gags are in place throughout the procedure to protect the bronchoscope. The normal trachea appears round to oval, with minimal laxity in the dorsal tracheal membrane (Figure 2.20). At the carina, the bifurcation into the left and right mainstem bronchi provides a reliable landmark for assessing location within the airways to allow further navigation into lobar and segmental bronchi (Figure 2.21). Normal airways appear round to oval in shape, demonstrate little change in shape or diameter throughout respiration, have minimal secretions, and are pale pink in color (Figure 2.22). All accessible airways should be evaluated, and abnormal regions with mucosal hyperemia or irregularity or areas with mucus accumulation should be identified as possible sites for BAL. If an obviously abnormal site is not visualized, the right middle lobe or caudal portion of the left cranial lobe is often a

worthwhile site to lavage, because they are both ventrally oriented and tend to accumulate secretions.

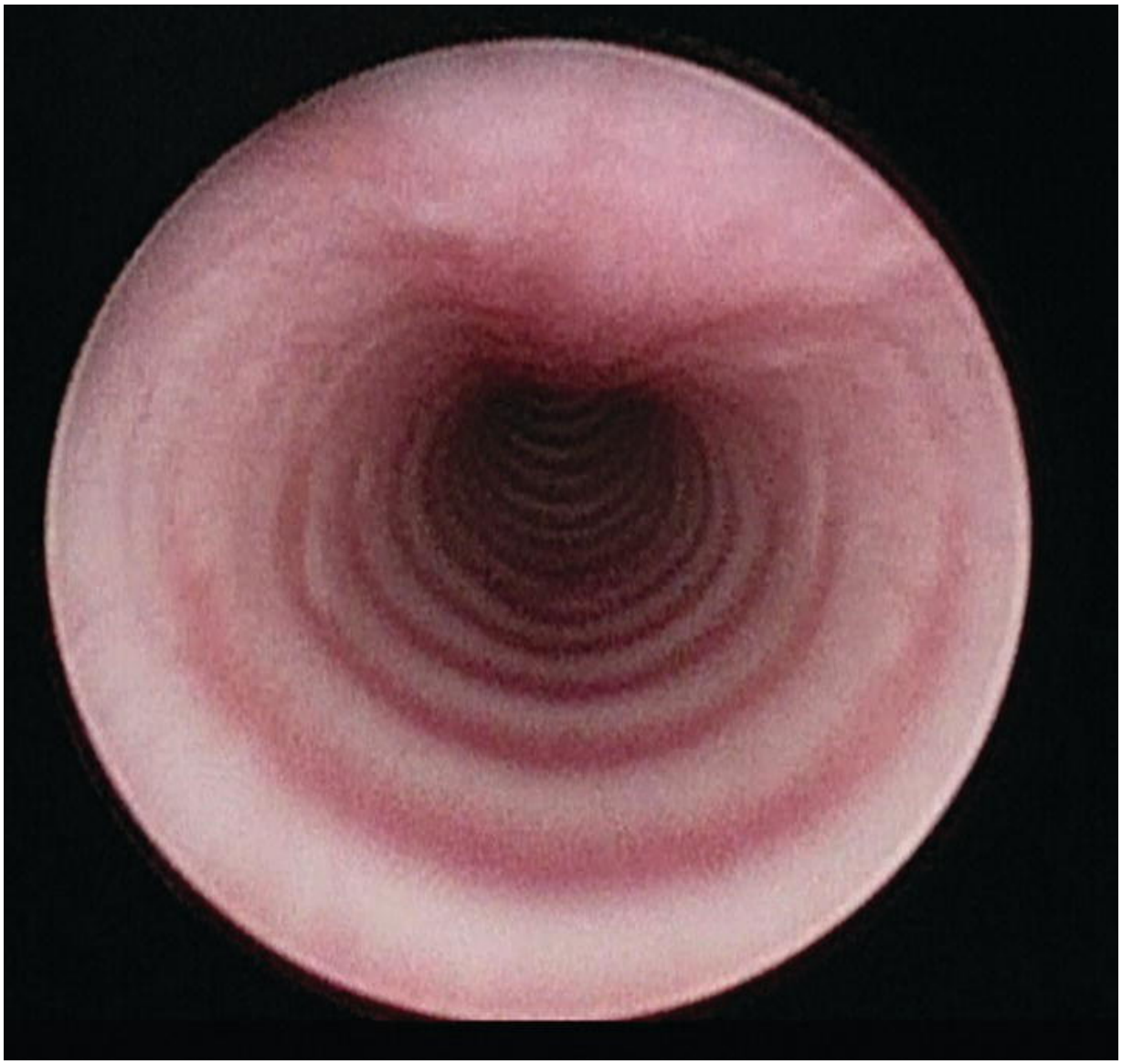


Figure 2.20 Endoscopic view of the normal canine trachea.

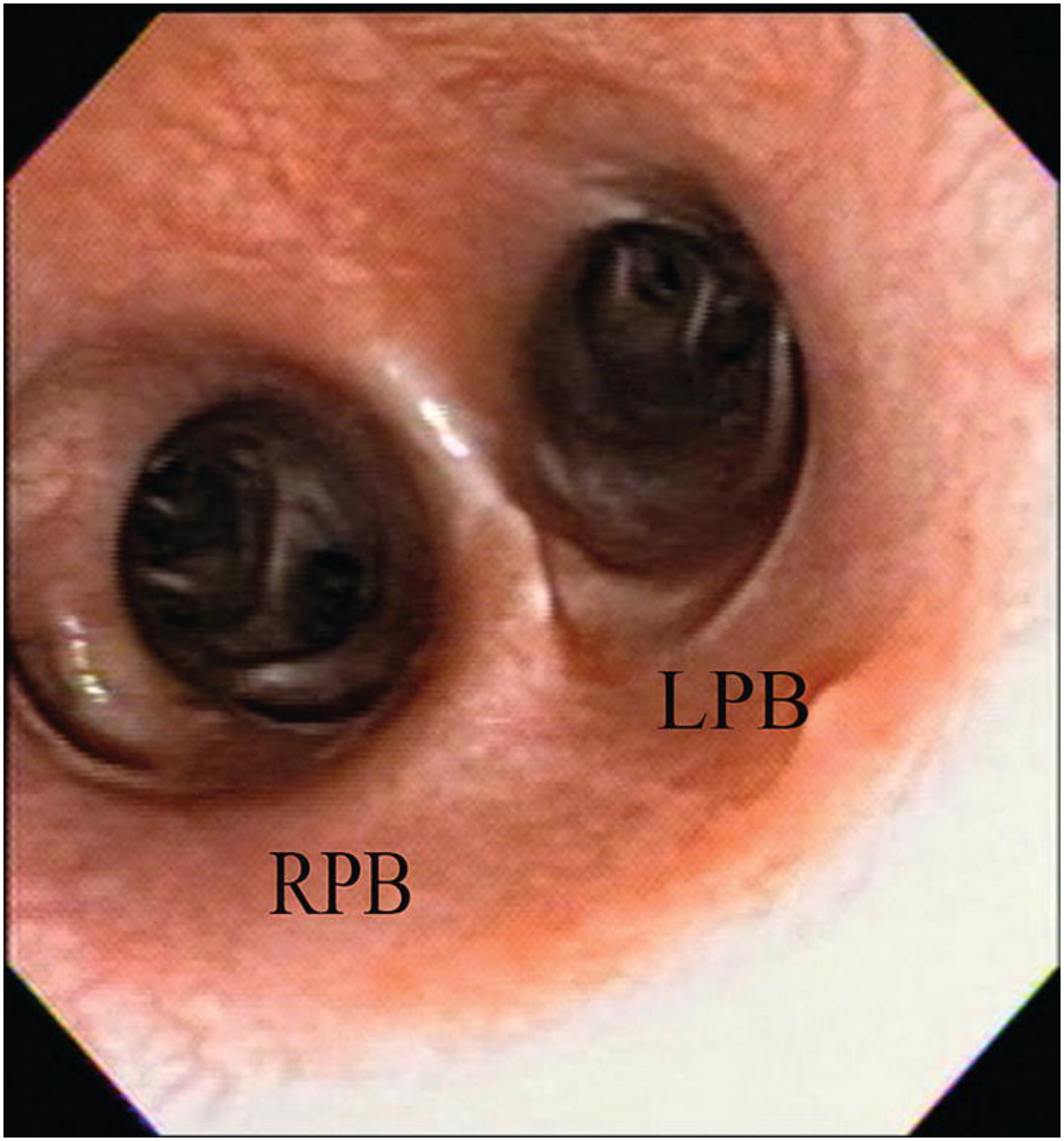


Figure 2.21 Endoscopic view of the carina illustrating the openings into the right principal bronchus (RPB) and left principal bronchus (LPB).

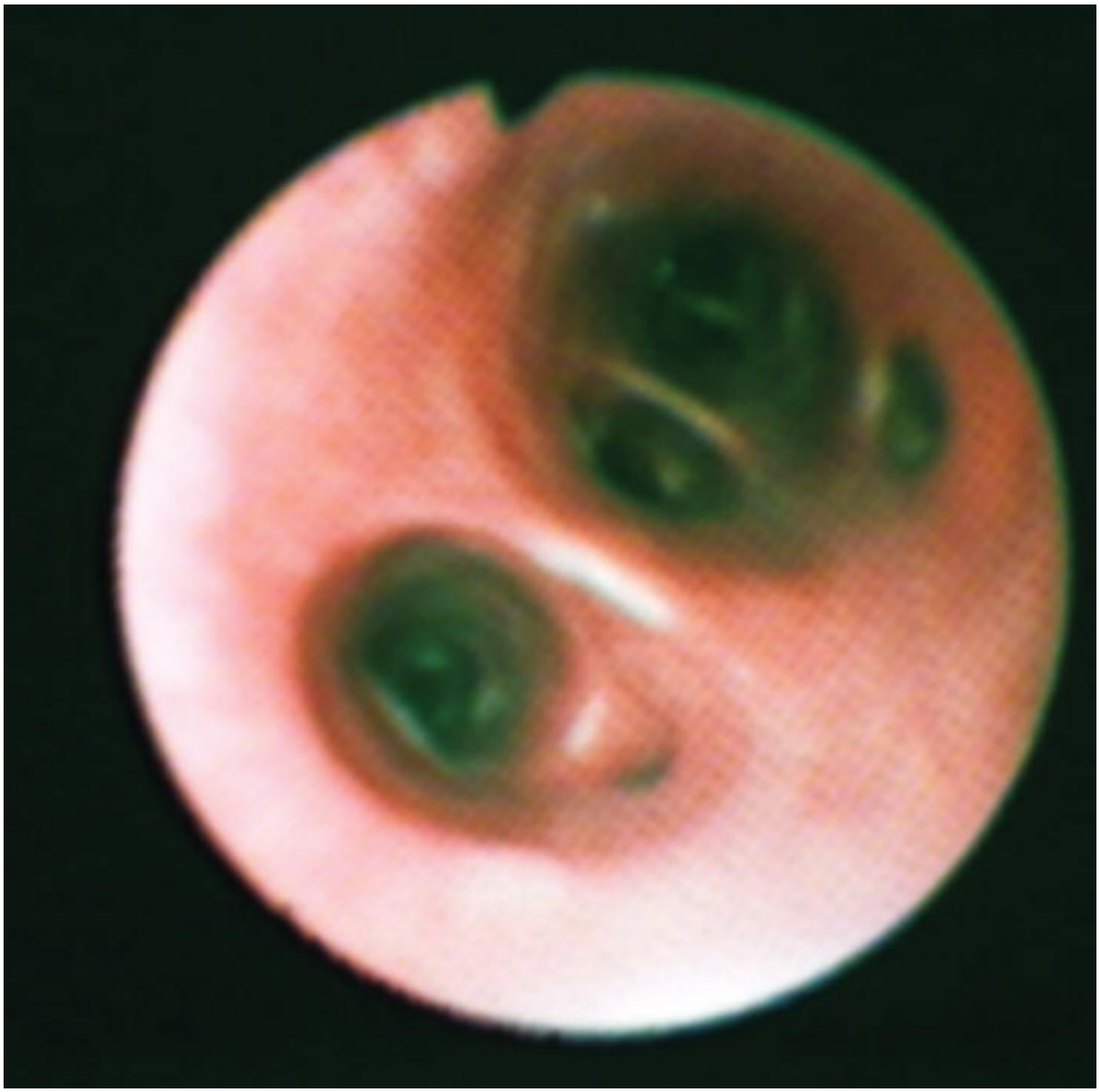


Figure 2.22 Distal airways in the dog exhibit relatively sharp bifurcations into round to oval airway openings. The epithelial surface is smooth.

After examining all visible airways, the scope is withdrawn from the airways, the outside of the scope is wiped off with saline-soaked gauze pads, and the biopsy channel is flushed with sterile saline. On the second entry to the airway, the scope should be kept in the center of the airways to limit upper airway and mucosal contamination when approaching the site for lavage. Success in achieving a diagnostic BAL will depend on the ability to wedge the bronchoscope

gently into a small airway and isolate a segment of alveolar volume (Figure 2.23). The goal is to flood this small wedge of lung with an aliquot of sterile non-bacteriostatic saline (5–20 ml), suspend the resident inflammatory cells, and gently aspirate back the fluid. Fluid should be fully ejected from the scope into the alveolar segment by flushing gently with a small volume of air (3–5 ml) before beginning the aspiration. The volume of fluid used for BAL depends on the size of the scope in relation to the size of the animal, experience of the operator, underlying disease process, and degree of respiratory compromise (Table 2.6), although ~1 ml/kg has been recommended (not to exceed 20 ml/lavage site). Aspirated fluid will be foamy because of the presence of surfactant at the alveolar surface. Flocculent material is usually mucus from bronchial contamination. If a sufficient sample is not recovered from the lavage (generally 50–70% of the fluid will be recovered), a second lavage should be performed at the same site. In human medicine, multiple lavages are commonly obtained and the first is not analyzed, because it represents more of the bronchial component rather than alveolar. It is unclear how often this is done in veterinary medicine. It is recommended to lavage at least two distinct lung sites because of inherent differences in the inflammatory cell populations among lung lobes and with different disease processes. Interpretation of differential cytology is most useful in defining disease processes (see later).

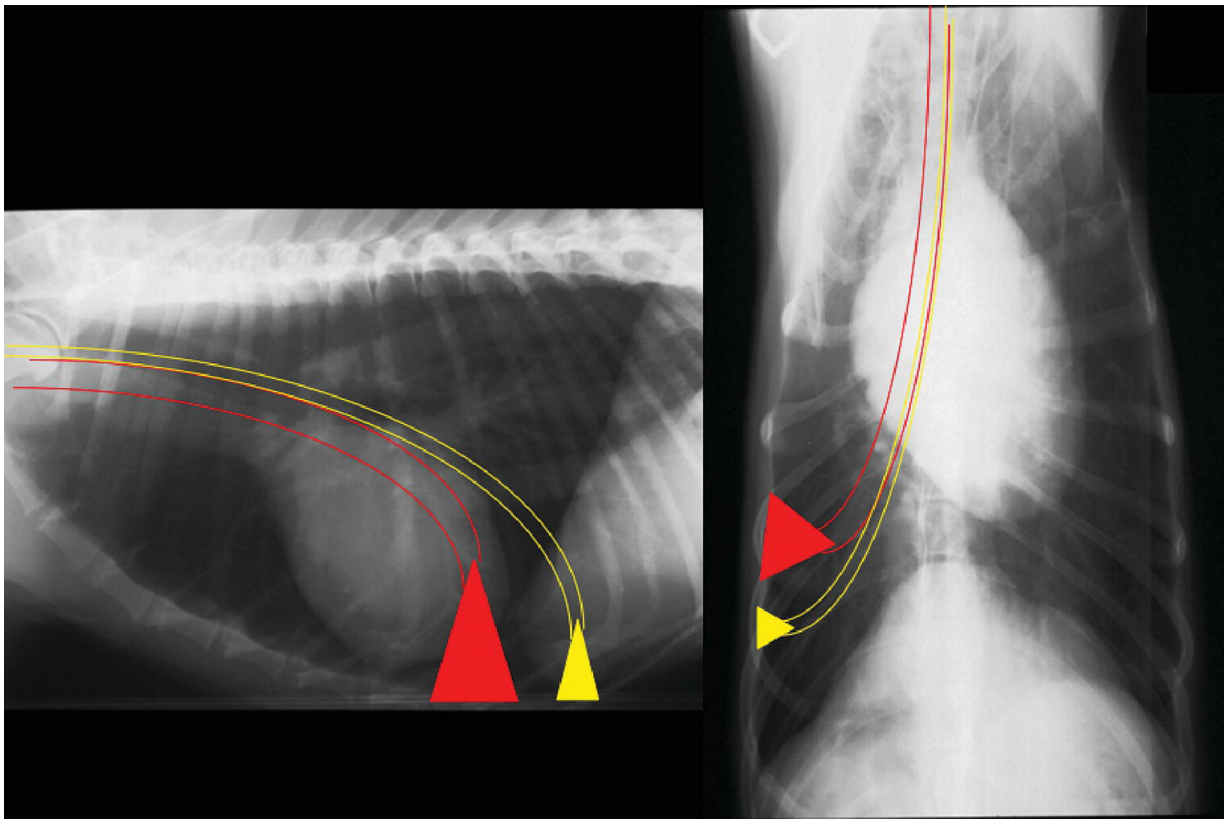


Figure 2.23 Bronchoalveolar lavage (BAL) is performed by gently wedging the bronchoscope into the smallest airway possible. The volume of the region lavaged (represented by red and yellow triangles) will depend on the size of the scope and the size of the animal.

Table 2.6 General guidelines for performing bronchoalveolar lavage (BAL).

Scope size	Animal size	Milliliters per aliquot
2.5–3.8 mm outer diameter	Cats	3–5 ml
	Dogs <6 kg	5–10 ml
4.9–5.5 mm outer diameter	Dogs	10–20 ml

When using a scope >6 mm outer diameter, consider passing sterile polypropylene tubing through the biopsy channel to wedge for BAL rather than using the channel. Beware that the tubing can puncture the airway if extended with force.

Thoracocentesis

Thoracocentesis is performed as a diagnostic and therapeutic technique. It can be done before radiographs are performed when physical examination suggests a pleural disorder and the animal is in distress, after thoracic ultrasound demonstrates pleural disease, or after radiographs indicate pleural space disease. The region of the seventh to ninth intercostal space is clipped and scrubbed in the ventral one-third of the chest for fluid and in the dorsal one-third for air. A 20 or 22 gauge butterfly needle is appropriate for use in small dogs and cats when small pleural effusion or mild pneumothorax is present. A 14–to 18 gauge catheter with extension set works well for larger dogs and can allow relatively rapid removal of large pleural effusions. In some animals, sedation is needed to perform a chest tap safely. Whenever possible, it is useful to have three people available to perform a chest tap. Prior to entering the chest, an extension set, three-way stopcock, and syringe should be assembled and ready for use. Rapid attachment of this system to the aspiration device will limit introduction of air into the pleural space after penetration with the needle or catheter. A large bowl, ethylenediaminetetraacetic acid (EDTA) and red-top tubes, and a culturette swab should also be readily available to allow efficient specimen collection.

A sterile preparation of the lateral thorax is completed and a site on the chest wall is chosen. The needle or catheter is advanced through tented skin and then walked off the cranial border of the rib to penetrate the pleural space at a perpendicular angle. This will avoid the vessels and nerves lying along the caudal rib margin. As soon as the pleura has been penetrated, the needle or catheter is directed downward to avoid injury to the lung parenchyma (Figure 2.24). The needle stylet is held stationary while the catheter is advanced over the needle into the pleural space. When the catheter is fully in the chest, the needle is withdrawn, and the extension set is rapidly attached. One person stabilizes the catheter system in the pleural space while another performs aspiration of fluid or air. The catheter might need to be re-positioned periodically to accomplish sufficient evacuation of the pleural space.

Fine-Needle Lung Aspiration and Biopsy

Fine needle aspiration (FNA) of the lung is a suitable technique for evaluating diffuse interstitial or alveolar disorders or peripheral mass lesions within the thorax. It can be performed as a blind technique or with ultrasound guidance. However, because it can be associated with pneumothorax or hemothorax, careful patient selection is advised to limit complications. In animals that are not severely tachypneic or hyperpneic, percutaneous FNA of the lung can be performed safely and with minimal sedation, using an agent such as butorphanol. In animals that are overly anxious, addition of dexmedetomidine might be required. This is a useful additive because effects of this drug can be readily reversed by administering an equal volume of atipamezole when the procedure has been completed. To perform a lung FNA, a small region of the chest is shaved and minor surgical preparation is completed. A 23–27 gauge 0.75–1.5 in. needle attached to a 3 ml syringe containing ~1 ml of air is passed perpendicularly through the skin and subcutaneous tissue cranial to the border of the rib. It is then inserted back and forth into the lung parenchyma gently and quickly; then the needle and syringe are removed together for preparation of cytologic specimens. The syringe is detached from the needle and filled with air, and contents of the needle hub are gently sprayed onto a slide or cover slip for cytologic examination and Gram staining, if sufficient material is obtained. Even when the sample appears to be of low cellularity, cytopathology is recommended to detect cellular atypia or inflammation.



(a) (b)

Figure 2.24 (a) To initiate thoracocentesis, the skin is tented and the catheter with needle is inserted perpendicularly between the rib spaces. (b) After the pleural space has been entered, the needle is directed ventrally and the catheter is advanced fully into the chest while the needle is held stationary.

Percutaneous lung biopsy can be obtained with use of an ultrasound-guided biopsy needle in the anesthetized patient. This is performed more commonly in dogs than in cats. A surgical preparation is performed, and a 16–18 gauge Temno™ biopsy needle (Merit Medical Systems, South Jordan, UT) is guided into the lesion to obtain a 2 cm core tissue sample for histopathology (Figure 2.25).

After either aspiration or biopsy, the animal should be placed in lateral recumbency with the aspirated side facing downward for 15–30 minutes to promote the development of a clot or seal at the aspiration site. Typically, an ultrasound is performed after the procedure to screen for hemorrhage or pneumothorax. Visualization of the normal “glide” sign as the lung slides across the pleura rules out one of these complications. An increase in respiratory rate or effort or detection of absent lung sounds near the site of aspiration would indicate hemorrhage or pneumothorax and the need for intervention.

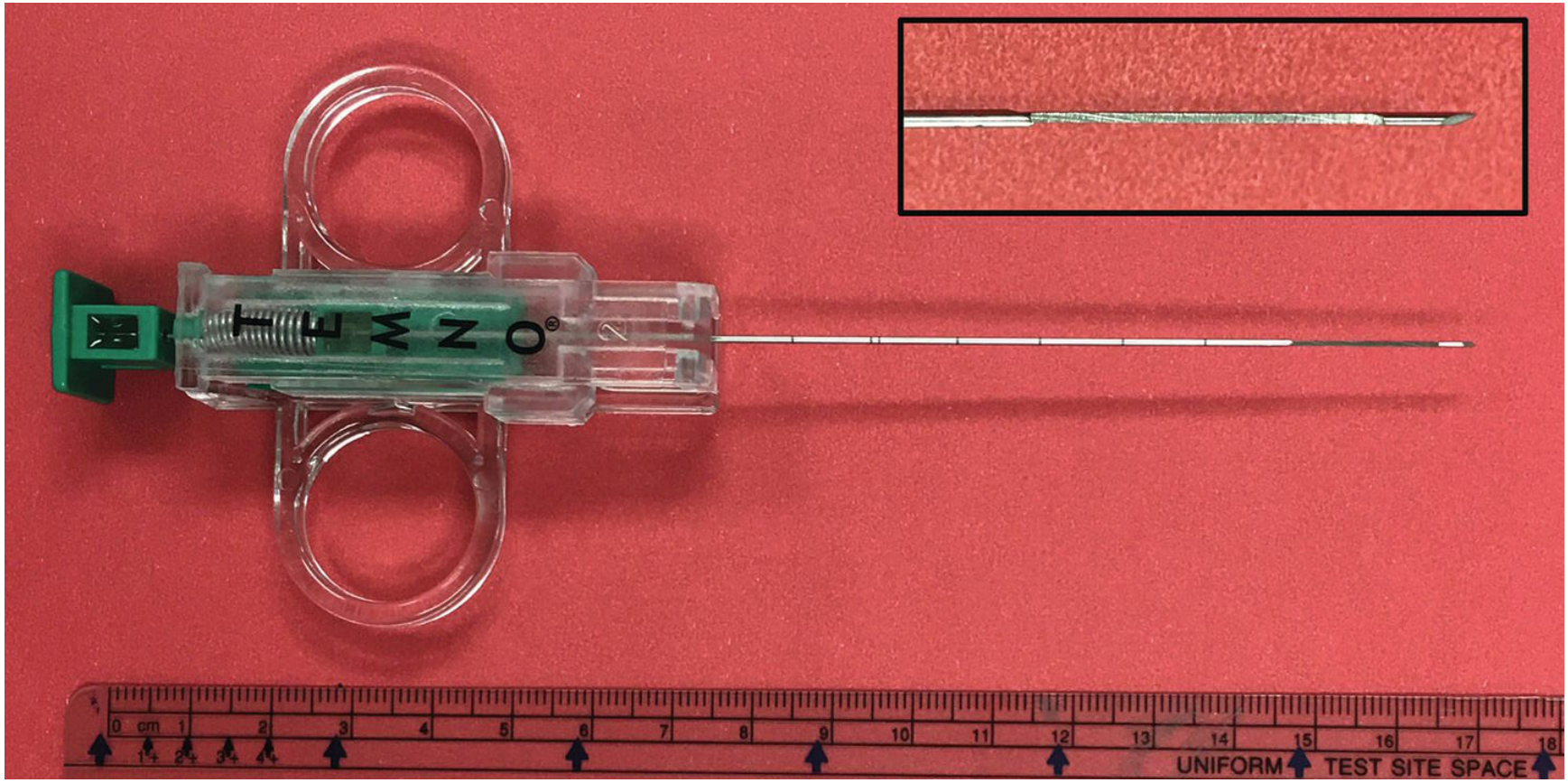

UNIFORM TEST SITE SPACE

Figure 2.25 Ultrasound guidance is used to obtain a lung biopsy using a Temno™ biopsy needle.

Sample Analysis

Nasal Cytology

Nasal cytology can be performed by pressing a microscope slide directly onto the nose of an animal or by obtaining material with a cotton swab and spreading it onto a slide. It is typically not possible to obtain an intranasal sample without sedation. Nasal cytology is non-invasive and inexpensive; however, there are substantial limitations to the amount of information obtained from this test. Its primary usefulness is in the diagnosis of nasal fungal infection with cryptococcosis (see Chapter 4). Accuracy in the diagnosis of nasal aspergillosis or neoplasia is poor unless an endoscopically obtained sample from a fungal plaque (De Lorenzi et al. 2006) or from a mass lesion is examined cytologically. If eosinophils are noted in a dog with cough and nasal discharge, the possibility of eosinophilic lung disease should be considered (see Chapter 6).

Nasal Culture

Bacterial culture of nasal discharge is not recommended. In fact, because most infections in the nose are secondary rather than primary, the value of culturing a deep nasal flush or culturette sample can also be questioned because of the difficulty in distinguishing normal flora from pathogens or opportunistic invaders. Interpretation of bacterial cultures is more difficult in animals that have been on multiple courses of antibiotic trials because this tends to favor the development of resistant species. Despite this, bacterial culture from a deep nasal swab or flush can provide some direction for antibiotic therapy in cats with chronic rhinosinusitis.

A study on the utility of fungal cultures in the diagnosis of canine nasal aspergillosis reported moderate sensitivity (77%) but high specificity (100%; Pomrantz et al. 2007). In that study, the material submitted for culture was from a visualized fungal plaque and

therefore a low number of false-positive values would be expected. In cases of cryptococcosis, culture and speciation can be helpful in determining the epidemiology of the infection, although subclinical colonization of the nasal cavity has been reported in 7–14% of dogs and cats (Malik et al. 1997).

Nasal Histology

Histopathology provides the diagnosis of aspergillosis in cases in which a plaque lesion has been sampled by direct visualization; however, a random sampling of the nasal mucosa or a blindly collected sample may not contain fungal elements, leading to a false-negative biopsy sample. Neoplasia can be difficult to confirm with a biopsy, because a rim of necrosis and inflammation often surrounds neoplastic cells. In some instances, neoplasia can be diagnosed on histopathology of a mass lesion in the nasopharynx when neoplastic cells are not evident in a sample from within the nasal cavity. This seems particularly common in feline nasal/nasopharyngeal lymphoma.

Airway Wash Cytology

Normal tracheal wash cytology is composed of ciliated columnar to cuboidal epithelial cells and rare macrophages or inflammatory cells. Normal BAL cytology contains primarily alveolar macrophages (65–75%), with 5–10% neutrophils, lymphocytes, and eosinophils; although in a cat, up to 18% eosinophils can be normal (Figure 2.26). Normal macrophages can exhibit variable appearances depending upon stimuli present within the lung, such as infection or inflammation. Activated macrophages contain intracellular inclusions, can appear foamy, and may be engulfing granulocytes or particulate matter in comparison to quiescent macrophages. Normal BAL cell counts have been reported for the dog and cat and are approximately 300–400 cells/μl, although not all laboratories report cell counts or even differential cytology. Interpretation of cell counts is complicated by the degree of dilution of the epithelial lining fluid by the volume of fluid instilled and the volume recovered. In general, BAL results in ~2% dilution of the epithelial lining fluid thus cell counts are likely diluted in similar fashion (Melamies et al. 2011).

Little progress has been made in standardizing the procedures for BAL, for handling fluid after collection, or for interpreting cell counts. Inflammatory cells can be trapped in mucus and straining a sample will artificially lower cell numbers. While hypercellular BAL fluid could be considered suggestive of an inflammatory process, not all laboratories report a total nucleated cell count and some do not supply a differential cell count. Whenever possible, these numbers should be requested from the clinical pathologist to aid in interpretation. Higher cell counts and/or an altered percentage of cells present within the lavage fluid are indicative of lower respiratory tract pathology.

Suppurative inflammation is characterized by >10% neutrophils and can represent pure inflammation, as in chronic bronchitis in the dog or cat, or can be an indicator of infection, as with pneumonia. The finding of degenerate neutrophils containing intracellular bacteria in tracheal wash fluid or in bronchoalveolar lavage fluid is a reliable indicator of bacterial infection (Johnson et al. 2013; Graham et al. 2021), although the absence of this finding does not rule out clinically important infection. Pyogranulomatous inflammation (activated macrophages and increased neutrophils) can be an indicator of fungal disease, and samples should be closely screened for cytologic evidence of fungal organisms (see Chapter 6). This type of inflammation in the absence of fungal elements can also be seen with very chronic bacterial or aspiration pneumonia or bronchiectasis.

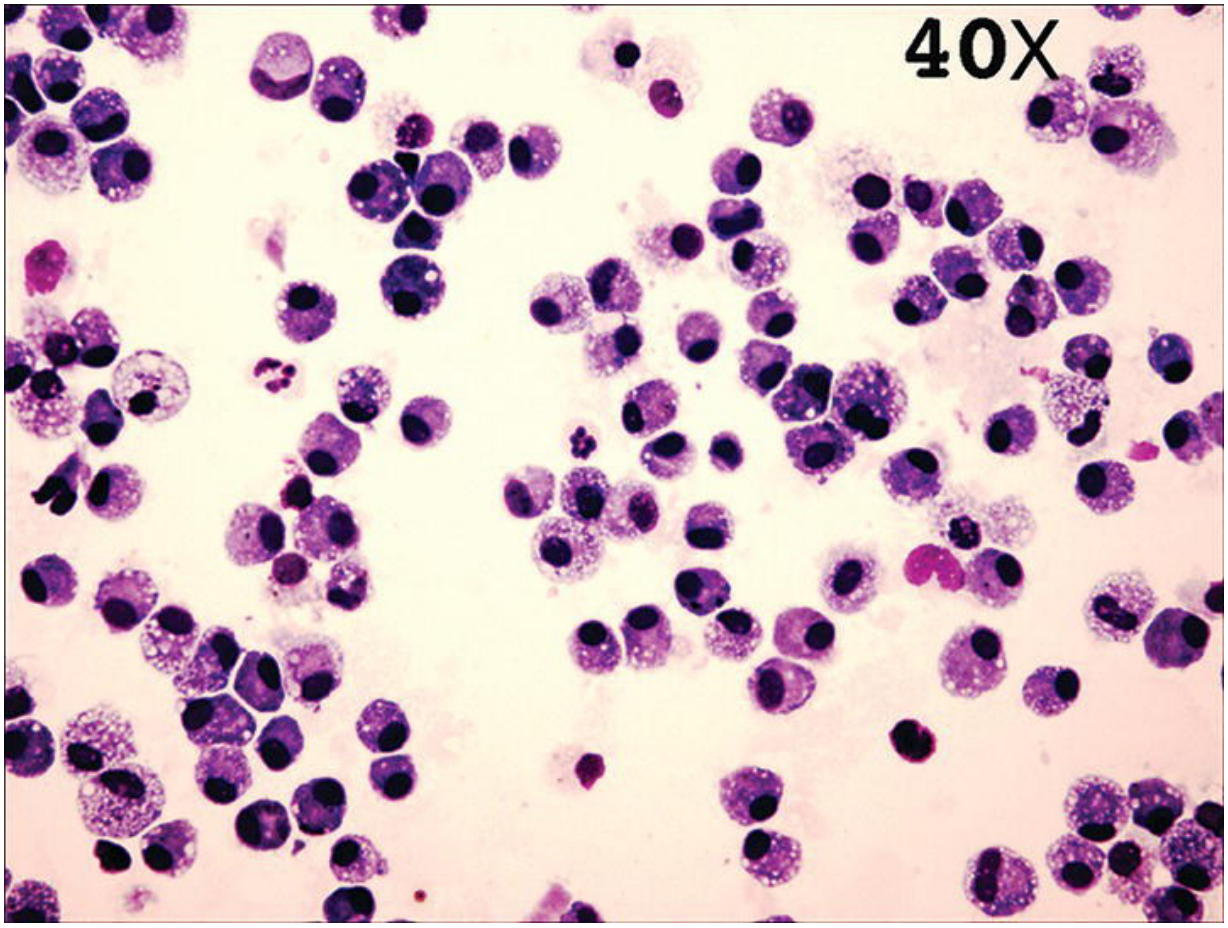


Figure 2.26 Cytocentrifuge of a normal BAL sample (40×) reveals primarily macrophages (65–75%), with the remaining percentage made up of neutrophils, lymphocytes, and eosinophils.

Eosinophilic inflammation is characteristic of some forms of feline asthma and can also be found with airway parasitism due to *Aelurostrongylus*, *Capillaria*, *Crenosoma*, or *Paragonimus*, in heartworm disease, or with larval migration of gastrointestinal parasites (*Toxocara*). Airway eosinophilia is a prominent feature of eosinophilic bronchitis or bronchopneumopathy in dogs.

Hemorrhagic inflammation can be found with rodenticide intoxication (vitamin K antagonists), heartworm or *Paragonimus* infection, foreign body, or trauma. Neoplasia and thromboembolic disease can also result in pulmonary hemorrhage. Evidence of previous airway hemorrhage (indicated by macrophages ingesting red blood cells or hemosiderin-laden macrophages) can be found in

some dogs with congestive heart failure, lung neoplasia, or with exercise induced pulmonary hemorrhage.

In rare instances, malignant cells can exfoliate into the airways with pulmonary carcinoma (primary or metastatic) or in pulmonary involvement with lymphoma and will be detected in BAL fluid. Characteristics of malignancy are similar to those in other tissues, including loss of contact inhibition, variation in cell size or nuclear size and shape, increased nuclear-to-cytoplasmic ratio, basophilia, multi-nucleate cells, or frequent cells undergoing mitosis. Neoplastic transformation can be difficult to confirm because dysplastic changes associated with severe inflammation can mimic neoplastic atypia. In addition, some lung tumors have a necrotic center or can become infected, which can complicate interpretation of abnormal-appearing cells or the presence of bacteria. Review of several samples can be required to confirm the presence of an underlying neoplasm.

Airway Culture

Positive bacterial and mycoplasmal cultures must be interpreted in conjunction with cytology. The presence of squamous cells or *Simonsiella* bacteria is suggestive of upper airway contamination, and in these cases, it is not uncommon to observe growth of two to four types of aerobic bacteria (usually oral flora) with or without *Mycoplasma*. Therefore, because approximately one-third of healthy dogs and almost three-quarters of healthy cats can have positive tracheal cultures (Table 2.7), strict attention should be paid to limiting upper airway contamination of BAL samples and appropriate interpretation of airway cultures in order to avoid overuse of antimicrobials. Quantitative bacterial cultures provide evidence for bacterial infection when $>1.7 \times 10^3$ bacterial colony forming units per milliliter of fluid grow on culture or when more than two intracellular bacteria are detected in any of 50 examined high-power fields (Peeters et al. 2000), although approximately one-quarter of cases with clinical lower respiratory tract infection lacked intracellular bacteria in one study (Johnson et al. 2013). Lower respiratory tract infections are often characterized by culture of several species of bacteria, including anaerobes (Johnson et al. 2013), although some studies suggest that infections are more

typically associated with isolation of a single organism. Importantly, recent administration of antimicrobials does not necessarily negate the value of airway cytology and cultures because positive results have been reported with analysis of either tracheal wash or BAL fluid in such circumstances (Johnson et al. 2013; Graham et al. 2021).

Table 2.7 Lower respiratory tract flora found in healthy dogs and cats.

Dogs (McKiernan et al. 1982)	**Cats (Dye et al. 1996)**
Bordetella	*Acinetobacter*
Corynebacterium	*Bordetella*
Escherichia coli	*Corynebacterium*
Enterobacter	*Enterobacter*
Klebsiella	*Flavobacterium*
Pasteurella	*Klebsiella*
Pseudomonas	*Pasteurella*
Staphylococcus	*Staphylococcus*
Streptococcus	*α-Streptococcus*
Mycoplasma	

Pleural Fluid Analysis

Initial analysis of pleural fluid should always include a packed cell volume (PCV), cell count, protein or specific gravity, and cytology. Smears can also be prepared for Gram staining to aid in decisions regarding empiric antibiotic therapy while awaiting culture results. Additional diagnostic tests for systemic disease such as a CBC, chemistry panel, urinalysis, or echocardiogram can be chosen after the character of the pleural fluid is determined (Table 2.8). Other tests to perform on pleural fluid include bacterial culture and susceptibility testing (aerobic and anaerobic cultures), protein electrophoresis, or a cholesterol/triglyceride ratio for the diagnosis of chylothorax. PCR can be useful for assessing the likelihood of effusive FIP, and various point of care tests might be efficacious in the diagnosis of septic pleural effusion (see Chapter 7).

Pleural Fluid Culture

When an exudative pleural effusion is obtained (protein >3 g/dl and cells >5000/μl), samples of pleural fluid should be cultured for both aerobes and anaerobes. In retrospective studies of pyothorax (Walker et al. 2000; Johnson et al. 2023), bacteria have been isolated from 90 to 96% of cases in spite of previous antimicrobial administration and were visible on cytology in 91–93% of cats. Obligate anaerobes were present in 73–89% of cases, and a mixture of obligate anaerobes and facultative organisms was found in approximately one-half of culture-positive cats. A median of three bacterial species were isolated from cats (Johnson et al. 2023). In dogs, bacteria were isolated from 78 to 92% of cases and were visible on cytology in 68–73% of samples (Walker et al. 2000, Johnson et al. 2023). Bacteria included obligate anaerobes in 36–45% of samples, and a median of one bacterial species was isolated in dogs. In dogs, enteric organisms and *Actinomyces* were the most common aerobic bacteria isolated, while in cats, *Pasteurella* species were isolated most commonly. Similar anaerobes were isolated from cats and dogs, with *Bacteroides*, *Fusobacterium, and Peptostreptococcus*, isolated most commonly. *Mycoplasma* has been proposed to play a role in pleural infection in cats, although this is poorly characterized and not recently documented.

Table 2.8 Characteristics of pleural fluid.

	Protein (g/dl)	Cell count (per µl)	Etiology
Transudate	<1.5	<1000	Hypoalbuminemia
Modified transudate	<2.5	500–2500	Right heart failure
			Pericardial disease
			Neoplasia
			Hernia
Exudate	>3.0	>5000	Feline infectious peritonitis
			Neoplasia
			Hernia
			Lung lobe torsion
			Pyothorax
Chylous	>2.5	>500	Idiopathic
			Cardiomyopathy
			Heartworm disease
			Neoplasia
			Lung lobe torsion
Hemorrhagic	>3.0	>1000	Trauma
			Coagulopathy
			Neoplasia
			Lung lobe torsion

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3
Respiratory Therapeutics

Considerations in Drug Therapy

Veterinarians are under increased scrutiny regarding use of antimicrobials in animal patients because of the development of resistant strains of bacteria that affect humans as well as animals, and some states require training in antimicrobial stewardship as part of the licensing process. However, antibiotics are often required for the management of acute and chronic respiratory diseases and are essential to reduce morbidity as well as mortality. It is critical to use the least potent antibiotic that is likely to be effective, to use it for the appropriate period of time, and to avoid using multiple, short courses of different antibiotics, particularly if culture and susceptibility testing has not been performed. Choosing the correct antibiotic for empiric therapy requires knowledge of the normal flora found in upper and lower respiratory tracts, as well as an understanding of the species most likely to be pathogenic. De-escalation of antimicrobial usage is also an important factor to consider where appropriate. Guidelines for antimicrobial usage in the respiratory tract were recently published by the International Society for Companion Animal Infectious Diseases (Lappin et al. 2017) and these should be consulted to ensure rational antibiotic usage.

Overuse of antifungal agents leading to development of resistant strains of fungal organisms appears to be less of a concern currently, but this could become an issue in the future. Inappropriate use of antiviral treatment has come under scrutiny because of the SARS-COVID 19 epidemic, which required restriction of specific anti-viral agents for human use alone. Recent (May 2024) availability of a compounded drug for treatment of the feline coronavirus infection that results in feline infectious peritonitis has contributed to close analysis of anti-viral use. The utility of famciclovir has become well-established for ocular diseases associated with feline herpesvirus, although determining the role for herpesvirus in upper respiratory conditions of cats remains challenging. It is important to use antivirals in a judicious manner to avoid the development of resistance. None of these agents should be tapered prior to use.

Opioid use or abuse in animals is problematic because of concerns for human use and abuse, as well as for potential exposure of family members to these drugs. This is particularly relevant when using narcotic cough suppressants in dogs with unrelenting cough.

Antibiotics for Upper Respiratory Tract Disease

Acute infectious upper respiratory tract disease in the cat is most commonly ascribed to viral infection, and when secondary bacterial invasion is suspected, empiric antibiotic therapy is often used initially. Flora of the upper respiratory tract (*Staphylococcus, Streptococcus, Pasteurella, Escherichia coli*, and anaerobes) can overwhelm local defenses and colonize the nasal cavity, leading to clinical signs of sneezing and mucopurulent nasal discharge. Other bacteria such as *Chlamydia*, *Mycoplasma*, *Bordetella*, and *Streptococcus canis* or *Streptococcus equi* var. *zooepidemicus* might act as primary pathogens. When purulent discharge is present or signs have been present for >10 days, antibiotics are commonly administered for 5–7 days to reduce bacterial numbers and decrease bacterial invasion of epithelium damaged by viral infection. Doxycycline at 5–10 mg/kg orally (PO)

once a day is recommended because of its efficacy against both typical and atypical bacteria, its tissue penetration, and because it is well tolerated by most animals. The primary adverse effect from this drug is esophageal stricture formation. To ensure that it passes completely into the gastrointestinal tract, water or food should be administered immediately after the pill is given. Commercially available doxycycline suspensions that have a high enough concentration to allow administration of the appropriate dose are less likely to induce esophageal damage but are not available in every country. The stability of compounded or liquid formulations of doxycycline is variable, and a compounded suspension more than 7 days old should not be used due to lack of efficacy (Papich et al. 2013). Administration of sucralfate substantially reduces doxycycline absorption and at least 2 hours should pass between dosing of these two drugs (KuKanich and KuKanich 2014). To avoid these complications, amoxicillin is a reasonable alternative antibiotic, although it is important to remember that penicillin derivatives are ineffective against *Chlamydia* and *Mycoplasma* spp., a cell-wall-deficient bacteria. If a kitten or cat with acute upper respiratory signs fails to respond to empiric treatment within 7–10 days, a diagnostic work-up is advised to rule out other nasal conditions (see Chapter 4). This would include collection of a sample for culture and susceptibility testing before use of an antibiotic with a different spectrum.

In chronic upper respiratory tract disease in the cat, mucosal tissue is often devitalized and there is accumulation of inflammatory products. Resolution of disease is difficult if not impossible to achieve; however aerobic bacterial infection is a common complication (Johnson et al. 2005) that can respond partially to treatment. Doxycycline and azithromycin are attractive drugs to use in such cases because they possess anti-inflammatory effects as well as antimicrobial action. Both of these drugs have efficacy against most of the organisms that have been isolated in cats with chronic rhinosinusitis, including anaerobes, and thus could be used for empiric therapy when owners cannot perform extensive diagnostic testing. Culture and susceptibility testing might indicate that a fluoroquinolone would be a rational antibiotic choice in some cases. This class of drugs has excellent efficacy against most Gram-negative bacteria and *Mycoplasma*. However, a high dose can be required for successful treatment of *Pseudomonas* infections, and this is not advisable in cats because of potential retinal toxicity. Newer fluoroquinolones (pradofloxacin and premafloxacin) have efficacy against anaerobic organisms as well as others, which is beneficial in some cases. For cats with underlying osteomyelitis or suspected anaerobic infections, a drug such as clindamycin could be effective in controlling clinical signs because it penetrates bone tissue. Caution is warranted when administering clindamycin because this drug has also been associated with development of esophageal strictures.

The appropriate duration of antimicrobial treatment for feline chronic rhinosinusitis in the cat has not been evaluated. When treating the bacterial component of chronic feline rhinosinusitis, consideration should be given to using a relatively long course of antibiotics (2–4 weeks) to achieve maximal control of bacterial numbers. In some cases, chronic use of antibiotics is required, although the benefit of this therapy has to be weighed against the risk of antimicrobial resistance, as well as the challenges of owner compliance. Also, the waxing and waning course of disease can make it difficult to assess therapeutic response as well as to decide when to discontinue medication.

Bacterial involvement in canine inflammatory rhinitis appears to be less prominent than in the feline syndrome, although few studies have evaluated bacterial isolation rates in dogs with nasal discharge (Windsor et al. 2004). Secondary bacterial infection can develop in dogs that have been treated for nasal aspergillosis infections because of destruction of turbinates and loss of normal nasal defense mechanisms. In those cases, 7–10 days of a

broad-spectrum antibiotic (e.g. amoxicillin-clavulanic acid) can help alleviate nasal discharge, although it will often recur. In these situations, recurrent nasal discharge could also indicate persistence of the fungal infection, warranting additional diagnostic testing.

Antibiotics for Lower Respiratory Tract Disease

Lower respiratory tract infection can be life-threatening and antibiotics should be based on culture and susceptibility testing whenever possible. However, when culture results are pending or when airway sampling is not clinically feasible, initial antibiotic choices must consider the likely species involved and reported susceptibility patterns of commonly encountered bacteria (Table 3.1).

Appropriate therapy for bacterial lower respiratory infection requires antibiotics directed at Gram-negative and Gram-positive aerobes, anaerobes, and *Mycoplasma* organisms. A rational choice for initial therapy of a serious, newly diagnosed infection (before final culture results are available) would include a fluoroquinolone with a penicillin drug. Dosing depends on whether the antibiotic is concentration-dependent or time-dependent (Table 3.2). More frequent administration is required for those drugs that are time-dependent. Parenteral administration is preferred for dogs with serious infection and systemic signs that require hospitalization. Enrofloxacin has good efficacy against most Gram-negative organisms as well as many Gram-positive organisms and *Mycoplasma* spp., and it has been demonstrated to accumulate in the epithelial lining fluid of the lung, making it a rational empiric choice. Ciprofloxacin, a generic human product similar to enrofloxacin, has variable absorption in the dog (Papich 2017) and is not preferred for use, even though it can be substantially cheaper than one of the veterinary formulations. An additional consideration is that fluoroquinolones have no efficacy against anaerobes, necessitating the addition of a second antibiotic such as a penicillin derivative while culture results are pending. The exception to this is pradofloxacin, as noted above. While this can be an appropriate choice for pneumonia in the cat, it is contraindicated in dogs because of bone marrow toxicity. Importantly, due to the emergence of bacterial resistance, beta-lactam type antibiotics are not recommended for infection with bacteria in the *Enterobacteriacae* family (*E. coli*, *Klebsiella*, etc.) (Rheinwald et al. 2015).

Anaerobic susceptibility testing is rarely performed by clinical laboratories because organisms are difficult to grow on susceptibility plates; however, most are sensitive to penicillins, and a potentiated penicillin is best to use for anaerobic infections. Other drugs with good anaerobic activity include clindamycin, metronidazole, and chloramphenicol, and these drugs also have excellent pulmonary penetration. *Bacteroides* spp. can be resistant to clindamycin (Jang et al. 1997) and a potentiated penicillin, metronidazole, or chloramphenicol would be a better choice when infection with this anaerobe is documented. Chloramphenicol has excellent efficacy against a number of organisms commonly implicated in respiratory infection; however, use of this drug is commonly associated with vomiting or anorexia and sometimes central nervous system depression or bone marrow suppression. Use of maropitant in the first several days of administration can lessen GI side effects, however, chloramphenicol is also a bacteriostatic drug and rarely indicated for in-hospital treatment, unless a multi-drug-resistant organism is isolated. If prescribed for therapy at home, owners must be instructed to wear gloves to administer the drug given concerns about human health.

Table 3.1 Gram-stain characteristics and antibiotic susceptibility for common bacteria.

Organism	Gram stain	First-line antibiotics
Bordetella	Negative coccobacillus	Aerosolized gentocin Doxycycline Chloramphenicol
Escherichia coli	Negative rod	Fluoroquinolones Amikacin, Gentocin Trimethoprim-sulfa
Klebsiella	Negative rod	Fluoroquinolones Amikacin, Gentocin Trimethoprim-sulfa
Pseudomonas	Negative rod	Fluoroquinolones Carbenicillin Amikacin Cephalosporin Gentocin
Pasteurella	Negative rod	Amoxicillin, amoxicillin-clavulanic acid Chloramphenicol Cephalosporin Trimethoprim-sulfa
Streptococcus	Positive coccus	Amoxicillin-clavulanic acid Ampicillin Cephalosporin
Staphylococcus	Positive coccus	Methicillin Cloxacin Cephalosporin
Mycoplasma	Not visible	Doxycycline Chloramphenicol Fluoroquinolones Azithromycin
Anaerobes	Positive or negative	Penicillins Clindamycin Metronidazole Chloramphenicol Cephalosporin

Table 3.2 Drug dosages of antibiotics commonly used for respiratory tract infection (Papich 2011) / with permission of Elsevier.

Drug	Static/Cidal	Dog dosing	Cat dosing
Amoxicillin	Cidal	6.6–20 mg/kg PO q8-12h	6.6–20 mg/kg PO q8-12h
Amoxicillin-clavulanate	Cidal	12.5–25 mg/kg PO q12h	62.5 mg/cat q12h
Ampicillin-sulbactam	Cidal	10–20 mg/kg IV, IM q8h	10–20 mg/kg IV, IM q8h
Azithromycin	Static	5–10 mg/kg/day for 5–7d then EOD	5–10 mg/kg/day for 5–7d then EOD
Chloramphenicol	Static	40–50 mg/kg PO q8h	12.5–20 mg/kg PO q12h
Clindamycin	Static	11–33 mg/kg PO q12h	11 mg/kg/day
Doxycycline	Static	3–5 mg/kg PO q12h	10 mg/kg/d
Enrofloxacin	Cidal	5–20 mg/kg/day PO, IM, IV	5 mg/kg/day PO, IM
Marbofloxacin	Cidal	2.75–5.5 mg/kg/day	2.75–5.5 mg/kg/day
Metronidazole	Cidal	15 mg/kg PO q12h	10–25 mg/kg/day
Minocycline	Static	5–12.5 mg/kg PO q12h	5–12.5 mg/kg PO q12h
Orbifloxacin	Cidal	2.5–7.5 mg/kg/day	2.5–7.5 mg/kg/day
Pradofloxacin	Cidal	Not recommended	5–10 mg/kg/day PO
Trimethoprim-sulfa	Cidal	15 mg/kg PO q12h	15 mg/kg PO q12h

Azalides (azithromycin and clarithromycin) have efficacy against Gram-positive and Gram-negative organisms and *Mycoplasma* spp. as well as some anaerobes. These drugs have the advantage of producing high and prolonged tissue levels, typically resulting in enhanced bacterial killing. In the cat, there is variability in drug half-life, but relatively high bioavailability (58%) and sustained accumulation of drug in tissues after a single oral dose of 5.4 mg/kg (Hunter et al. 1995), allowing it to be administered on an every other day basis. The clinical efficacy of azithromycin in feline respiratory diseases is not yet known; however, its pharmacokinetic properties and pulmonary penetration could prove valuable in the treatment of both upper and lower respiratory infections.

In general, antibiotic treatment should be used for immediate control of infectious lung disease and the length of therapy in dogs with uncomplicated pneumonia is based on clinical response. Reduction in clinical signs of cough and tachypnea, improvement in parameters of oxygenation (when available), and resolution of an inflammatory leukogram would signify appropriate response to therapy. Future studies might identify specific biomarkers that could signal when adequate antimicrobial therapy has been achieved. Currently, treatment for 7–14 days is often considered sufficient for control of disease, and achieving radiographic resolution of infiltrates is no longer recommended for determining the length of antimicrobial therapy (Wayne et al. 2017; Vientos-Plotts et al. 2021). However, chronic antibiotic therapy can be required to control clinical signs in dogs with bronchiectasis and animals with ciliary dyskinesia because mucus accumulation with trapping of bacteria in secretions can result in severe and recurrent or persistent pneumonia. In these cases of complicated pneumonia, long-term antimicrobial therapy should be determined by results of bacterial culture and sensitivity, as well as

considerations of the anticipated side effects of medications (Table 3.3). The antibiotic chosen should have proper efficacy, should penetrate the airways and lung parenchyma, and should be relatively free of side effects.

Table 3.3 Side effects of commonly used antibiotics.

Penicillins and cephalosporins	Hypersensitivity response Immune mediated hemolytic anemia (humans)
Trimethoprim-sulfa	Keratoconjunctivitis sicca Folate deficient anemia Decreased thyroid function Arthropathy (black and tan dogs) Hepatotoxicity
Enrofloxacin	Retinal toxicity (cats) Cartilage injury (immature animals)
Metronidazole	Neurotoxicity
Doxycycline	Esophageal stricture Photosensitivity Hepatotoxicity
Chloramphenicol	Bone marrow toxicity
Aminoglycosides	Renal toxicity Ototoxicity
Clindamycin	Esophageal stricture Diarrhea

If a fluoroquinolone is needed in an animal that is being treated with theophylline, it is important to note that methylxanthines inhibit the metabolism of theophylline, and use of the two drugs together results in toxic plasma levels (Intorre et al. 1995). At least a 30% reduction in theophylline dose is recommended when a fluoroquinolone is used concurrently.

Antifungal Therapy

Fungal infection in the respiratory tract most commonly involves *Cryptococcus neoformans* or *Aspergillus fumigatus* in the nasal cavity of cats or dogs respectively (see Chapter 4), and *Histoplasma capsulatum*, *Blastomyces dermatitidis*, or *Coccidioides immitis* organisms in the lower respiratory tract. *Pneumocystis* spp. are also responsible for fungal pneumonia, although treatment relies on the use of trimethoprim-sulfa rather than standard antifungal medication discussed here. Nasal aspergillosis is also a special condition, which responds best to extensive debridement of fungal plaques and single or multiple infusions of topical antifungal therapy rather than oral therapy (see Chapter 4). When treating lower respiratory tract infection associated with fungal organisms, long-term therapy (from 6 weeks to over 12 months) must be anticipated. Depending on the severity of disease, the presence of concurrent illness, and the initial response to therapy, fungistatic or fungicidal agents administered orally or parenterally should be chosen (Table 3.4).

The triazoles (itraconazole, fluconazole, voriconazole, posaconazole) are fungistatic agents that inhibit the P450 enzymes involved in the synthesis of ergosterol, a key component of the fungal cell membrane. Itraconazole (Sporanox®, Itrafungol®) can be used as sole therapy for pulmonary fungal infection, or it can be used following initial fungicidal therapy with amphotericin B for prolonged control of disease. Itraconazole is excreted by the liver,

and side effects of therapy include hepatic toxicity, dermatotoxicity, and anorexia. Capsules and suspensions have different bioavailability, resulting in different dosing recommendations. Also, capsules should be given with food, while the solution is administered on an empty stomach. Compounded formulations of itraconazole are not advised because of variable absorption, which can negatively influence response to therapy. Fluconazole is renally excreted, thus a reduced dosage is recommended for animals with renal insufficiency. Fluconazole is available in generic form and can be preferred for animals that require long-term therapy due to cost savings, although bioequivalence among different generic preparations should not be presumed. Monitoring steady state serum concentration (after ~3 days of treatment) for therapeutic efficacy can be important to ensure resolution of disease because of individual variations in bioavailability, as well as the general variability in the pharmacokinetic properties of fluconazole (KuKanich et al. 2020). In animals that achieved clinical remission from various fungal infections, the median (range) serum fluconazole concentrations were 19.4 (8.1–79.0) μg/ml (dogs) and 35.8 (6.0–95.2) μg/ml (cats) (KuKanich et al. 2020). Compounded and generic formulations of fluconazole can have variable pharmacokinetic properties and stability (LaPorte et al. 2017; KuKanich et al. 2020) and therefore should be avoided, as for itraconazole. Fluconazole has no efficacy against *Aspergillus* species.

Table 3.4 Antifungal drug therapy.

Drug	Formulation	Dose	Mechanism	Indications	Side effects
Fluconazole	50, 100, 200 mg tablets	10 mg/kg BID (dog) 50–100 mg/cat/day	Static	Best for CNS penetration	Renally excreted
				Might be the best drug for histoplasmosis in cats	
				Not effective in *Aspergillus* infection	
Itraconazole	100 capsules	5 mg/kg daily to BID or 10–12.5 mg/kg daily with food	Static	Can be used alone or in combination with amphotericin B	Liver toxicity
	5 or 10 mg/ml oral solution	1.0–4.0 mg/kg of the liquid on an empty stomach			Dermatotoxicity
Voriconazole	50 and 200 mg tablets	2.5–10 mg/kg PO daily to BID	Static	Any susceptible fungal infection	Liver toxicity
	40 mg/ml oral suspension			Consider for canine nasal aspergillosis that has breached the cribriform plate	Neural toxicity in the cat
	10 mg/ml solution for IV use	Dilute to 5 mg/ml or less and infuse at a maximum rate of 3 mg/kg/hour over 1–2 hours			
Posaconazole	40 mg/ml oral suspension	Cats: 30 mg/kg PO loading	Static	Any susceptible fungal	

Drug	Formulation	Dose	Mechanism	Indications	Side effects
		dose of suspension followed by 15 mg/kg/48 h, or 15 mg/kg PO loading dose followed by 7.5 mg/kg/24 h		infection Preferred drug for feline sino-orbital aspergillosis	
	100 mg delayed-release tablet	Dog: 5 mg/kg PO EOD (delayed-release tablets)		Consider for nasal aspergillosis that has breached the cribriform plate	
Terbinafine	250 mg tablet	One-fourth of 250 mg tablet daily (cat) 30 mg/kg PO BID (dog)	Static	Might have synergistic effects when used with azoles	
Flucytosine	250 mg capsule	30–50 mg/kg PO TID–QID	Static	For CNS infection with *Cryptococcus* in combination with an azole	Cats only
	75 mg/ml oral suspension				
Amphotericin B	50 mg vial	0.5–1.0 mg/kg IV EOD to total dose of 5–14 mg/kg	Cidal	Fungicidal treatment of fungal pneumonia	Nephrotoxic
					Drug fever
					Thrombophlebitis
Amphotericin B lipid complex, liposomal amphotericin	5 mg/ml in a 20 ml vial, 50 mg/vial	0.5–1.0 mg/kg IV EOD to a total dose of 10–20 mg/kg	Cidal	Fungicidal treatment of fungal pneumonia	Less/no nephrotoxicity
					Drug fever

BID, twice a day; CNS, central nervous system; EOD, every other day; IV, intravenously; PO, orally; QID, four times a day; TID, twice a day.

Voriconazole (Vfend®, Pfizer, New York) and posaconazole (Noxafil®, Merck&Co., Inc, Whitehouse Station, NJ) are newer triazoles with improved antifungal activity. Use of these drugs has been limited by their expense, as well as reports of neurotoxicity in cats administered voriconazole. Posaconazole appears to be the favored medication for treatment of sino-orbital aspergillosis in the cat, and a pharmacokinetic study suggested that 30 mg/kg PO followed by 15 mg/kg every other day would attain trough levels similar to those proven efficacious in humans (Mawby et al. 2016). The suspension has low bioavailability (16% in cats, 26% in dogs) and there is variable absorption of the delayed-release tablets in dogs, with values up to 159% (Kendall and Papich 2015; Mawby et al. 2016); however, posaconazole has been associated with relatively few side effects when used clinically. Because the delayed-release tablet can be administered every other day, it could be cost-effective for use in cats as well as dogs.

Terbinafine is an allylamine fungistatic agent that acts through inhibition of squalene epoxidase used in the synthesis of ergosterol for the fungal cell membrane. Side effects are relatively rare, and it can be used in combination with azole-type medications for improved effectiveness against infection. Flucytosine is a pyrimidine analog that also inhibits fungal synthesis. It is used only in combination with other antifungal agents because it is a relatively weak antifungal drug and because of rapid development of resistance. It is indicated primarily for treatment of central nervous system cryptococcosis in cats only.

Amphotericin B is a fungicidal drug that kills fungal organisms by creating holes in the fungal cell membrane. Because it is highly nephrotoxic, aggressive diuresis with 0.9% saline (20–40 ml/kg over 1–3 hours) is recommended prior to administration. After saline diuresis, the infusion line must be flushed with 5% dextrose to avoid precipitation of the amphotericin in saline. A central vein is recommended for administration to avoid thrombophlebitis, and the drug should be protected from light prior to infusion. A test dose of 0.5 mg/kg in 5% dextrose solution is administered intravenously over 5–6 hours on the first day of therapy to assess the patient's response to the drug. Body temperature is continually measured during the infusion to detect development of a drug fever. On the day after administration, renal parameters are measured, and if creatinine has not risen more than 0.3 mg/dl (88.4 µmol/l), a dose of 1.0 mg/kg can be administered on the following day. Temperature is again monitored and if drug fever develops, the infusion is slowed or a low dose of a non-steroidal anti-inflammatory agent can be administered. Every other day administration (of 1 mg/kg amphotericin) and monitoring is continued until acute renal injury necessitates discontinuation of therapy or until fungal disease is under control, which can require cumulative amphotericin doses of 5–14 mg/kg. If residual disease is suspected or the animal can no longer tolerate intravenous amphotericin therapy, oral triazole treatment is used for continual control of disease.

Subcutaneous administration of amphotericin B has been used successfully to treat fungal infections in fractious animals, those that cannot be hospitalized, or those that cannot be treated with oral medications (Malik et al. 1996). For this protocol, amphotericin B at a dose of 0.5–0.8 mg/kg was diluted in 400–500 ml of 0.45% sodium chloride/2.5% dextrose and administered subcutaneously two to three times weekly until disease resolved. Animals must be monitored for development of subcutaneous abscessation when this form of administration is used.

To reduce the likelihood of renal insufficiency during treatment with amphotericin, administration of lipid-complexed or liposomal amphotericin B is recommended. This drug

is given as a 20–30-minute infusion of 0.5–3.0 mg/kg to a cumulative dose of 12 (cat) – 36 (dog) mg/kg, and pretreatment with aggressive saline diuresis is not a requirement. This drug is more expensive than standard amphotericin B and is formulated in a single-use vial, which adds to the expense of therapy; however, this is countered by the requirement for less monitoring of renal function during therapy.

Antiviral Therapy

Viruses (feline herpesvirus-1: FHV-1; feline calicivirus: FCV) have been implicated as major etiologic agents in acute feline upper respiratory disease. Because clinical signs are generally self-limiting and correlation of molecular test results with disease state is poor, specific diagnostic tests to identify infecting organisms are rarely performed. Nonetheless, therapeutic trials using a drug known to assist in control of ophthalmic manifestations of FHV-1, famciclovir, are being performed in cats with upper respiratory tract signs, with varied clinical results. One study revealed a lack of effect on clinical signs but reduced conjunctival shedding of FHV-1 in kittens treated with famciclovir (Cooper et al. 2019). In a separate study of 22 cats with a 50% FHV-1 detection rate by qPCR (albeit in low copy numbers), famciclovir-treated cats had decreased risk of worsening clinical signs (Reinhard et al. 2020). In privately housed kittens with sneezing and naso-ocular discharge, FHV-1 was isolated by qPCR in only 30% of cases; kittens were treated with doxycycline and placebo or doxycycline in combination with famciclovir, and no difference in disease remission was noted (Kopecny et al. 2020). Therefore, the role of famciclovir in management of the acute infectious upper respiratory syndrome remains unclear, and in the chronic disease syndrome (feline chronic rhinosinusitis), presence of the upper respiratory viruses is poorly correlated with disease status, and there are no controlled studies evaluating efficacy. Fortunately, the drug is safe in kittens and cats, therefore a clinical trial using an appropriate dose of famciclovir (40–90 mg/kg q12h) could be considered in animals with severe manifestations of chronic upper respiratory tract disease.

Use of pheromone diffusers has been investigated as a means to reduce stress in shelters and thus limit the impact of FHV-1 in kitten populations. Both positive and neutral results have been reported, but no side effects of this adjunct therapy were noted.

Lower respiratory tract disease due to viral infection is less common, but can occur with some upper respiratory tract viruses or due to infection with the mutated coronavirus that causes feline infectious peritonitis (FIP). Many respiratory manifestations of FIP are related to the host's immunologic response and subsequent vasculitis, and definitive diagnosis of FIP remains difficult. Controversy surrounding viral pathogenesis of disease and of diagnostic methodology for the diagnosis make it difficult to determine whether antiviral therapy is warranted in suspect cases, although protease inhibitors and remdesivir or its metabolite (GS-441524) have provided promising results in control of the wet form of disease (see Chapter 7).

Viruses associated with canine infectious respiratory disease complex can cause severe pneumonia in dogs; however, specific antiviral therapy has not been investigated for use in canine viral pneumonias.

Glucocorticoids

Glucocorticoids are indicated for long-term control of feline bronchial disease, chronic bronchitis, and canine eosinophilic lung disease. Glucocorticoids reduce inflammation by inhibition of phospholipase A2, the enzyme responsible for the initial metabolism of arachidonic acid into inflammatory mediators. Glucocorticoids also decrease migration of

inflammatory cells into the airway, thus decreasing the concentration of granulocyte products and reactants (major basic protein, eosinophil cationic protein, reactive oxygen species) that perpetuate epithelial injury.

Short-acting oral glucocorticoids are preferred for management of inflammatory airway disease in the dog or the cat. Use of this class of drug will allow accurate titration of the dose to control clinical signs while inducing minimal side effects. Prednisolone is the preferred glucocorticoid to use in the cat, while either prednisone or prednisolone can be used in the dog. Long-acting glucocorticoids such as dexamethasone, triamcinolone, and methylprednisolone acetate do not have a therapeutic advantage over prednisone, and use of a repositol steroid agent could result in progression of inflammation between doses that allows perpetuation of disease. The duration and dose of glucocorticoid therapy will depend upon the severity and chronicity of respiratory signs, the extent of infiltrates on radiographs, and the degree of inflammation on cytology. An individualized approach to anti-inflammatory treatment is required for each case, with a gradual reduction in dose to the minimal level that controls clinical signs. Ideally, the goal is to achieve alternate day therapy to re-establish the hypotholamic–pituitary–adrenal axis as soon as possible.

The length of treatment required to alleviate signs is unknown; however, long-term therapy (2–3 months for dogs with chronic bronchitis and 4–6 months for dogs with eosinophilic disease) can be anticipated in most cases. Discontinuation of medication can be possible in dogs, although many cats with inflammatory airway disease will require lifelong medication continually or intermittently. Absence of clinical signs does not necessarily equate to control of airway inflammation, therefore caution is warranted when considering discontinuation of medication. If disease worsens during lowering of the dose, a return to the higher dose of glucocorticoid that controlled clinical signs is generally required. Alternatively, treatment with inhaled glucocorticoids, bronchodilators, or antitussive agents can be added depending on the disease process (see later and Chapter 5).

Bronchodilators

The two main classes of bronchodilators used in veterinary medicine are methylxanthine derivatives (theophylline) and beta-agonists. Methylxanthines provide minimal bronchodilation while beta agonists trigger immediate airway dilation; however either class of drug can be clinically helpful in reducing signs in dogs or cats with bronchitis or in allowing a reduction in the dosage of glucocorticoid required to control signs.

Methylxanthines

Extended-release theophylline, a methylxanthine derivative, was used extensively in human medicine as a bronchodilator, but it has fallen out of favor in recent years and is no longer manufactured commercially in the US. The drug can be obtained from various compounding pharmacies, although pharmacokinetic and pharmacodynamic studies are available for few preparations (Cavett et al. 2019; Reinhart et al. 2022). Despite the historically widespread use of theophylline, its mechanism of action remains obscure. Although known pharmacologically as a phosphodiesterase inhibitor, the dose of theophylline used clinically does not result in sufficient accumulation of cyclic adenosine monophosphate to cause smooth muscle relaxation. Instead, the clinical effects of methylxanthines likely result from adenosine antagonism or from alterations in cellular sensitivity to calcium. Theophylline might provide beneficial effects other than bronchodilation such as increasing diaphragmatic muscle strength, improving pulmonary perfusion, reducing respiratory effort, and stimulating mucociliary clearance (in dogs, but

not in cats). Previous studies evaluating specific brands of extended-release theophylline suggested a dose of 10 mg/kg PO every 12 hours in a dog and 15–19 mg/kg PO once daily in the evening for the cat to approximate the human therapeutic range of 10–20 µg/ml (Bach et al. 2004; Guenther-Yenke et al. 2007). These doses are commonly used when prescribing compounded medications; however, animals must be monitored closely for signs of toxicity as well as for evidence of efficacy.

Adverse effects of methylxanthines are likely related to adenosine antagonism and include gastrointestinal upset, tachycardia, and hyper-excitability. It is essential to individualize drug therapy because there is a wide variation in the dose that causes side effects in the individual. Theophylline metabolism is influenced by many factors, including fiber in the diet, smoke in the environment, congestive heart failure, and the use of other drugs. Because of concerns about metabolism and unknown bioavailability, a reduced dosage can be considered initially (5 mg/kg every 12 hours in a dog and 5–10 mg/kg once daily in the cat), and if the animal tolerates the drug, the dosage can be increased as needed.

Methylxanthines have very weak bronchodilatory activity (if any at all) and while they can be beneficial for adjunctive therapy in control of clinical signs, they are not recommended for use in an acute or emergency situation. Aminophylline is not advised because of its short half-life.

Beta-agonists

Administration of a beta-2 agonist (terbutaline or albuterol) results in bronchodilation due to direct relaxation of airway smooth muscle, and intravenous terbutaline has been shown to reduce airway resistance acutely in cats with constricted airways (Dye et al. 1996). Preliminary pharmacokinetic studies have established the safety of the drug, and the recommended dose for use in an emergency situation is 0.01 mg/kg parenterally (intravenously, intramuscularly, or subcutaneously). Repeat administration can be performed after 10–20 minutes if therapeutic response is inadequate. This drug does have some beta-1 activity and can lead to an increased heart rate, therefore monitoring is advised. Active bronchoconstriction does not play a role in canine chronic bronchitis as it does in a subset of cats with bronchitis, making use of beta-agonists of questionable efficacy in the canine disease. Theoretically, chronic use of a beta-agonist can result in downregulation of beta-receptor numbers and decreased efficacy of the drug, although it is unclear if this is recognized clinically. As with methylxanthines, beta-agonists can cause excitability or tremors during initial therapy, but animals usually become accustomed to the drug. Beta-2 agonists can be administered orally and are also available for inhaled therapy; however, prolonged use of specific isoforms of albuterol (R, S and S enantiomers) can potentially worsen airway inflammation in cats (Reinero et al. 2009).

Mucolytics

Marked controversy exists concerning the utility of mucolytic agents in human medicine, and there is little information on the use or efficacy of these preparations in veterinary patients. Clinical experience suggests that some dogs and cats with excessive production of airway secretions associated with chronic infectious or inflammatory diseases can benefit from their use. Conditions that might respond to mucolytic agents include feline chronic rhinosinusitis, canine lymphoplasmacytic rhinitis, chronic bronchitis, bronchiectasis, eosinophilic lung disease, and bacterial pneumonia associated with the production of viscous secretions (e.g. *Mycoplasma* pneumonia).

Mucolytic/expectorant agents such as *N*-acetylcysteine, bromhexine, ambroxol, and guaifenesin are proposed to thin the viscosity of mucin-containing secretions. These drugs act by a variety of mechanisms, including breakage of disulfide bonds in airway mucoproteins, stimulation of serous airway secretions, or breakdown of acid mucopolysaccharide fibers in sputum. N-acetylcysteine is also reported to provide a variety of antioxidant and endothelial effects that might prove beneficial in respiratory patients. This neutraceutical can be administered orally or by inhalation, although nebulization with *N*-acetylcysteine could trigger bronchoconstriction and can cause epithelial injury, therefore this route is not routinely recommended. *N*-acetylcysteine is typically available in 600 mg capsules, and an empiric dose of 30–60 mg/kg (not to exceed 600 mg) PO two to three times a day can be clinically efficacious in improving evacuation of mucus. All other mucolytic agents are designed for oral use. Guaifenisin is combined with dextromethorphan (a cough suppressant) in an over-the-counter medication. Bromhexine and ambroxol can also be obtained over the counter as either liquid or pill preparations. None of these medications have had clinical trials performed to establish efficacy.

Antitussive Agents

The cough reflex is of major importance in animals because it serves the essential function of clearing secretions from the airway. Suppression of this reflex before resolution of inflammation or infection can be deleterious, because mucus can become trapped in small airways, and prolonged contact between the inflammatory mediators in mucus and epithelium perpetuates airway injury. If infection is present, cough suppression can lead to serious pneumonia. When clinical signs suggest that inflammation is resolving yet cough persists, cough suppression is desirable, because chronic coughing can lead to repeated airway injury and syncopal events. Cough suppressants are used almost exclusively in dogs rather than cats and are often required in dogs with airway collapse or irritant tracheitis.

Over-the-counter dextromethorphan-containing compounds are only occasionally efficacious in some animals with airway disease, but they appear to be generally safe for use if not administered in excess. When more potent suppression of a dry cough is required, narcotic agents are typically prescribed. Hydrocodone bitartrate (0.22 mg/kg PO every 6–12 hours) or butorphanol tartrate (0.5 mg/kg PO every 6–12 hours) can be used in dogs. These agents must be given at an interval that suppresses coughing without inducing excessive sedation. Giving these drugs frequently in the first 24–48 hours can help break the cycle of cough and airway injury. The drug should then be administered less frequently, with gradual downward tapering of the dose to the lowest amount that controls clinical signs. Long-term therapy can be required in some patients; however, overuse should be avoided because tolerance can develop which diminishes efficacy.

Tramadol has been suggested for use as a cough suppressant, although it has not been well-studied and does not appear to provide much cough suppression. Clinical use thus far suggests it is of limited benefit. Gabapentin has also been suggested to have some utility in managing cough that is mediated by central neural system sensitization or a neuropathic response, but this has not been specifically examined in dogs.

Routes of Administration

Parenteral versus Enteral

For treatment of life-threatening disease, parenteral administration of a microbiocidal agent rather than a static drug provides optimal therapy. An exception to this might be the animal with severe pulmonary infiltrates associated with fungal pneumonia. Rapid killing of large numbers of organisms with a drug such as amphotericin B can lead to acute respiratory distress syndrome when an exuberant inflammatory response damages the alveolocapillary membrane, resulting in non-cardiogenic pulmonary edema (see Chapter 8). In a severely affected animal with marked tachypnea and elevated work of breathing, consideration should be given to achieving a controlled kill of organisms with a fungistatic drug, if possible.

Parenteral administration of drugs is indicated for any animal with a swallowing disorder, vomiting, or malabsorptive intestinal disease. Renal and hepatic function should be evaluated and monitored throughout therapy, because many drugs (particularly antifungal medications) rely on renal or hepatic excretion for removal from the body or can cause organ dysfunction.

Nebulization

Nebulization can be used to hydrate airway secretions or to administer drug directly to the epithelial surface of the respiratory tract. With upper respiratory tract disease, a standard humidifier can be used for hydration; however, liquefication of lower airway secretions requires use of an ultrasonic or compressed-air nebulizer that will generate particles <4–5 μm in size. These are readily available through respiratory supply companies or via the internet.

When nebulization is performed to administer medication, a facemask must be used to provide direct delivery of the agent to the respiratory tract, and specific drug formulations should be utilized. Not all liquid drugs will physically form into micelles that can be distributed via nebulization. Some antibiotics (primarily aminoglycosides) can be nebulized, and these are generally indicated for treatment of surface infection with *Bordetella bronchiseptica* when clinical signs cannot be managed with orally administered drugs alone. A retrospective study reported improved response with nebulization of undiluted 5% gentocin q12h compared to gentocin diluted in saline, with a shorter median duration of treatment (4 versus 6 weeks) (Cannone et al. 2020). Importantly, topical administration of gentocin does not result in toxic serum levels (Biénès et al. 2023). Albuterol, a beta-2-agonist bronchodilator, can be nebulized and is clinically efficacious in reversing bronchoconstriction in cats with asthmatic disease. Budesonide is a glucocorticoid that can be nebulized, but it typically requires use of a compressed-air jet nebulizer rather than an ultrasonic nebulizer. N-acetylcysteine, a mucolytic agent, is available in a form designed for nebulization; however, it can trigger bronchoconstriction when administered this way and also can be somewhat toxic to airway epithelium. Therefore, it is not recommended for use by inhalation.

Nebulization can also be used simply to hydrate airway secretions and facilitate removal of mucus from the lower airway. This can be beneficial for animals that suffer from diseases resulting in excessive mucus production or pooling of secretions in the lower airways, including bronchitis, bronchiectasis, and infectious or inflammatory pneumonia. Use of sterile 0.9% saline dispensed as single-use vials without addition of preservatives is recommended for most cases; hypertonic (3%) saline has been used in various human conditions associated with excessive mucus accumulation but hasn't demonstrated better results in clinical patients to date. A small aquarium, animal carrier, or plastic container

can be modified to allow introduction of the nebulized liquid and venting of exhaled carbon dioxide (Figure 3.1). Nebulization can be performed for 10–20 minutes 2–4 times daily, as tolerated by the animal. Gentle exercise or coupage (Figure 3.2) following nebulization will encourage evacuation of airway mucus when treating lower respiratory disease.



Figure 3.1 Nebulization is administered in a cat carrier covered in plastic by using an ultrasonic nebulizer that creates particles <5 μm in size.



Figure 3.2 Chest coupage is performed after nebulization by using cupped hands to percuss the chest in a ventral to dorsal and caudal to cranial manner.

Metered-Dose Inhalers

Various glucocorticoid preparations are available as metered-dose inhalers (MDIs). Because animals will not actively inspire on command, administration of inhaled medication requires attachment of the MDI to a spacer device with facemask. Spacers are available from many respiratory supply companies, and Trudell Medical International makes units specifically designed for cats and large and small dogs (AeroKat®, AeroDawg®, London, Ontario, Canada; www.trudellmed.com). The spacer device collects aerosolized drug generated by the MDI, holds the drug in the spacer behind a one-way valve, and tidal respiration carries the particles into the lower airways. An investigation into drug delivery in dogs using a MDI demonstrated adequate lower airway distribution, although deposition was improved when using a nebulizer in comparison to the MDI (Chow et al. 2017). Clinically, administration of medication via MDIs has proven efficacious in controlling clinical signs in dogs with various respiratory diseases (Bexfield et al. 2006; Chan and Johnson 2023), although not always with eosinophilic lung disease (see Chapter 6). A tightly fitting but comfortable facemask is critical for successful therapy, and it is important to ensure that the animal breathes normally for 8–10 breaths. Brachycephalic dogs often can be fit with a facemask designed for a cat or one obtained from a local pharmacy or respiratory supply company, because the shape of the face is fairly similar to humans. For dolichocephalic breeds, anesthetic or cone-shaped facemasks can be better tolerated. Specific studies of drug delivery in animals with various facial conformations or in animals with respiratory disease are lacking.

In dogs or cats with moderate-to-severe clinical manifestations of disease, standard doses of oral glucocorticoids are generally recommended during the first few weeks of inhaled therapy because of a theoretical delay in the efficacy of inhaled medications. The oral dose can then be tapered downward as the animal responds clinically. However, in a recent study (Chan and Johnson 2023), reduction in cough by at least 50% was observed within the first 2 weeks of treatment with inhaled medications alone, obviating the need for systemic therapy unless there are concerns that excessive mucus lining the airways could interfere with the local effect of drugs.

The most commonly recommended glucocorticoid for inhalation is fluticasone propionate inhalation aerosol, which is available in an MDI containing 120 doses to deliver 44, 110, or 220 µg/puff (from US distributors). Any of these drug dosages can reduce experimentally induced airway eosinophilia in cats (Cohn et al. 2010); however, the appropriate dose to use in naturally occurring disease is unknown. In dogs and cats with lower respiratory tract disease, starting with 110 mcg/puff has been efficacious clinically with development of few side effects. The MDI must be shaken well prior to actuation and attached to the spacer before the dose is ejected. Side effects of inhalational therapy are uncommon, although some dogs can develop signs related to glucocorticoid excess including polyuria, polydipsia, and polyphagia. Oral fungal infection is not common in animals as it is in humans, but an ill-fitting facemask can be associated with chronic ocular or facial trauma.

In addition to glucocorticoids, inhaled beta agonists are available in MDIs and can be used in the emergency situation to control an asthmatic crisis. As mentioned above, long-term use is not advised due to concerns about inducing inflammation. Inhaled preparations containing both glucocorticoids and beta agonists are widely used in human medicine and also in some veterinary practices, although it is unclear how necessary these are for feline conditions.

While inhaled medications are more expensive than oral medications, they can improve owner compliance, particularly when animals are difficult to medicate orally and chronic therapy is required. In dogs, this method of therapy is particularly advantageous when side effects of glucocorticoids are severe or when concurrent diseases (diabetes, heart disease, pancreatitis, obesity, or renal disease) make oral glucocorticoid therapy undesirable. Similarly, cats with cardiac disease, diabetes, or renal dysfunction that have concurrent lower airway inflammation are better managed with inhaled therapy. Many owners find that animals tolerate inhalation treatment readily, although problems can be encountered. Some cats are frightened by actuation of the MDI, but they can become habituated to the sound with training. The cat that suffers from acute asthmatic attacks might not tolerate application of the facemask in the emergency situation. An additional concern might be the competence of drug delivery to the epithelial surface because owners lack the ability to deploy the device correctly, or because mucus-filled airways prevent the drug from interacting with its receptor. In the latter situation, instituting nebulization to liquefy secretions or employing oral glucocorticoids can be beneficial. Finally, breath holding by the dog or cat can be a reason for treatment failure, although the newest spacing chamber created by Trudell Medical has a Flow-Vu indicator that allows visualization of respiratory movements at the valve of the chamber.

Adjunct Therapy

Oxygen Therapy

Supplemental oxygen should be provided to any animal presenting with respiratory difficulty as indicated by tachypnea, hyperpnea, cyanosis, or collapse, although it is important to realize that upper airway obstructive disease and pleural diseases are poorly responsive to oxygen administration alone. In those situations, alleviation of the obstruction and removal of pleural fluid or air to allow lung expansion are of critical importance. Oxygen can be supplied rapidly by attaching a facemask to an oxygen line and providing a high flow rate of oxygen directly to the patient. The disadvantage of this system is the need for continual patient restraint. An oxygen cage is generally less stressful to the patient and provides stable oxygen flow rates; however, examination of the animal is hindered. Nasal oxygen administration is suitable for animals that are able to breathe through the nose, and this method allows easy access for repeat examinations and greater freedom of movement for the animal. To provide nasal oxygen, the outer surface of a red rubber tube is lightly coated with anesthetic gel and directed into the ventral nasal meatus. Tubes are advanced into the caudal aspect of the nasal cavity (approximately to the level of the medial canthus of the eye) to supply oxygen to the pharyngeal region and are glued or sutured in place (Figure 3.3). Oxygen flow rates of 1–5 l/min can provide 30–50% fraction inspired oxygen depending upon the size of the dog. Alternately, nasal prongs used in human medicine can be applied to the nose of a dog and will supply 30–40% inspired oxygen in a convenient manner. Finally, an emergency oxygen tent can be created by inserting an oxygen supply tube into an Elizabethan collar covered with plastic wrap. An exhaust vent should be provided for the exit of carbon dioxide.



Figure 3.3 Transected skull shows placement of a nasal oxygen catheter through the ventral nasal meatus into the caudal portion of the nasal cavity just rostral to the soft palate.

Oxygen supplementation at home can be helpful in dogs or cats with severe interstitial lung disease, particularly when the condition is complicated by pulmonary hypertension. This type of therapy obviously requires a dedicated owner and benefits are not easily quantifiable, although nightly administration can improve daytime activity in some animals. An oxygen chamber can be constructed from plexiglass or from an aquarium or with a commercially available pop-up unit, and it must contain inlet and outlet valves. Oxygen is provided through a tank or compressor-driven system at the inlet and the outlet allows egress of carbon dioxide (oxygen4pets.com, pawprintoxygen.com, and others). The fraction of inspired oxygen can often be maintained around 40–50% to provide an oxygen-enriched environment.

The level and extent of oxygen supplementation that can be supplied to a given animal without risking oxygen toxicity must be considered. Generally, moderate levels of oxygen (40–60%) can be administered for 24–48 hours without risking toxicity; however, the underlying disease process alters susceptibility to oxygen toxicity. Animals with aspiration lung injury, which generates both inflammatory and oxidative damage, are likely more susceptible to oxygen toxicity. For at-home management of chronic diseases, intermittent oxygen therapy is unlikely to be associated with toxicity.

Animals with hypoxemia that are refractory to supplemental oxygen, or those with excessive work of breathing resulting in respiratory muscle fatigue, require ventilatory support until lung disease or hypoventilation is adequately treated. Excessive respiratory muscle activity during breathing, ventilatory fatigue, or development of hyperthermia

associated with the metabolic cost of breathing can also be indications for mechanical ventilation. Objective indicators for the need to provide mechanical ventilation are obtained from arterial blood gas values. An elevated partial pressure of carbon dioxide (P_aCO_2; normal <45 mmHg) indicates hypoventilation, and values that continue to increase over time (above 60 mmHg) generally require intervention. When rising P_aCO_2 or low partial pressure of oxygen (P_aO_2 <60 mmHg or pulse oximetry reading consistently <91%) fails to respond to supplemental oxygen therapy, mechanical ventilation should be considered. Because this requires constant monitoring and is both labor intensive and technically challenging, referral to a critical care specialist is usually required.

Nutritional Therapy

Obesity is a common finding in the pet population and animals with chronic respiratory disease suffer from worsening of cough and respiratory effort when obesity causes poor lung expansion, reduced thoracic volume, or increased work of breathing. Obesity worsens clinical signs in dogs and cats with chronic bronchitis by decreasing thoracic wall compliance and increasing abdominal pressure on the diaphragm. Improvements in exercise tolerance and arterial oxygenation can be seen with weight loss alone.

Owners should be given reasonable goals for an animal's optimal weight and the time within which a sufficient amount of weight loss can be achieved. A 1–2% weight loss per week is desirable, but highly difficult to achieve (German et al. 2007). Advising owners that it will take 20 weeks (5 months) for a pet to achieve a 20% weight reduction can aid in communication and achievement of weight loss goals. Dietary calorie restriction and rigorous owner cooperation are required. Close monitoring of owner compliance and using positive reinforcement seem to enhance overall success. Animals can be started on 80% of their previous caloric intake. Alternatively, the resting energy requirement (RER in kcal/day) can be used to calculate the daily calories to provide an obese animal when starting a weight loss program: $RER = 70 \times (\text{body weight in kg})^{0.75}$. Use of a high-fiber, high-protein diet can improve participation in a weight loss program by enhancing satiety in patients and thus reducing food-seeking behavior (Weber et al. 2007). Allowing owners to save 10% of the daily calories to provide as treats can increase owner satisfaction with the process. When possible, the animal should be encouraged to participate in gradually increasing amounts of exercise.

Chest Tube Placement

A chest tube is required for treatment of tension or recurrent pneumothorax and pyothorax. It is sometimes used to drain a large-volume effusion from the pleural space. When placing a chest tube, all necessary tools should be collected prior to initiation of the procedure and sterile technique should be used. Chest tube placement is usually performed in lateral recumbency. Sedation or anesthesia is used depending on the stability of the patient. The side of the thorax is liberally clipped for surgical preparation, surgical scrub of the hands is performed, and sterile gloves are worn.

The chest tube can be placed in the dorsal third of the chest cavity for management of pneumothorax or in the mid to ventral third of the chest when pyothorax is present. The chest tube will be directed ventrally and toward the elbow to provide optimal drainage of fluid, and it should lie just ventral and slightly cranial to the heart. The tube is positioned higher in the chest when used for evacuation of air. Ensure that any fenestrations in the tube will lie within the thoracic cavity to reduce the risk of subcutaneous emphysema or

iatrogenic pneumothorax. Pay attention to where the depth markings are on the chest tube to know how far to insert it into the chest.

Large-Bore Chest Tubes

An Argyle™ trocar catheter is a commercially available tube system for chest tube placement that has a sharp and rigid trocar to guide the chest tube into the pleural space. Alternatively, a sterile red rubber catheter (18 French) with a 10 French urinary catheter inserted for support can be used. If a viscous pleural fluid is present, additional side holes should be made in the red rubber catheter to limit clogging of the openings with fibrinous material (Figure 3.4). The animal is usually placed in lateral recumbency and sedation is employed, but debilitated animals may not be able to tolerate excess anesthesia. Prior to inserting the chest tube, the desired position of the tube within the thorax should be visualized (Figure 3.5). Ideally, the chest tube will enter the skin at approximately the 10th intercostal space and will enter the thorax at a more ventral position at the 8th intercostal space.

The site of the skin incision at the 10th intercostal space is infiltrated with local anesthesia (0.2–0.5 ml of lidocaine). An area ventral and cranial to the skin incision is chosen for entry of the chest tube into the thorax at the eighth intercostal space. This site should also be infiltrated with lidocaine down to the level of the pleura. Recall that the intercostal vessels and nerves lie on the caudal border of the rib. Thus, the tube should be inserted close to the cranial rib border to avoid trauma to these structures. After local anesthesia is instilled, the sterile surgical preparation is completed.

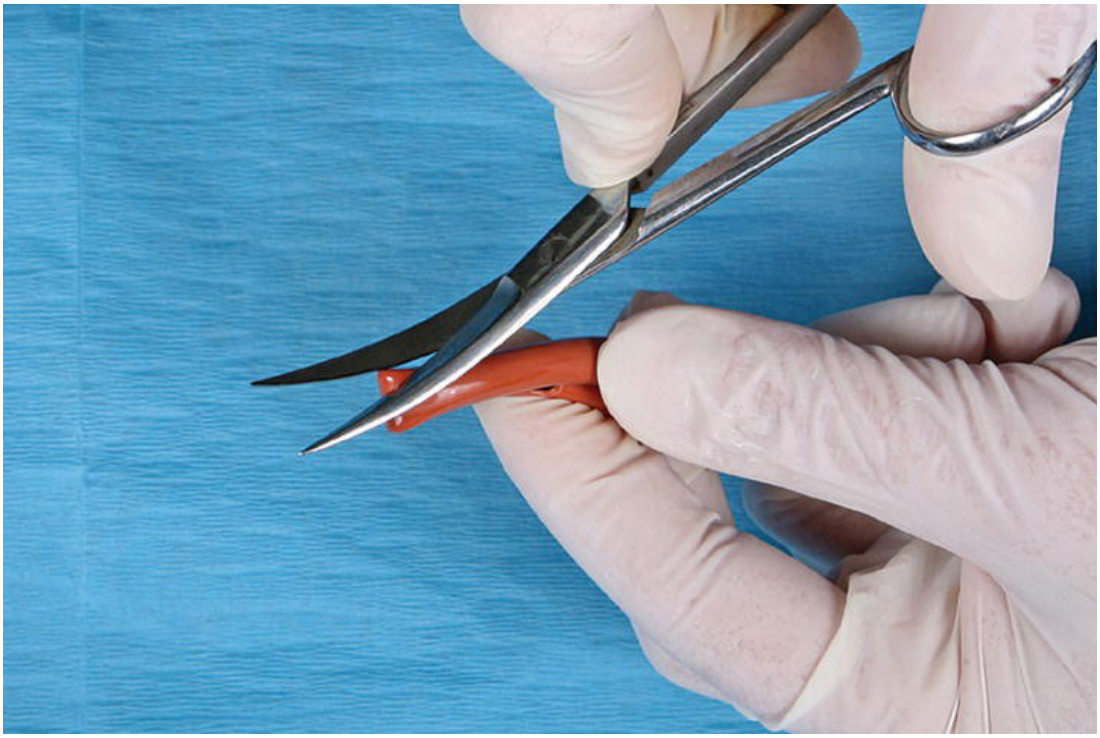
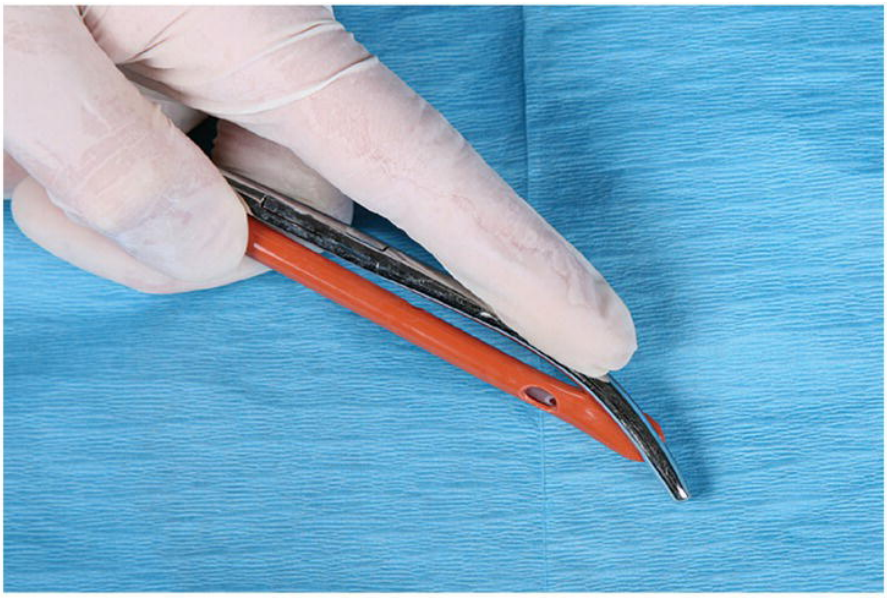


Figure 3.4 For removal of viscid pleural fluid associated with pyothorax, additional side holes can be cut in a red rubber catheter. Caution is warranted to avoid weakening the catheter with holes that are too large or placed too close together.



Figure 3.5 This cat is in left lateral recumbency with the head to the right of the image. The chest tube should be placed through the skin at the 10th intercostal space and through the thorax at the 8th intercostal space. Ideally, it should lie on the ventral portion of the thorax for removal of fluid. Any additional side holes made in the tube must be within the thoracic cavity.

A stab incision is made at the caudal site on the thorax to allow easy entry of the chest tube through the skin. This incision should not be too large, because it must be sutured closed with a purse-string pattern at the end of the procedure. Long curved forceps are used to grasp the red rubber tube, ensuring that the supporting catheter is not trapped by the forceps. The sharp ends of the forceps will precede entry of the tube through the ribs (Figure 3.6). Use of a commercially available chest tube avoids the need for long forceps and provides a sharp trocar for use in penetrating the chest cavity.



(a)



(b)

Figure 3.6 (a) The red rubber catheter and stabilizing catheter are assembled and the red rubber only catheter is grasped with large curved hemostats. Approximately 1–2 cm of the instrument should precede the red rubber catheter into the chest cavity. (b) Commercially available trocarized chest tubes come in a variety of sizes that can be tunneled under the skin for insertion into the pleural cavity.

The skin is retracted cranially, and the intercostal muscles are gently dissected at the site of entry to the pleural cavity. The instrument is grasped 2–3 cm from the tip and controlled downward force is used to insert the tube rapidly through the rib space. After the tube is advanced partially into position towards the ventral aspect of the chest cavity, the stylet or trocar is slowly withdrawn or held in place while the chest tube is properly placed. When the stylet or trocar is fully withdrawn, the end of the tube is quickly clamped with a large hemostat to prevent entrance of air into the chest. A purse-string suture is used to close the skin incision. The distal end of the tube can be secured to the lateral aspect of the chest by

using a finger trap suture (Figure 3.7). This will prevent the tube from being pulled out of the thorax if traction is applied to the tube.

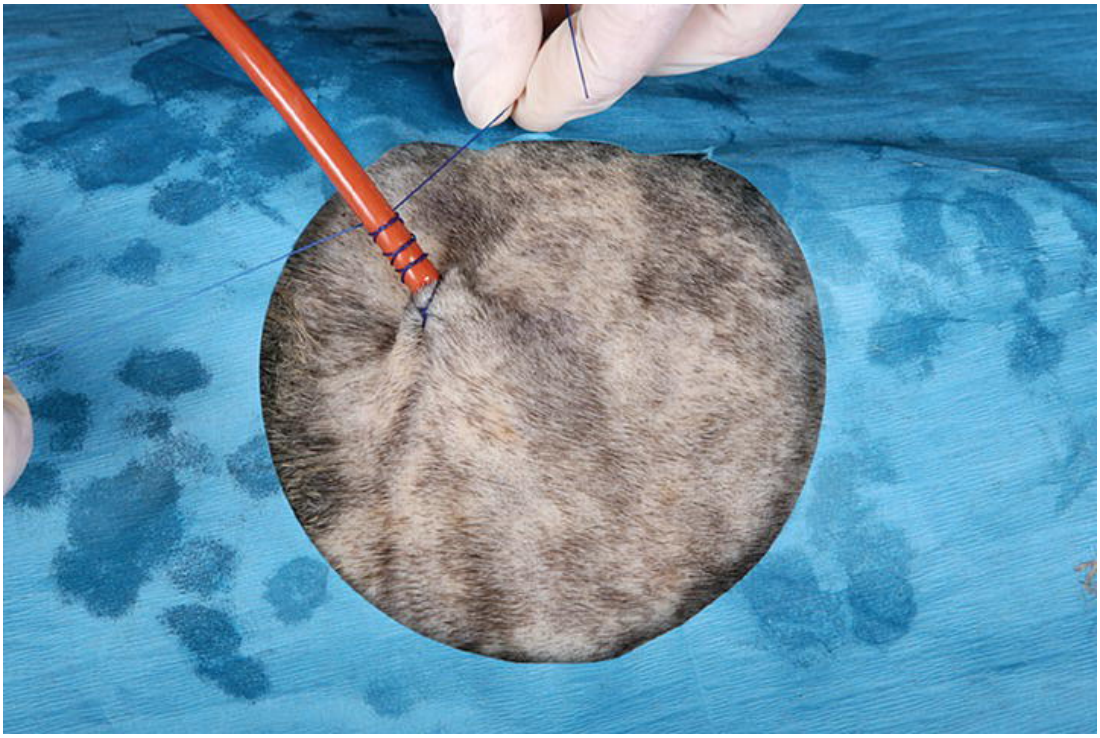


Figure 3.7 A purse-string suture and finger cot pattern are used to close the incision and secure the chest tube in place.

When the tube has been sutured firmly in place, extension tubing with a three-way stopcock and syringe is attached to the chest tube to insure a tight seal against leakage. The plastic flange on the extension set should be engaged in the closed position, the three-way stopcock (between the extension set and the syringe) is turned off to the patient, and a syringe completes the air seal. Gauze sponges loaded with antiseptic ointment are applied to the site on the chest where the tube exits the body and the tube is bandaged in place.

Small-Bore Chest Tubes

An easier method for placing a chest tube is by use of a commercially available small-bore Mila® chest tube (MILA International, Florence, KY, USA). Mila catheter kits (Figure 3.8) allow placement of a smaller-bore chest tube using a catheter-over-guidewire (modified Seldinger) technique. Catheters are radio-opaque and are available in 12 and 14 gauge sizes, with multiple fenestrations placed in the tube up to the 4 and 8 cm points on the chest tube catheter to allow for improved drainage. The chest tube can be connected to a one-way valve provided in the kit for intermittent aspiration. It can also be attached to a continuous drainage device, although this might not be as effective as when using a large-bore chest tube.

Lidocaine anesthesia is instilled between the seventh and ninth intercostal spaces by injecting at sites through the skin and subcutaneous tissue, down to the level of the pleura. The skin is tented at the site of the caudal-most lidocaine block and a stab incision is made with a #11 blade. The 14 gauge catheter-over-needle introducer is passed through the skin and subcutaneous tissue towards the elbow to penetrate the pleural cavity off the cranial

border of the rib. Once the pleura has been entered, the needle is retracted while the introducer catheter is passed into the pleural cavity. This will be used to insert a floppy ended J wire into the pleural space. The plastic sheath on the J wire contains a groove that allows smooth passage of the wire through the catheter (Figure 3.9). The J wire is initially retracted fully into the blue plastic sheath, the sheath is firmly seated into the hub of the catheter, and the J wire is passed floppy end first into the pleural space.

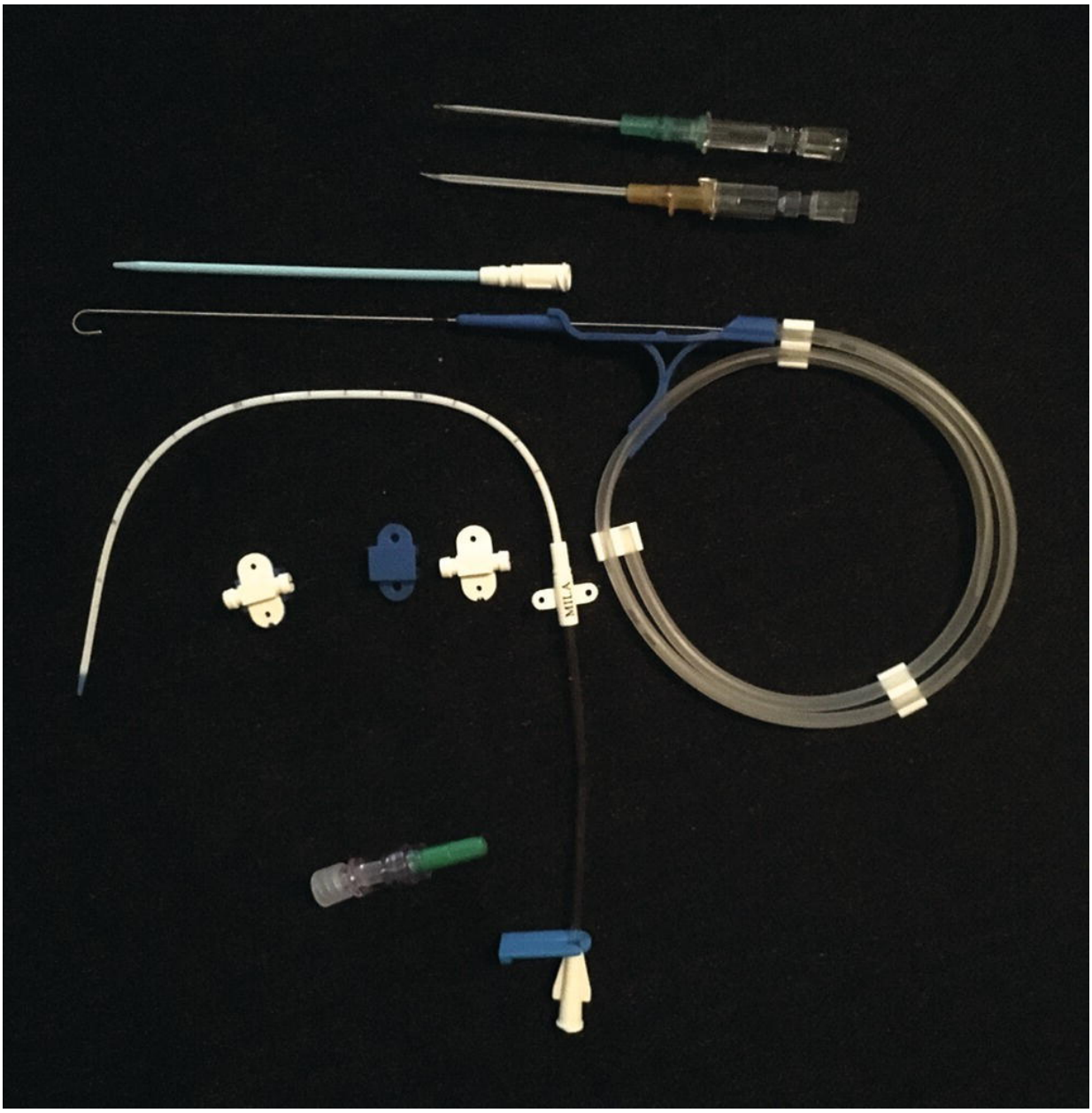


Figure 3.8 Mila small-bore chest tube kit contains (from top to bottom) 14 and 18 gauge catheter-over-needle introducers, a dilator catheter, a floppy-ended J wire and guide sheath, a chest tube with multiple fenestrations, suture anchors, and a one-way valve.

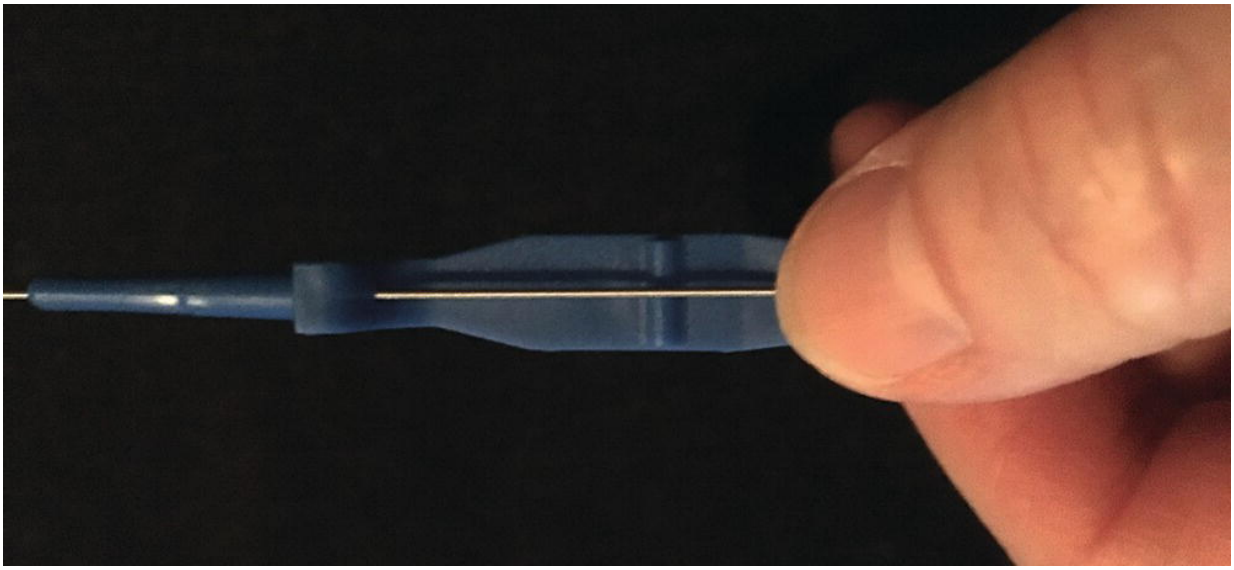


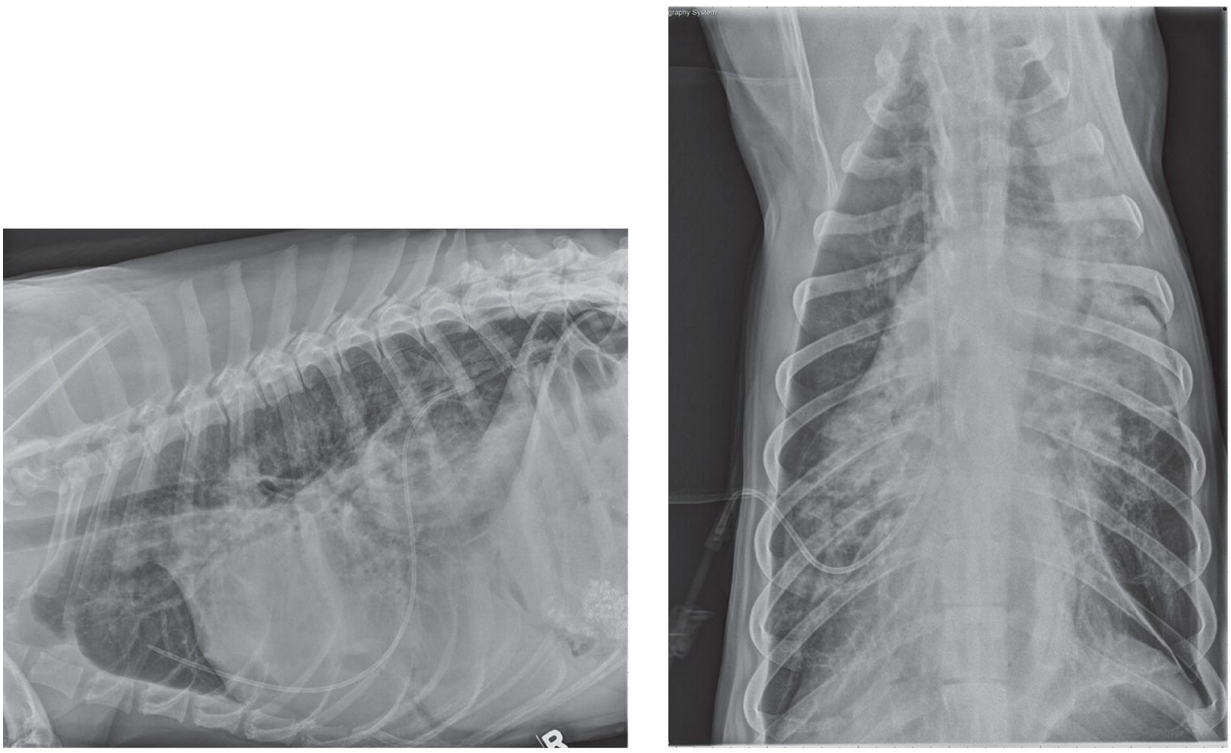
Figure 3.9 The plastic sheath used to deploy the J wire contains a groove to use when deploying the guide wire through the catheter into the chest cavity.

After approximately one-third to one-half the length of the J wire is passed into the pleural space, the introducer catheter can be removed. The J wire should always be held in place and secured using sterile technique throughout these maneuvers. A sterile-gloved assistant can be helpful for this purpose. If the smaller (18 gauge) introducer catheter has been used, the dilator catheter might be needed to widen the opening through the thoracic wall in preparation for the chest tube. Otherwise, place the end of the Mila chest tube catheter over the wire and advance it until the wire exits the distal end of the chest tube. Do not let the chest tube enter the skin until the wire is secured at the distal end.

As the Mila catheter approaches the chest wall, tent the skin to ease its passage over the wire into the chest. Gently twist and push the catheter into the appropriate position within the chest, withdraw the wire, and attach the one-way valve adaptor to the catheter to confirm that it aspirates fluid or air. The chest tube is sutured to the skin of the chest wall using the butterfly wings on the chest tube catheter. If too much of the chest tube is within the thorax, retract the catheter and place an anchor on the tube prior to suturing in place. Place sutures through the skin and keyhole on either side of the tube and tie in place. For further stability, pass the suture around the groove on the hub of the catheter and tie with a surgeon's knot. A sterile dressing should be placed over the insertion site. Catheter care of the insertion site is performed daily as part of standard patient management when chest tubes are in place.

After placement of the chest tube, orthogonal radiographs are performed to assess position of the tube (Figure 3.10). If a significant fluid volume is still present within the pleural space, placement of a second tube should be considered.

The pleural space can be evacuated by use of continuous suction, when the animal exhibits respiratory distress, or on a predetermined schedule. Volume should be recorded to assess the production of air or fluid and to determine when the chest tube can be removed.



(a) (b)

Figure 3.10 (a) Right lateral and (b) dorsoventral radiographs in a dog, showing proper placement of a chest tube for treatment of pyothorax.

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4
Nasal Disorders

Structural Diseases

Stenotic Nares and Brachycephalic Obstructive Airway Syndrome

Pathophysiology

Brachycephalic obstructive airway syndrome (BOAS) is a congenital and heritable disorder (Bannasch et al. 2010) of dogs and cats resulting from primary conformational defects of structures in the upper airway caused by severe shortening of muzzle. Resultant crowding of bony and soft tissue structures within the nose and pharynx as well as stenotic nares cause severe airflow obstruction. Elongation of the palate as well as macroglossia cause further obstruction. Increased velocity of air flow and pressure effects on the soft tissue structures of the larynx result in inflammation that leads to secondary findings of everted laryngeal ventricles, thickening of the soft palate, and, in the final stages, laryngeal collapse. In the Bulldog, tracheal hypoplasia can be encountered as an additional component of BOAS. In some dogs (particularly Pugs) BOAS can be accompanied by caudal protrusion of nasal turbinates into the nasopharynx (Figure 4.1), resulting in further obstruction of nasal air-flow (Ginn et al. 2008). Interestingly, severe brachycephaly is associated with cardiopulmonary and systemic abnormalities, including pulmonary hypertension, gastrointestinal problems, hypercoagulability (Crane et al. 2017), and augmented production of inflammatory mediators (Rancan et al. 2013), indicating that this syndrome is multi-systemic.

History and Signalment

Brachycephalic syndrome is common in Bulldogs (English and French), Pugs, Pekingese, Shih Tzu, and Boston Terriers, and is also

seen in Persian, Himalayan, British Shorthair, and Scottish Fold cats (Figure 4.2). Clinical signs include stertor, snoring or snuffling, gagging, exercise intolerance, respiratory difficulty, and collapse. Some dogs (particularly French and English Bulldogs) have vomiting or regurgitation due to concurrent gastroesophageal disease caused by reflux, inflammation, or hiatal hernia (Poncet et al. 2005; Reeve et al. 2017), and in certain cases gastrointestinal signs are more pronounced than respiratory. Animals can be very young or elderly (6 weeks to 14 years of age) when clinical signs require evaluation and correction.

Physical Examination

In many reports, stenotic nares is the most common abnormality identified, but this likely depends on the breed being evaluated. This finding can be readily visualized on physical examination of the patient and comparison to the breed standard. Audible stertor is due to turbulent airflow through the nasal cavity, past everted laryngeal ventricles, or past an elongated soft palate, and is often evident on inspiration and expiration. If laryngeal collapse is present, inspiratory stridor can sometimes be heard during auscultation over the larynx. Stridor or a high-pitched inspiratory wheeze can also be heard in some dogs with tracheal hypoplasia. The remainder of the physical examination is usually within normal limits, although obesity is relatively common in brachycephalic dogs and worsens the clinical presentation. Conversely, dogs that are severely affected by gastrointestinal manifestations of disease can be very thin.

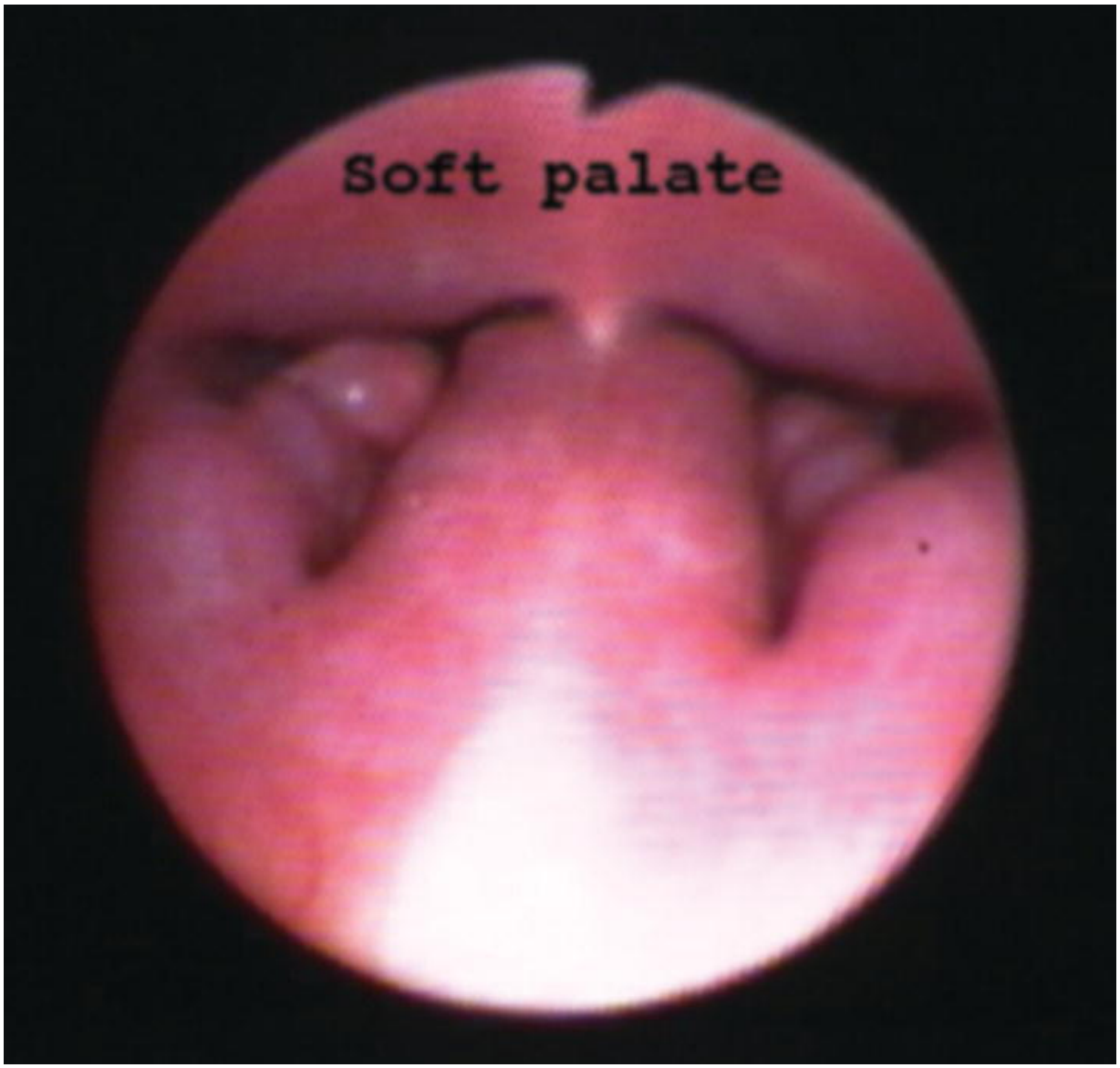


Figure 4.1 Retroflex view of the choanae in a Pug shows hyperemic and swollen turbinates that are bulging into the nasopharynx and contributing to upper airway obstruction.

Diagnostic Findings

Cervical and thoracic radiographs are useful for subjective evaluation of the soft palate, although caution is advised in interpretation because of the difficulty in discerning soft tissue boundaries in the cervical region. In normal dogs, the soft palate should end at the tip of the epiglottis, while in brachycephalic animals, the palate can extend well beyond the epiglottis into the larynx (Figure 4.3). In

some cases, the palate might appear to be of an appropriate length but thickened, however on visual inspection, it is elongated but folded back into the naso- or oropharynx. In other cases, the palate is obviously thickened. Pharyngeal collapse can sometimes be visualized on the cervical radiograph and is often more readily apparent during fluoroscopic examination. Thoracic radiographs are used to assess tracheal height when tracheal hypoplasia is suspected. Two methods have been reported to evaluate tracheal size. One compares tracheal lumen height in the thoracic region to the third rib. A normal dimension is >3.0 (Suter 1984). In the second method, height of the tracheal lumen at the thoracic inlet is compared to the height of the thoracic inlet. The normal ratio in the Bulldog is >0.127; in the non-Bulldog brachycephalic is >0.160; and in the normal dog it is >0.204 (Harvey and Fink 1982). Often, the diagnosis of tracheal hypoplasia is made based on subjective evaluation rather than precise measurements.



Figure 4.2 Stenotic nares in a brachycephalic cat.

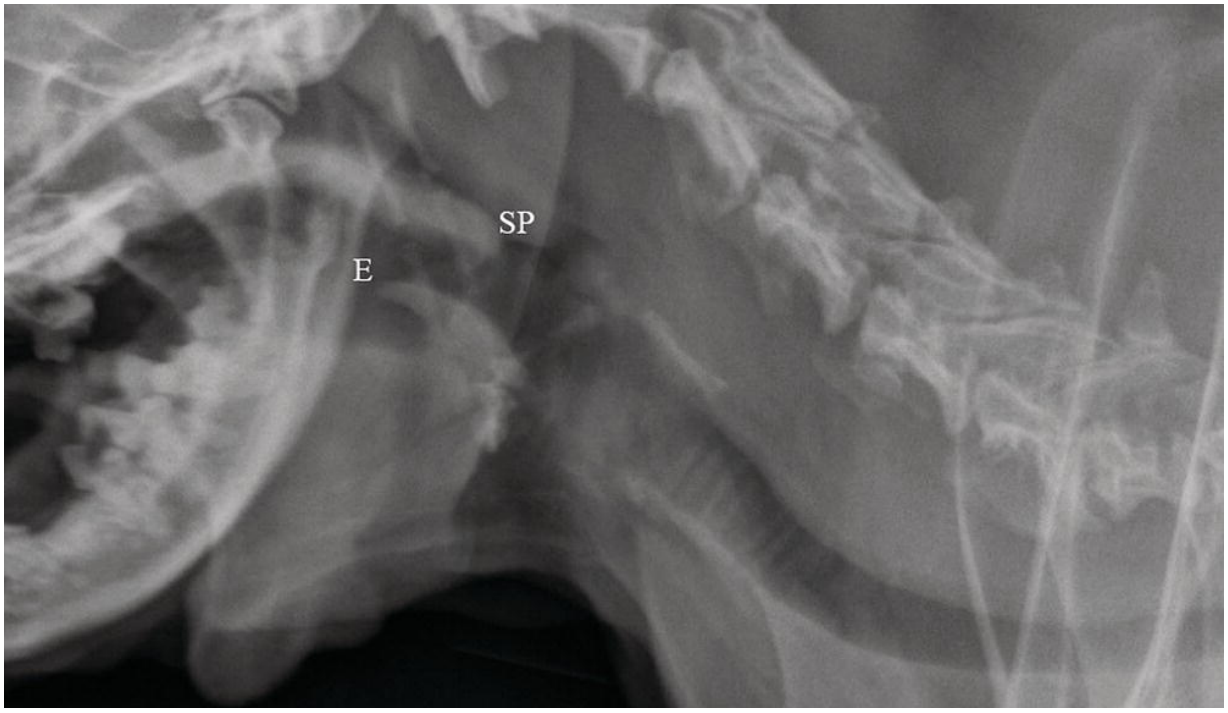


Figure 4.3 Position of the soft palate in a brachycephalic dog. E represents the cranial tip of the epiglottis and the caudal extent of the soft palate is indicated by SP.

Documentation of soft palate elongation and assessment of laryngeal structures require sedation for direct visualization and, because of anesthetic concerns with brachycephalic breeds, surgical correction should be planned at the time the diagnosis is confirmed. Normally, the soft palate should extend only a few millimeters caudal to the tip of the epiglottis or the caudal edge of the tonsillar crypt. Eversion of laryngeal ventricles can be visualized as rounded and bulging soft tissue structures emerging from the ventral portion of the laryngeal aditus, just lateral to the vocal folds (Figure 4.4). Laryngeal ventricular eversion is sometimes referred to as grade 1 laryngeal collapse. More severe and clinically important forms of laryngeal collapse can be recognized as medial displacement of the arytenoid cartilages (Figure 4.5). It is unclear whether this condition is related to airflow dynamics and chronic weakening of the laryngeal abductor muscles or to a form of chondromalacia. Laryngeal collapse must be distinguished from laryngeal paralysis, a disorder in which arytenoid cartilages do not abduct on inspiration but are normally positioned. Laryngeal collapse is designated grade 2 when the cuneiform processes are involved and grade 3 when the corniculate processes are collapsed.

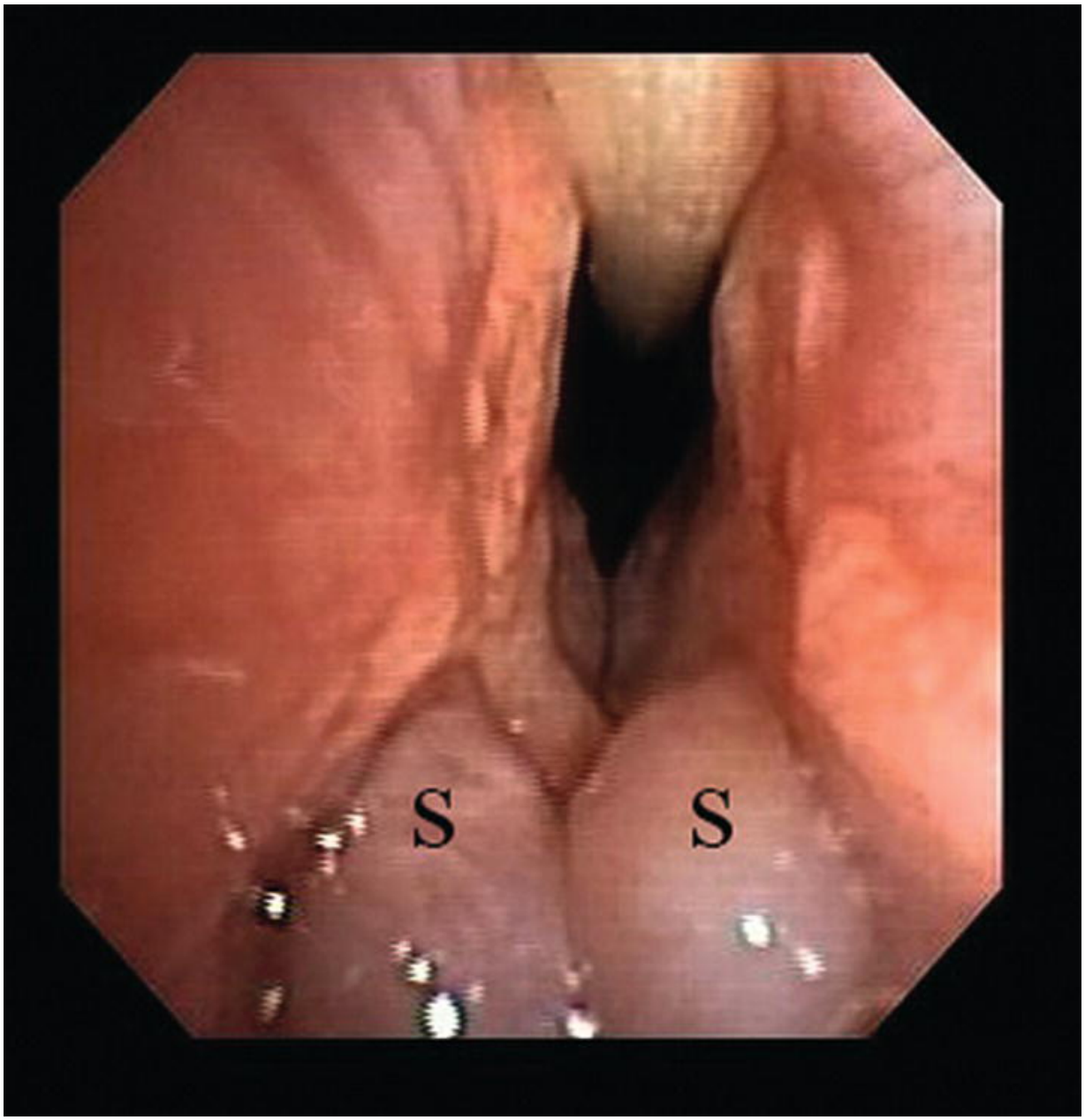


Figure 4.4 Everted laryngeal ventricles (S) are evident at the ventral-most portion of the image.

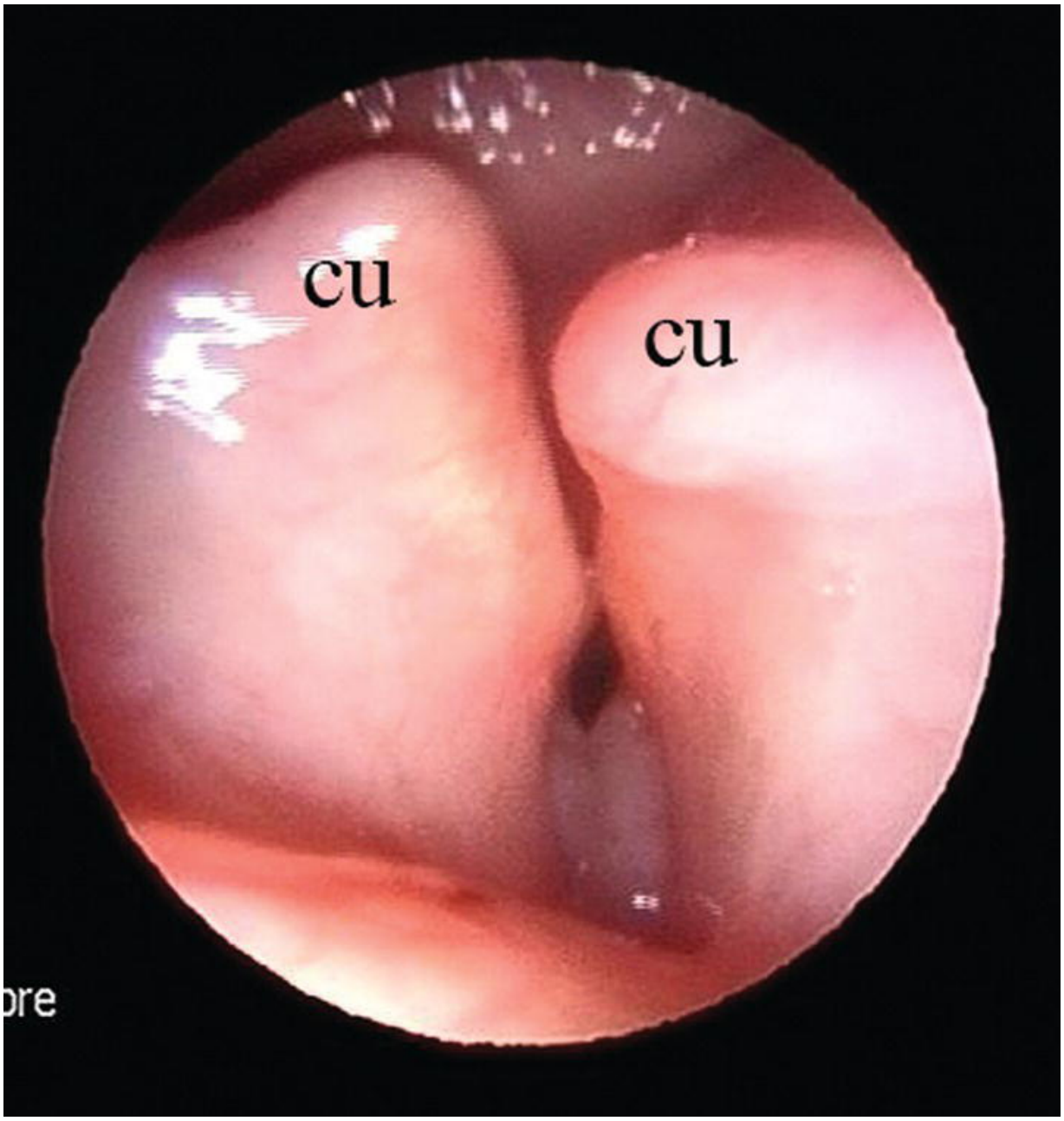


Figure 4.5 Laryngeal collapse in a 2-year-old Norwich Terrier. Cuneiform processes (cu) are displaced medially and almost overlapping.

If a flexible endoscope is available, a retroflex examination of the nasopharynx should be performed to document the presence of nasopharyngeal turbinates, as these can lead to continued obstructed breathing following surgical correction of other lesions.

Treatment

Weight reduction is essential to reduce the work of breathing in animals with brachycephalic syndrome, and when possible this should be achieved prior to surgery to reduce complications associated with anesthesia. Prior to anesthesia, consideration can be given to use of acid suppressants to reduce the severity of aspiration injury to the lung. Anesthetic induction should proceed after adequate pre-oxygenation, and it is helpful to have several different sizes of endotracheal tubes available. It can also be beneficial to have a floppy ended guidewire or a small urinary catheter to pass through the laryngeal aditus to guide the endotracheal tube into place.

Stenotic nares and elongated soft palate are amenable to surgical resection with a scalpel or a carbon dioxide laser via wedge resection and staphylectomy, respectively. Thinning of the palate through folded flap palatoplasty has been recommended by some surgeons, although there is limited consensus on the best approach to management of dogs with various features of BOAS. Excessive shortening of the soft palate is generally not recommended, because this can result in nasal or nasopharyngeal regurgitation, although some surgeons believe it is an appropriate technique that provides enhanced alleviation of airway obstruction.

Ventriculectomy is considered a controversial surgery by some surgeons because edema and eversion of these soft tissue structures are secondary complications related to turbulent air flow. In some cases, ventricular eversion will resolve when airflow has improved; however, in some breeds such as the Norwich Terrier, surgical options other than ventriculectomy are limited. Also, in certain dogs, chronic protrusion of the ventricles results in irreversible hyperplasia that requires resection. Some surgeons elect to perform unilateral removal of a ventricle rather than removing both in order to avoid mucosal apposition during the healing phase that could result in laryngeal stenosis or webbing. Others will remove ventricles bilaterally as standard of care, while some surgeons place a temporary tracheostomy tube following ventriculectomy in the event that post-operative swelling in the upper airway results in airway obstruction.

Currently, no specific treatment is available for laryngeal collapse, and the success of unilateral lateralization is questionable. For dogs with severe stridor or respiratory distress, a permanent tracheostomy should be considered when weight loss and surgical correction of other lesions fail to alleviate respiratory difficulty.

More aggressive therapy for brachycephalic syndrome includes laser resection of internal nasal turbinates, although this requires advanced training and is performed at few institutions (Oechtering et al. 2016). It could be considered in dogs that fail to improve following routine surgical procedures.

Finally, the age at which this surgery should optimally be performed is unknown. With increasing age, the risk of secondary complications increases, including the need for a temporary tracheostomy post-operatively (Worth et al. 2018). Older dogs also seem to be more prone to perioperative swelling, and then have more difficulty restoring normal eating behavior post-operatively. It would seem wise to correct conformational disorders early in life (~6–9 months) to prevent development of secondary obstructive disease; however, it is also important for facial and skeletal structures to have matured to a certain extent.

In the immediate post-operative period, careful monitoring is advised to detect soft tissue swelling that can lead to obstruction or aspiration events that could lead to pneumonia or acute respiratory distress syndrome. Animals should be maintained in a cool, calm environment, and one study from the United Kingdom reflected less complications from surgery when owners were present at recovery to keep the dogs calm (Camarasa et al. 2023), although this likely depends on the temperament of the dog as well as the owner. During the first 24 hours, hand feeding of soft meatballs of food can be considered to avoid disruption of the palatal surgery site. Gradual return to normal feeding can be used.

Prognosis

Surgical resection of upper airway obstruction is associated with an excellent outcome in the vast majority of dogs, although outcome in cats is less clear. Cats do display improved activity levels and reduced breathing noises were reported after ala vestibuloplasty (Gleason et

al. 2023). Perioperative mortality in dogs and cats is low and post-operative complications are generally mild, unless upper airway obstruction necessitates temporary tracheostomy, yet this condition is readily managed with additional hospitalization and nursing care. Pigmentation changes around the surgical site of nares resection gradually resolve. Ventricular remnants can undergo hyperplasia or hypertrophy and cause obstruction that necessitates additional surgery. Dehiscence of the palatal repair is the most serious event encountered but occurs rarely. Animals that have concurrent gastroesophageal signs often have resolution or abolition of gastrointestinal signs following surgery (Poncet et al. 2006), although some dogs can require continual use of prokinetic and acid reducing drugs, and some require hiatal hernia repair.

Nasal Foreign Body

History and Signalment

Foreign material can be aspirated directly into the nasal cavity through the nares or can lodge in the nasopharynx when the animal retches material from the oral cavity into the area above the palate. Animals with a nasal foreign body usually present with an acute onset of paroxysmal sneezing or reverse sneezing, nasal discharge, epistaxis, and pawing or rubbing at the face, although chronic signs can also be seen. Dogs can become subclinical despite the continued presence of nasal foreign material, which makes diagnosis and management challenging. The decision to move forward with evaluation of the nasal cavity relies on clinical suspicion of disease (Figure 4.6). Foreign bodies that are firmly lodged in the nasal cavity or in the nasopharynx can also result in chronic nasal discharge or halitosis.



Figure 4.6 Rhinoscopic view of the left nasal cavity of a dog that had acute onset of sneezing after running in the fields. Clinical signs were absent at the time of rhinoscopy; however two foxtails (grass awns) are visible in the ventral portion of the image.

Physical Examination

Affected animals usually display unilateral mucopurulent or serosanguineous nasal discharge, and nasal airflow is typically preserved unless a large or round foreign body obstructs the choana.

If a foreign body obstructs the nasopharynx, bilateral signs can be seen along with loss of nasal airflow. In chronic cases, or if secondary nasal aspergillosis results, regional lymph node enlargement can be found.

Diagnosis and Treatment

Animals must be fully anesthetized for a comprehensive evaluation of the nasal cavity. Imaging is usually recommended prior to examination of the nasal cavity to help guide removal of a radiodense foreign body; however, organic objects are usually not visible radiographically or on computed tomography (CT). In more chronic cases, secondary changes of increased fluid density or bony lysis on radiographs or CT can help locate the site of the foreign material.

Whenever possible, the caudal nasopharynx should be examined for a foreign body, as well as both nasal cavities. If a flexible endoscope is not available, copious antegrade and retrograde flush of the nasal cavity can dislodge a foreign body (see Chapter 2). If the nasal cavity cannot be fully visualized with available equipment, gentle probing with alligator forceps can be successful in retrieving a foreign body. In rare instances an exploratory rhinotomy could be required. This is most likely when a large, smooth foreign body (such as a stone) cannot be removed endoscopically or if a tooth root has migrated into the nasal cavity. After foreign body retrieval, a broad-spectrum antibiotic (e.g., amoxicillin-clavulanate) is sometimes administered for 7 days to treat secondary infection.

Prognosis

In some cases, a foreign body can cause permanent damage to the nasal structures that allows the development of secondary fungal rhinitis or results in chronic nasal discharge associated with turbinate destruction and alterations in mucus production. In these cases, continued production of mucus can be encountered, and antibiotic therapy may be needed for control of clinical signs.

Tooth Root Abscess or Oronasal Fistula

History and Signalment

Dental-related nasal disease usually arises near canine teeth or premolars in older animals and results in unilateral mucopurulent to hemorrhagic nasal discharge. The animal might also display difficulty or pain while eating or opening the mouth. Anorexia, drooling, and halitosis can be reported. A palatal defect can result in an oronasal fistula (Figure 4.7) and can be congenital or acquired. Water or liquid meals can be seen exiting the nasal cavity in some cases, but typically food and foreign material will become impacted in the nasal region via the oral route. Both abscesses and fistulae result in antibiotic-responsive clinical signs that recur when medications are discontinued.



Figure 4.7 An adult cat evaluated for chronic nasal discharge was placed under anesthesia for evaluation. With the cat in dorsal recumbency, a defect in the hard palate could be visualized.

Physical Examination

Unilateral nasal discharge should raise dental-related nasal disease higher on the differential diagnosis list, particularly in older dolichocephalic dogs with obvious periodontal disease. However, it is important to note that dental disease or gingivitis may not be obvious during examination, and a palatal defect or oronasal fistula can be particularly challenging to document in the awake animal prior to advanced imaging, dental probing, and close scrutiny of the palate. Nasal airflow is typically preserved in animals with dental-related nasal disease. Oral or facial pain or swelling and regional lymphadenopathy can be found in some cases. With a carnassial tooth abscess, an expanding facial swelling will sometimes develop immediately below the eye on the affected side (Figure 4.8). The swelling might decrease during antibiotic therapy and then return.

Diagnostic Findings

Skull or dental radiographs targeting the affected area can reveal bony loss surrounding a tooth root or a retained tooth root. In cases with chronic dental disease, destruction of nasal turbinates can be seen on radiographs, CT, or rhinoscopy. Use of a periodontal probe to detect deep periodontal pockets (>1 mm in the cat and >1–3 mm in the dog) can identify occult tooth root disease. This should be performed with the animal in dorsal recumbency and after advanced imaging and rhinoscopy, because of the potential for dental probing to cause bleeding, which would affect imaging results and visual inspection.



Figure 4.8 An adult DMH cat has obvious facial swelling on the left side of the maxilla associated with a tooth root abscess.

Treatment

Effective treatment requires removal of the tooth and all roots, and in some instances bony curettage can be needed. In some instances, rhinoscopy can be used to remove an impacted tooth but sometimes the tooth is walled off by cystic structures, or it is beneath the mucosa, and not accessible to rhinoscopic equipment. Surgical debridement and closure of a fistula can sometimes require referral to a dental surgeon, particularly if a large lesion necessitates use of bone graft. A 7–10-day course of antibiotics (with a potentiated penicillin or clindamycin) is often used to treat secondary infection.

Prognosis

Generally dental-related nasal discharge will resolve with tooth removal, management of periodontal disease, or closure of a fistula; however, as with a foreign body, alterations in turbinate structures can result in continued mucus production.

Nasopharyngeal Stenosis

Pathophysiology

The opening to the caudal nasopharynx in dogs and cats is normally 1–2 cm across and can be greatly reduced or obliterated by a web of scar tissue, resulting in obstructed airflow, abnormal breathing sounds, or chronic nasal discharge as well as esophageal dilatation with difficulty swallowing. Nasopharyngeal stenosis (NPS) is thought to occur either as a congenital lesion in which the caudal opening of the choanae is malformed, or as an acquired lesion resulting from chronic inflammation in the caudal aspect of the nasal cavity that forms a cicatrix. Inflammation can result from chronic upper respiratory tract disease or from regurgitation of esophageal or gastric contents into the nasopharynx. Post-anesthetic regurgitation is a common cause of the syndrome in the dog. The scar can be unilateral or extend across the entire choanae (Figure 4.9).

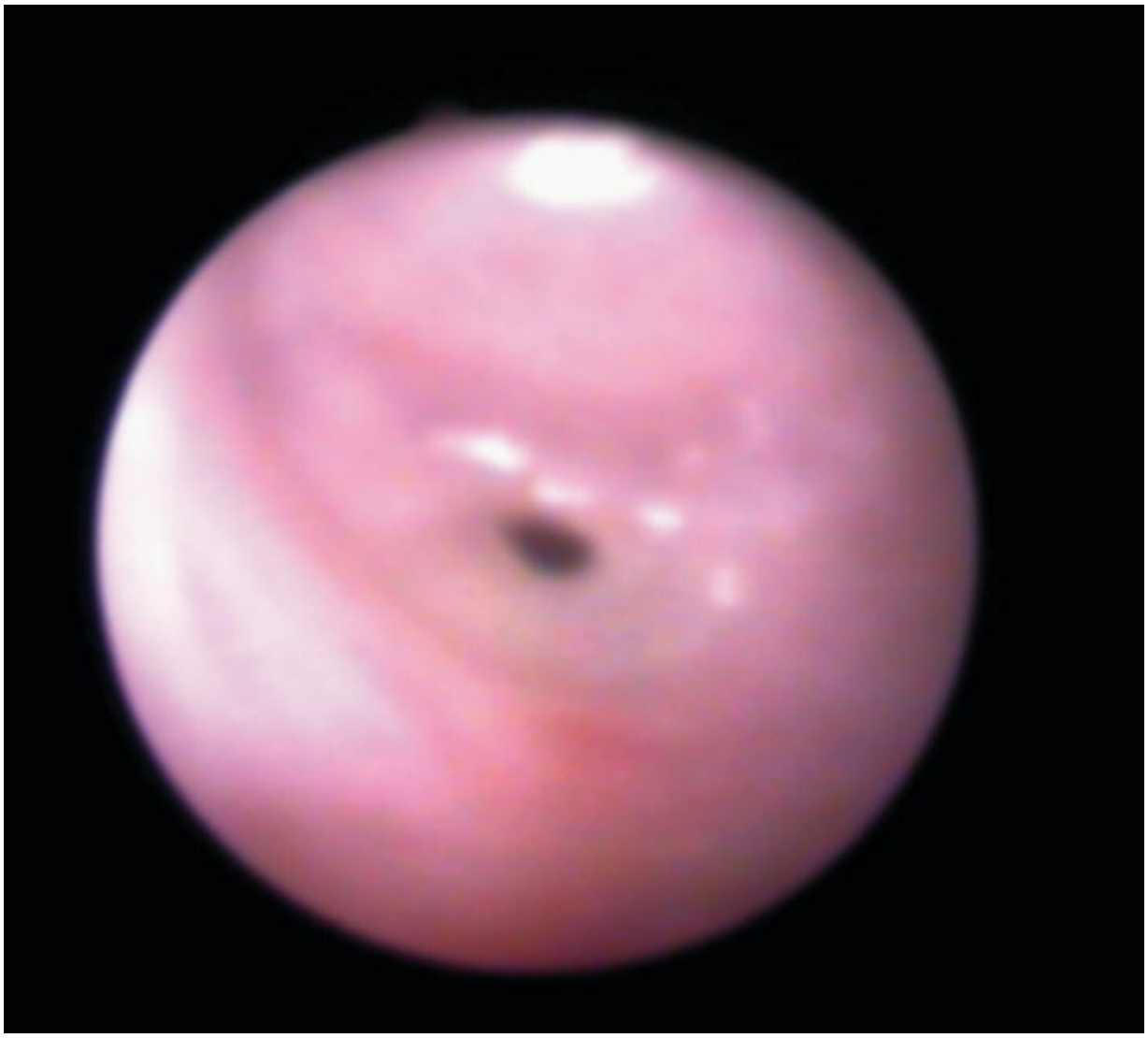


Figure 4.9 Retroflex view of the choanae in a 17-year-old spayed female domestic short hair (FS DSH) presented for an 8-year history of difficulty breathing. In this case, stenosis of the nasopharynx reduced the diameter of the choanae to less than a millimeter. Compare to the normal opening into the choanae in Figure 2.10.

History and Signalment

The predominant clinical feature of NPS is obstruction of airflow through the nasal cavity. Loud, noisy respiration is commonly reported. In some cases, this condition is preceded or accompanied by nasal discharge. When the deformation or scar is bilateral or circumferential, the animal will display open mouth breathing because of an inability to breathe through the nose. This can be

challenging to detect in a cat because of their propensity to hide any affliction from potential predators. NPS is usually non-progressive and not associated with systemic disease, although inappetence has been reported in some cats as well as difficulty swallowing.

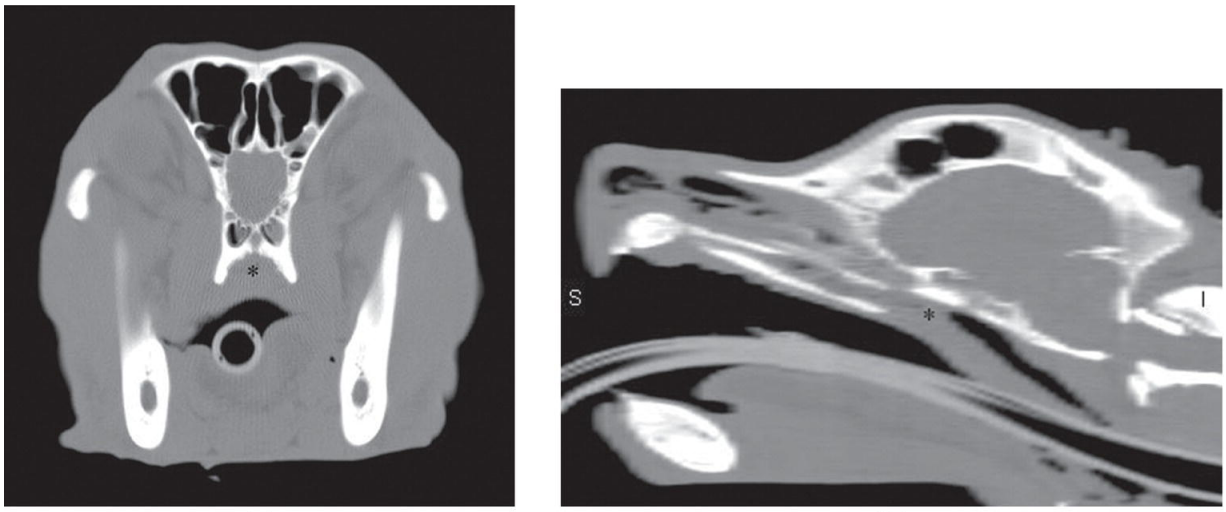
Physical Examination

The primary recognizable examination feature is a loud upper respiratory noise that can be stertorous or stridorous. Animals that have unilateral stricture or stenosis are often subclinical and anatomic narrowing is detected on imaging or endoscopy performed for other reasons. When present, respiratory difficulty is detected on inspiration and there is reduced nasal air flow, depending on the extent of stenosis. With a complete stricture, respiratory distress occurs when the mouth is closed and nasal breathing is required.

Diagnostic Findings

Primary differential diagnoses include nasal obstruction due to neoplasia, a nasopharyngeal polyp, cryptococcosis (in the cat or dog), or aspergillosis (in the cat). NPS can be seen on CT as a soft tissue density in the nasopharyngeal region (Figure 4.10a). The obstruction can occur anywhere within the nasopharynx or caudal nasal cavity. In cats, it is most commonly encountered toward the caudal-most aspect of the soft palate and it is usually a relatively thin band of tissue. In the dog, the obstruction tends to be more firm or fibrous and encompasses a longer segment of the nasal cavity or nasopharynx. NPS is most easily visualized when an open mouth CT is performed or with sagittal reconstruction of the image (Figure 4.10b). Administration of contrast material can help differentiate mucus from tissue, although endoscopy can also define the type of obstruction present.

NPS is typically easily diagnosed using a flexible endoscope to obtain a view of the nasopharynx. Alternately, the obstruction can be appreciated by attempting to pass a 3–8 French catheter caudally through each of the ventral nasal meati into the oropharyngeal region (see Figure 3.3). In the normal animal, the catheter should pass easily into the pharynx; however, a stenosed region will block passage of the catheter.



(a) (b)

Figure 4.10 Computed tomography images from a young dog with nasopharyngeal stenosis (*) in standard view (a) and in sagittal reconstruction (b).

Treatment

Treatment of this obstructive breathing disorder is best achieved by balloon dilation of the region, using fluoroscopic or endoscopic visualization. The procedure seems to be more successful in cats, which have a thin tissue stricture, in comparison to dogs, where a long fibrous band can obstruct the caudal nasal column. First, a wire is passed antegrade or retrograde to span the nasal cavity between the rostral opening and the nasopharynx. In dogs, a needle or catheter passed under fluoroscopy might be required to breach the fibrous tissue. Vascular dilators can then be employed to open up the region, or cutting balloons (expandable balloons that project small cutting blades after inflation of the balloon) can be inserted to release the scar tissue. Subsequently, esophageal balloons (from 7 to 15 mm in outer diameter) are passed over the wire to span the stenosed region and these are inflated several times. Post-dilation, oral glucocorticoids are often employed in an attempt to keep the region from scarring over. Cats usually respond to a single intervention, but several episodes can be required to open the stenosis permanently, especially in dogs. When balloon dilation is unsuccessful, stent placement could be considered. Both permanent (nitinol) and temporary (red rubber or peel-away catheters) have

proven successful in alleviating the obstruction, although each type is susceptible to removal or obstruction, and complications of the procedure should be anticipated (Burdick et al. 2018).

Prognosis and Prevention

NPS represents a benign lesion; however, some owners report loss of appetite or lethargy related to nasal obstruction. In cats with concurrent rhinitis, it would seem likely that stenosis would impact clinical response to therapy.

If an animal is observed to regurgitate material out the nose after anesthesia, it would seem prudent to re-anesthetize and intubate the patient, to pack the back of the throat with a moistened surgical laparotomy pad, and to perform copious nasal flush. Removal or dilution of gastric juices containing acid and other inflammatory products could lessen the development of NPS.

Infectious Diseases

Acute Feline Upper Respiratory Tract Disease

Pathophysiology

The organisms most commonly implicated in upper respiratory infection (URI) in kittens include feline herpesvirus 1 (FHV-1), feline calicivirus (FCV), *Chlamydia felis*, *Mycoplasma*, *Bordetella*, and *Streptococcus* (*canis* and *equi* var. *zooepidemicus*). Other currently unrecognized viruses could also be involved. Infection occurs via inhalation or via contact of mucosal membranes of the nose or ocular surface with viral particles. Viral infection of the epithelial cells results in cell death and predisposes the respiratory tract to bacterial infection. However, some of the bacteria involved can also act as primary respiratory pathogens, and infection with bacteria alone can result in substantial clinical disease. Pathogenic streptococcal organisms have been implicated in severe rhinitis and bronchopneumonia syndromes in cats from high-intensity environments where multiple species are housed, suggesting a potential role for cross-species contamination and fomites in spread

of disease (Frymus et al. 2015). Importantly, *C. felis* results in systemic infection, although clinical signs are typically manifest in the conjunctiva alone.

Upper respiratory viral infection is usually self-limiting, with resolution of disease within 7–10 days. Viral shedding occurs within 1–3 days of infection and persists for up to 3 weeks, providing a constant source of virus in the environment. Both FHV-1 and FCV persist in the cat population in a carrier state, and viral shedding can be reactivated during stressful periods. Thus, carriers and intermittent shedders of these viruses serve as an important reservoir for continual infection in cat populations. A virulent form of FCV has been associated with outbreaks of ulcerative lesions around the face, facial and forelimb edema, and fatal pneumonia, with mortality rates of ~40% (Hurley et al. 2004) although this has not been reported recently.

History and Signalment

Young kittens (2 weeks to 4 months old) are affected most commonly, although older kittens and cats can develop signs of acute URI when exposed to high concentrations of pathogens in a shelter environment, when particularly virulent organisms are encountered, or when stress results in reactivation of viral replication. Older cats are more severely affected by the virulent form of FCV, and any age of cat can develop *Chlamydia* conjunctivitis.

Physical Examination

Sneezing and serous to mucoid oculonasal discharge are the classic findings in acute feline URI. Fever and systemic signs of illness (lethargy and anorexia) are commonly seen in young kittens as well as in some older animals suffering exacerbations of disease. FHV-1 has a predilection for ocular infection, and conjunctival hyperemia and corneal disease are common. Tracheitis and pneumonia are also reported secondary to FHV-1 infection, but these are less commonly recognized clinically than URI. FCV can cause lingual ulcers and also can result in pneumonia occasionally; co-infection in cats with FHV-1 results in worsened disease. *Chlamydia* is most likely to cause severe chemosis, which can be unilateral or bilateral.

Diagnostic Findings

In general, feline URI is a clinical diagnosis in the individual cat presented to the veterinarian, although various laboratory tests are available that can detect the organisms currently implicated in the disease syndrome. FHV-1 can be identified through culture or polymerase chain reaction (PCR); however, the presence of virus does not correlate with disease (Maggs et al. 1999). Quantitative PCR for FHV-1 is still being evaluated to determine whether a high number of viral particles can be associated with clinical disease. The presence of FCV can be confirmed through virus isolation or reverse transcriptase PCR for the RNA virus, although positive tests are expected in chronic shedders, making it difficult to correlate the test result with disease state. The virulent form of FCV is diagnosed based on clinical signs and physical examination. Bacteria can be identified by standard culture and susceptibility testing, but sampling of nasal secretions is not advised because of the likelihood that commensal organisms will be isolated. When indicated based on a history of chronic antibiotic usage, a deep nasal sample can be collected under anesthesia for culture (see Chapter 2).

During disease outbreaks in high-density environments, diagnostic tests including virus isolation, bacterial culture, and PCR of combined nasal, oropharyngeal, and conjunctival swabs should be considered, particularly when high morbidity or mortality occurs. Combined culture and PCR techniques have demonstrated the commonality of co-infections in cats with URI (Litster et al. 2015). Caution is warranted in the interpretation of results, because positive results will be obtained when normal flora are detected and because of interference by viral vaccination. Multiple animals should be sampled to identify potential infecting organisms and to institute appropriate control measures. In a shelter study, shedding of FHV-1 was shown to increase from 4 to 52% after cats had been housed for 1 week (Pedersen et al. 2004), highlighting the role of stress and intermingling of animals on viral shedding.

Treatment

In high-density situations, separation of affected from non-affected animals is critical for limiting the spread of disease. Both

environmental and staff activities should be modified to ensure decreased spread through fomites. Larger housing spaces are important, along with use of areas where cats can hide and portals in cages through which animals can escape scrutiny. Pheromone sprays and misters have been suggested to reduce stress and hence viral shedding; however, variable results have been reported. For the individual cat or kitten, supportive care should be instituted to aid in resolution of signs related to viral infection. The eyes and nose should be kept clear of exudate, hydration and adequate nutrition should be ensured, and animals should be kept in a warm environment. Steam inhalation to humidify inhaled air and use of lubricating eye ointment to manage virally-mediated keratoconjunctivitis sicca (KCS) can also improve overall health.

If clinical signs extend beyond 10 days or are worsening in association with fever or anorexia, systemic antibiotic therapy should be considered to manage primary or secondary bacterial infection. Various antibiotics including amoxicillin, amoxicillin-clavulanate, and pradofloxacin have demonstrated efficacy in control of clinical signs of URI, although the current recommendation is to employ doxycycline for 7–10 days for initial therapy (see Chapter 3). Treatment of *Chlamydia* requires 4–6 weeks of treatment with doxycycline at 10 mg/kg/day, and it is essential that all in-contact cats receive adequate treatment.

Lysine has been recommended to reduce FHV-1 replication and decrease clinical signs associated with FHV-1 infection. However, dietary supplementation did not prove efficacious in a natural disease setting (Maggs et al. 2007) and bolus administration of 250–500 mg orally twice a day (PO BID) is required to reduce viral replication. Directed therapy against FHV-1 can be achieved using famciclovir, and trial therapy can be considered in seriously ill cats or kittens, despite the inability to confirm that the disease is caused by FHV-1. Famciclovir is a nucleoside analog that is metabolized to penciclovir and reliably reduces replication of FHV-1 through inhibition of DNA polymerase. The currently recommended dosage is 90 mg/kg PO BID (Sebbag et al. 2016), although a dose of 40 mg/kg PO three times a day (TID) resulted in improvement of oculorespiratory signs in naturally affected cats (Thomasy et al.

2016). In a placebo controlled study evaluating the effects of doxycycline and famciclovir on signs of URI in privately housed kittens, there was no significant difference between cats treated with doxycycline plus famciclovir versus those treated with doxycycline plus placebo, although detection of viral DNA was low in that study (Kopecny et al. 2020). Thus, the use of antivirals in acute feline URI requires further study.

A novel antiviral therapy for FCV that blocks virus synthesis by molecular interference with the initiation of translation was shown to reduce the severity of oral ulcers and reduce FCV shedding in an outbreak situation (Smith et al. 2008), although clinical studies are lacking. Parenteral interferon or intranasal vaccination showed promise in reducing clinical signs in cats with URI lasting 3–4 weeks (Fenimore et al. 2016), although no further studies have been performed.

Prognosis

Most kittens survive acute URI and it is unclear whether severe or poorly managed infection at an early age plays a role in development of chronic rhinosinusitis (CRS). When upper respiratory disease is observed in a shelter or cattery situation, implementation of control measures with improved hygiene and environmental modification is needed. Aerosolization is the prime method of infection, and isolation of sneezing or coughing cats can help limit spread. However, fomites can also spread disease, and general infection control should be stressed. FHV-1 is labile in the environment and is readily killed by bleach or detergent, but FCV can persist for up to 1 month and is more resistant to standard cleaning methods.

Prevention

Vaccination against upper respiratory viruses (FHV-1 and FCV) reduces clinical signs and can help limit spread of disease but does not prevent infection. The 2024 World Small Animal Veterinary Association vaccination guidelines advise core vaccinations against FHV-1, feline panleukopenia, and FCV to kittens every 2–4 weeks from after 6 weeks to 16–18 weeks of age with a booster

administered at 6 months of age. Additional parenteral booster vaccinations are done every 3 years.

Cryptococcosis

Pathophysiology

Cryptococcosis is an invasive fungus that exists in the yeast form in the animal. Various species enjoy a specific geographic distribution. *Cryptococcus neoformans* is found in bird guano worldwide, while *Cryptococcus gattii* is typically localized to wood, such as eucalyptus trees in Australia and numerous fir trees in Vancouver, Canada. Disease is thought to be spread primarily through inhalation, with initial infection in the nasal cavity and subsequent spread to the nasopharynx or central nervous system, although direct inoculation causing skin infection might also occur. Systemic disease (pneumonia or abdominal involvement) is more common in the dog than in the cat.

History and Signalment

Cryptococcal infection has been reported in all ages of animals, although young adult, immunocompetent animals appear to be affected most often. Disease is reported much more commonly in cats than in dogs, with Siamese, Birman, and Abyssinian cats over-represented in some studies. American Cocker Spaniels appear to develop cryptococcosis more commonly than other dog breeds (Trivedi et al. 2011). *C. gattii* is the more common pathogen in cats, while *C. neoformans* affects dogs more often. Respiratory complaints include facial distortion (particularly a Roman nose appearance), sneezing, chronic mucopurulent nasal discharge, and stertor. Lower respiratory infection occurs much less commonly, but signs of pneumonia can be present. Non-respiratory complaints include non-healing craterous skin lesions, blindness due to retinal detachment or optic neuritis, and central nervous system signs such as circling, seizures, ataxia, or vestibular disease. Disease appears to be disseminated into parenchymal organs more commonly in dogs than in cats, with neurologic signs identified more often in dogs than in cats.

Physical Examination

The classic finding for nasal cryptococcosis in the cat is a firm swelling along the dorsum of the nose. It can be central or unilateral, at the bridge of the nose or on the tip (Figure 4.11a). In some cases a mass can be seen protruding from the nose (Figure 4.11b), while other cases might develop a nasal or nasopharyngeal granuloma, identifiable by a deviation of the palate into the oral cavity and a palpable mass effect, similar to a nasopharyngeal polyp. Regional lymphadenopathy is not uncommon. In cases with lower respiratory tract disease, tachypnea can be noted and abnormal lung sounds detected because of lobar consolidation. In some animals, particularly cats, ulcerated and craterous skin lesions are evident. Every animal suspected of cryptococcosis should have a thorough fundic examination to detect chorioretinitis. This inflammatory condition of the choroid and retina can appear as a hyporeflective, round to geographic, white to gray, sometimes raised fluffy lesion when active, or as a dark circular region on the retina when the lesion has scarred or healed.



(a) (b)

Figure 4.11 (a) The dorsal portion of the nose is distorted by a mass lesion in the nasal cavity diagnosed as a cryptococcal granuloma. (b) The fleshy soft tissue mass protruding from the left naris was diagnosed as a cryptococcal granuloma.

Diagnostic Findings

Diagnosis involves identification of a fungal organism (5–8 μm in size) encircled by a clear polysaccharide coat (~30 μm in diameter) in cytology of exudate, aspirates, impression smears, or a squash preparation of a biopsy specimen (Figure 4.12). Wright's stain, Diff-Quik™, or iodine stain can be used. Because the fungal organism is so characteristic, cytologic examination of nasal smears from all cats with chronic nasal discharge is warranted for quick differentiation of a fungal infection from other causes of nasal discharge, although non-encapsulated forms of *Cryptococcus* will not be readily identified using this method. Serology (latex capsular agglutination titer: LCAT or cryptococcal antigen latex agglutination serology: CALAS) is a sensitive and specific method for confirming the diagnosis through detecting cryptococcal antigen in serum. A point-of-care test (cryptococcal lateral antigen flow assay: CrAG LFA; IMMY, Norman, OK) has been validated for use and has high sensitivity and specificity for diagnosis of *Cryptococcus*. When positive, a quantitative titer should still be obtained, because the magnitude of the titer can be serially assessed to determine response to therapy.

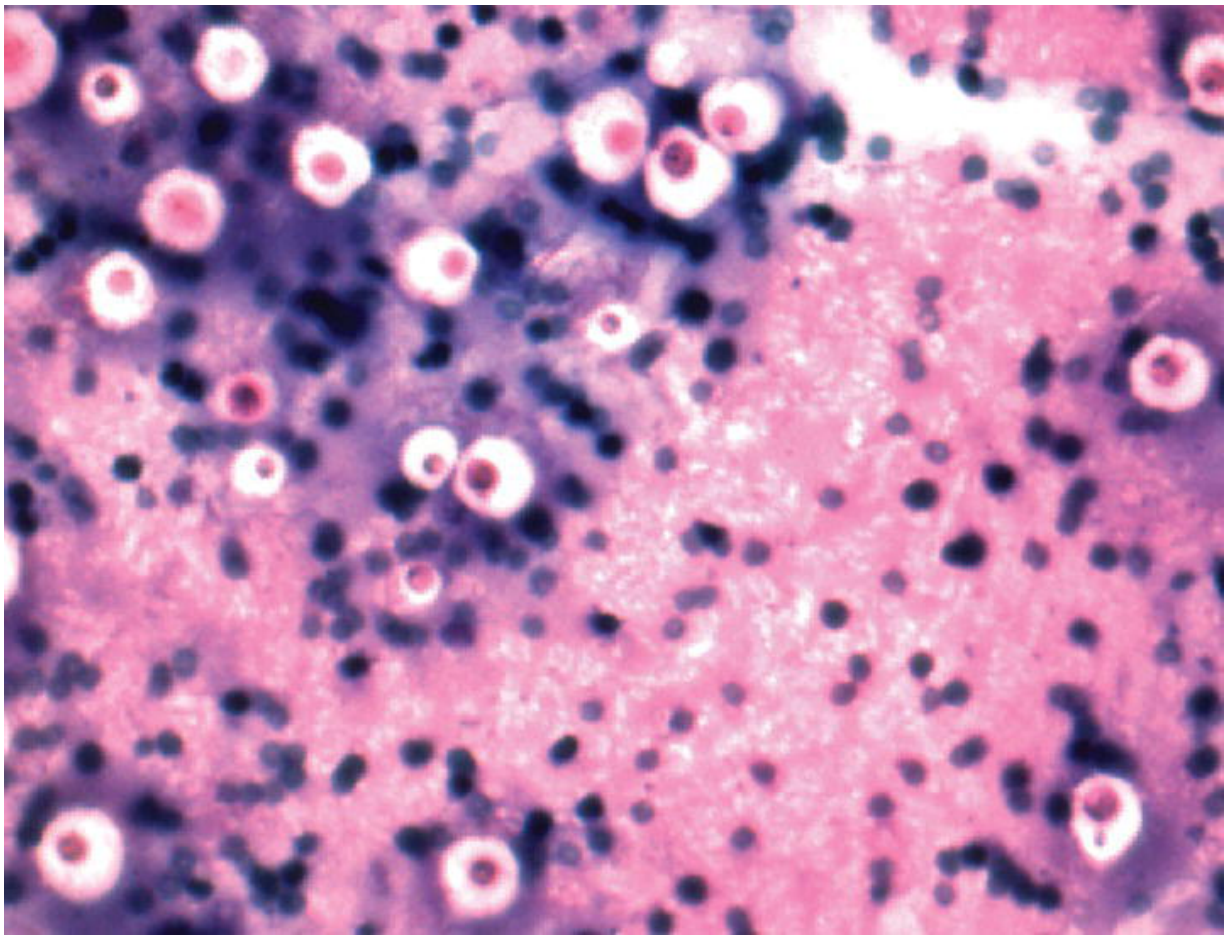


Figure 4.12 Cytology of an impression smear from a nasal mass in a cat. Wright's stain has been applied and reveals multiple 3–8 μm round organisms surrounded by a clear capsule ranging in size from 10 to 30 μm. Fungal culture was positive for *Cryptococcus gattii*.

Culture of a nasal swab or biopsy is used to identify the infecting species and perform susceptibility testing. Typically this is performed when an animal fails to respond to initial drug therapy, but testing can be important in both choosing and assessing drug therapy. *C. gattii* isolates display a wider range of susceptibilities in comparison to isolates of *C. neoformans*, and regional susceptibility to antifungal agents has been identified (Singer et al. 2014). Fungal susceptibility testing is typically performed by a microdilution method and an established laboratory should be used to ensure accurate results. Culture of nasal discharge alone should not be used to diagnose cryptococcal infection, because it can occasionally be

positive in the absence of clinical disease due to colonization of the nasal cavity without infection.

Depending on the clinical presentation and physical examination findings, thoracic radiographs or abdominal ultrasound should be performed to stage disease, particularly in dogs. A complete blood count, chemistry profile, and urinalysis are performed to assess the general health of the animal, and retroviral testing should be performed in the cat. Concurrent immunosuppressive disease due to feline leukemia virus may be associated with a worse prognosis for cure or control of disease, and feline immunodeficiency virus infected cats may require longer treatment.

Treatment

Cryptococcosis is typically treated with oral azole therapy, and prolonged therapy (4–12 months) should be anticipated (see Chapter 3). Cryptococcal serology is repeated every 2 months during therapy to detect a reduction in titer, indicating successful control of disease. It is important to send serum samples to the same laboratory for analysis, because the methodology and conditions within the lab can impact the values determined. Treatment is continued until the titer is negative. If the titer fails to decline, a different azole should be administered or susceptibility testing performed. Alternately, terbinafine, a synthetic allylamine, can be added to therapy in cats that do not respond appropriately to azole therapy alone or those that develop side effects while treated with azoles.

Itraconazole, fluconazole, or posaconazole is likely to be efficacious in controlling disease in the majority of cases (Singer et al. 2014). Duration of treatment required was significantly shorter with fluconazole than with itraconazole in one study (4 versus 9 months; O'Brien et al. 2006). Fluconazole is preferred if ocular involvement is documented, because of better penetration of the blood–ocular barrier. If central nervous system involvement is suspected or confirmed based on physical examination, clinical signs, brain imaging, or cerebrospinal fluid tap, fluconazole is used in combination with flucytosine because of improved efficacy in penetrating the blood–brain barrier. The utility of posaconazole has

not yet been evaluated in such situations, but it is also likely to be efficacious.

Fungicidal treatment is needed in cases with severe cryptococcosis, and amphotericin B has proven effective in inducing remission (details in Chapter 3). Subcutaneous administration of amphotericin B can be considered in animals that cannot be hospitalized or cannot be medicated orally. Nephrotoxicity is limited with this mode of administration, although cure of cryptococcosis can require a cumulative dose over 20 mg/kg.

Prognosis

In general, cats with cryptococcal infection are more responsive to therapy than dogs. Cats with intranasal cryptococcosis have a slightly lower percentage of resolution of disease than those with cutaneous signs only, and central nervous system infection is the least responsive form of disease. Cats that fail to show a reduction in antigen titer over several months are less likely to achieve resolution of disease and could be resistant to the antifungal drug in use. In these cases, culture and susceptibility testing should be considered. Recurrence of cryptococcosis can occur months to years after apparent cure, and a relapse rate of 17% has been reported (O'Brien et al. 2006).

Canine Nasal Aspergillosis

Pathophysiology

Aspergillus is a branching septate mold that is ubiquitous in the environment. Climactic changes affecting temperature and gusting wind patterns, alterations in soil properties, and increasing areas with decaying vegetation or excavation impact the number of spores present at any given site. Nasal aspergillosis can result from infection with several different *Aspergillus* species, although infection with *Aspergillus fumigatus* is most common. Nasal aspergillosis appears to occur most often as a primary infection in healthy dogs, but the fungus can also colonize the nasal cavity and/or frontal sinuses following trauma, inhalation of a foreign body, or rarely in conjunction with a neoplastic process. *Aspergillus* results in mucosal

infection of the nasal cavity and/or sinuses, with the formation of fungal granulomas or plaque lesions surrounded by a biofilm, which allows continued growth and perpetuation of infection as it induces local immunosuppression (Valdes et al. 2020). Toxins produced by the fungus and the local inflammatory response are likely responsible for the severe destruction and collapse of turbinates that occurs with infection. The nasal mucosa responds to infection by upregulation of proinflammatory cytokines – interleukin (IL)-6, IL-12, IL-18, and tumor necrosis factor (TNF)-α – as well as the immunomodulatory cytokine IL-10, which might serve to reduce tissue injury but also limits the host's ability to clear the organism from the nose (Peeters et al. 2006; Valdes et al. 2020). Ongoing research supports the understanding that nasal aspergillosis occurs in immunocompetent dogs as cytokines involved in cell-mediated immunity – interferon (IFN)-γ and IL-12 – by T helper (Th)-1 lymphocytes are actually upregulated in peripheral blood mononuclear cells of affected dogs (Vanherberghen et al. 2013). Interestingly, the proinflammatory effects of Th2 immunity (as evidenced by increased IL-4) and dysregulation of the Th17 immune response (IL-17A) likely counteract the ability of Th1-mediated immunity to clear the infection (Valdes et al. 2020).

History and Signalment

Nasal aspergillosis is most commonly encountered in young to middle-aged dolichocephalic and mesaticephalic dogs. Large breeds predominate. Animals tend to have a long-standing history (4–6 months) of purulent or mucohemorrhagic nasal discharge and sneezing. Dogs can become head-shy or exhibit pain around the head region. Development of neurologic signs such as seizures or obtundation suggests fungal invasion of the central nervous system through the cribriform plate.

Physical Examination

Nasal discharge is commonly unilateral but becomes bilateral over time when disease erodes through the septum. Dogs typically have preservation of nasal airflow because of marked turbinate destruction. Depigmentation of the nares with or without ulceration

is found in approximately 40% of canine cases (Figure 4.13). Some dogs display marked facial or skull pain on palpation. Ipsilateral lymphadenopathy is found occasionally due to a reactive lymph node response; however, affected dogs remain systemically healthy unless pain interferes with appetite or activity.



Figure 4.13 Depigmentation at the entrance to the right nasal cavity.

Diagnostic Findings

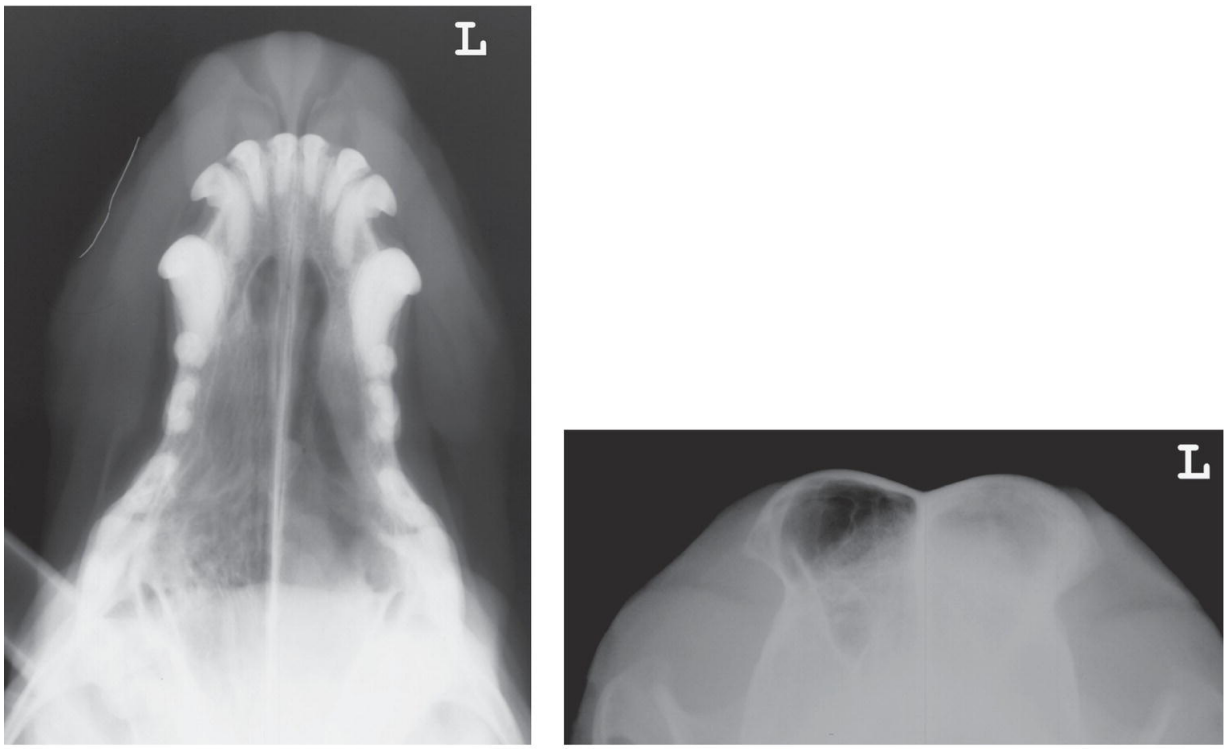
A minimum database is typically unremarkable, but can show evidence of chronic infection, with neutrophilia, monocytosis, and hyperglobulinemia. An agar gel immunodiffusion test (AGID) using an *Aspergillus* antigen prepared from cultures of *A. fumigatus*, *A.*

niger, and *A. flavus* has proven useful in confirming the clinical suspicion of aspergillosis in dogs. Positive AGID performed at the University of California, Davis laboratory for *Aspergillus* spp. was highly suggestive of nasal aspergillosis in one study, with a positive predictive value of 94%; however, false-negative results were found in almost one-third of cases (Pomrantz et al. 2007), indicating that the disease cannot be ruled out in a dog with negative serology. Whether results from other laboratories can be used similarly to rule in aspergillosis in a dog with nasal discharge is unknown. Tests for galactomannan, the *Aspergillus* antigen, are not indicated for dogs suspected of nasal aspergillosis, because the fungal infection is not systemic.

A study on cytologic diagnosis of aspergillosis demonstrated that direct smear of nasal discharge revealed fungal hyphae in a minority (<20%) of cases (De Lorenzi et al. 2006). Cytology of a swab or biopsy sample collected endoscopically was more likely (>90%) to demonstrate fungal spores, indicating that a visualized sample of a plaque lesion in the nasal cavity should be obtained whenever possible. Similarly, a study on the utility of fungal cultures in the diagnosis of canine nasal aspergillosis reported moderate sensitivity (77%) but high specificity (100%; Pomrantz et al. 2007). In that study, material submitted for culture was also from a visualized fungal plaque and therefore a low number of false-positive values would be expected. Fungal culture of nasal discharge has been associated with much lower sensitivity and specificity and is not recommended.

More definitive diagnosis and disease staging are obtained by finding the characteristic imaging findings with radiography or CT scan and with rhinoscopic detection of plaque lesions. Skull radiographs show variable degrees of turbinate lysis (unilateral or bilateral) and increased radiolucency in the nasal cavity (Figure 4.14a). The majority of dogs (75% or more) have frontal sinus involvement, and a frontal view of the skull should be included in the radiographic examination to look for a fungal granuloma in the sinus (Figure 4.14b). In some cases, the frontal sinus might be the only location in which fungal organisms can be identified (Johnson et al. 2006). CT is preferred for evaluation of dogs suspected of nasal aspergillosis. CT scans typically reveal unilateral loss of turbinate structures

(Figure 4.15a) and amorphous fungal mats, particularly in the frontal sinus (Figure 4.15b). The integrity of the cribriform plate can also be assessed (Figure 4.15b). Dogs with destruction of the cribriform plate have historically been considered more susceptible to central nervous system complications during topical treatment from edema or inflammation resulting from contact of the vehicle or antifungal medication with the meninges; however, this has not been borne out in clinical practice. Owners should be advised of the potential for complications, but damage to the cribriform plate is not an immediate contraindication for topical treatment.



(a) (b)

Figure 4.14 Open mouth radiographic view (a) of the nasal cavity in a 2-year-old male castrated (MC) Golden Retriever presented for left-sided nasal discharge. Asymmetry is evident, with lucency noted intranasally on the left side. An amorphous soft tissue density can be appreciated caudally. Turbinate structures on the right appear within normal limits. Frontal sinus image (b) of the same dog reveals a heterogeneous soft tissue density within the left frontal sinus. Sinuscopic examination and histopathology confirmed a fungal granuloma within the sinus.

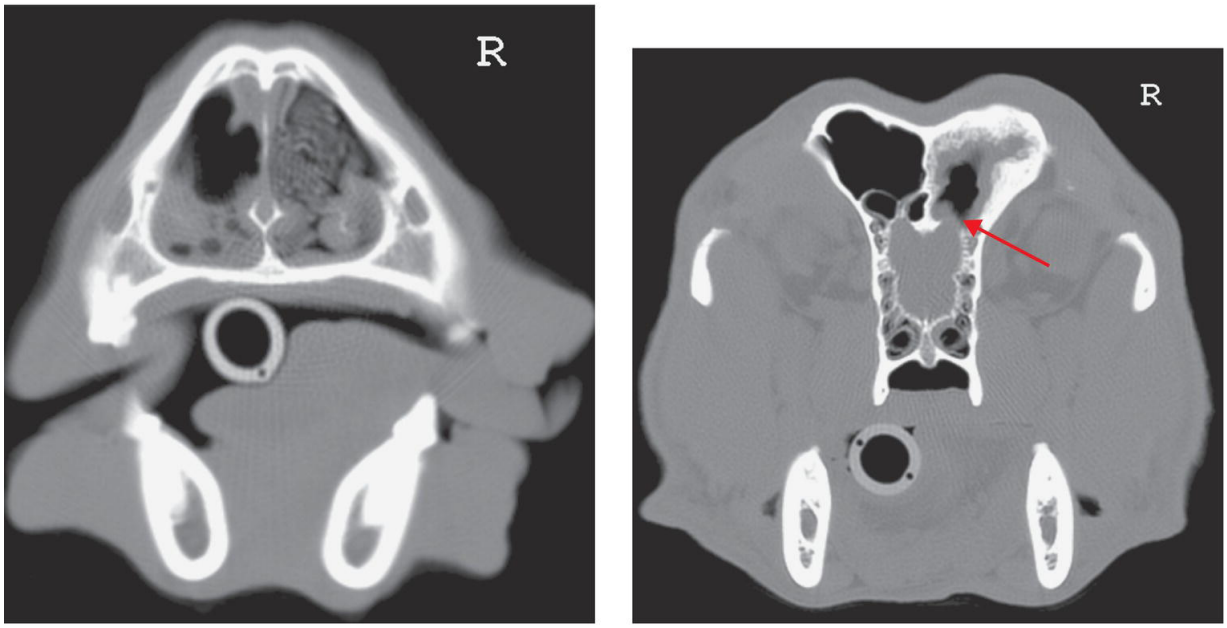


Figure 4.15 Computed tomography (CT) images from two dogs with confirmed sino-nasal aspergillosis. Rostrally (a) cavitation of the nasal cavity is noted on the left side with collapse of turbinates. In a CT slice through the region of the frontal sinus (b) hyperostosis of the right frontal sinus is seen along with a soft tissue density adhering to the wall of the sinus. On the ventral floor of the right frontal sinus, a breach in the cribriform plate is noted (red arrow) with local destruction by fungal infection.

Rhinoscopic examination of the nasal cavity typically reveals severe destruction of turbinates with increased space within the nasal cavity. It is not uncommon for the septum to be eroded in severe or chronic cases. Fungal plagues can be white, green, or black and are surrounded by granulomatous and hemorrhagic inflammation (Figure 4.16). It is critical to obtain a sample from the fungal plaque for cytologic, histopathologic, and mycologic evaluation (Figure 4.17). Definitive diagnosis of aspergillosis relies on a combination of serology, findings on diagnostic imaging, rhinoscopic examination, and cytologic or histopathologic changes.

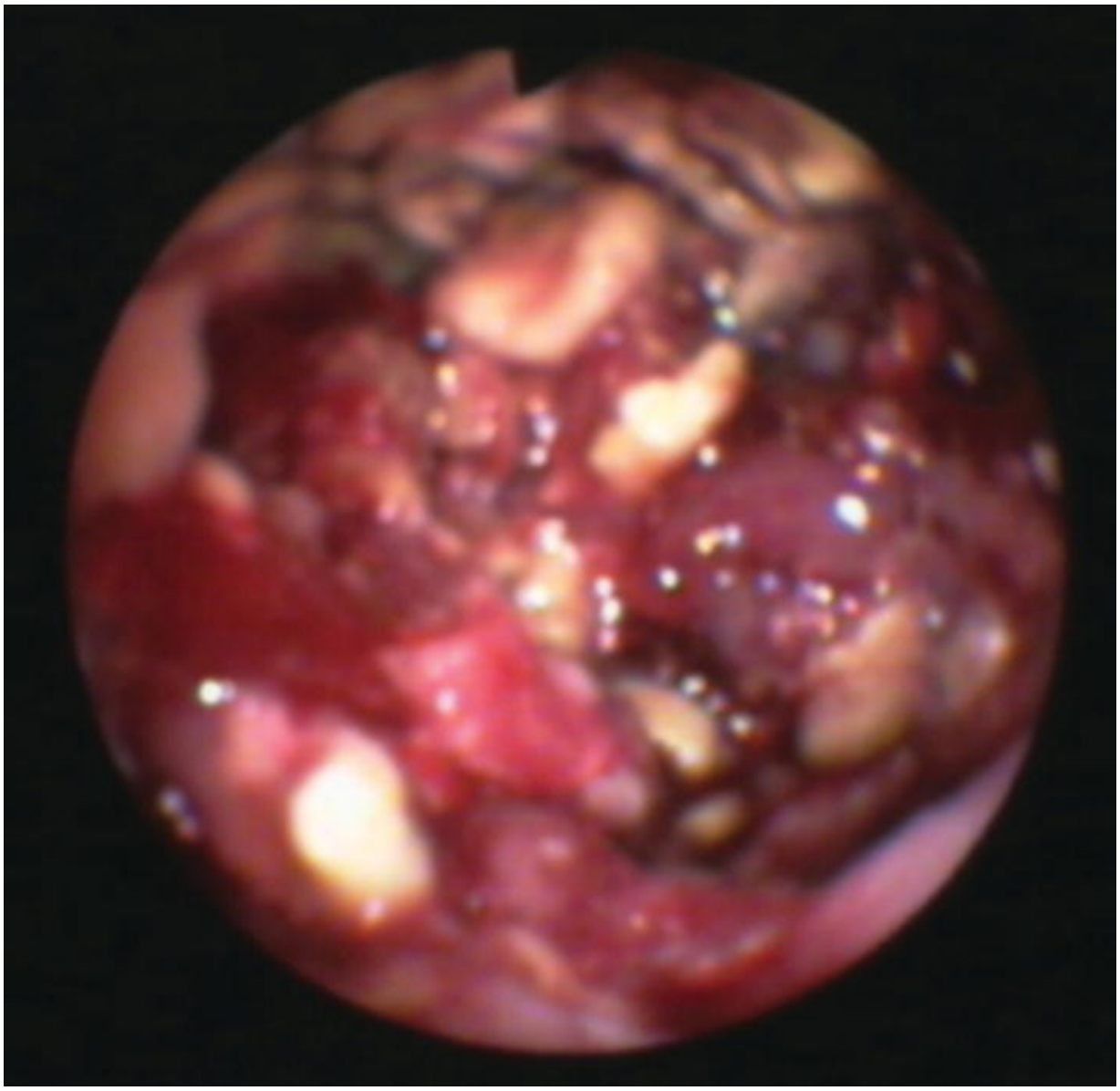


Figure 4.16 Fungal plaques identified during endoscopy in a dog with sino-nasal aspergillus. This would be an appropriate sample to submit for cytology or culture.

Treatment

Nasal aspergillosis in the dog is best treated with local instillation of clotrimazole or enilconazole, with resolution of disease reported in up to 67–85% of cases following multiple infusions (Zonderland et al. 2002; Pomrantz and Johnson 2010). Fungal plaques must be meticulously debrided from the nasal cavity and frontal sinus prior to instillation of topical therapy. This can result in substantial

bleeding, although it is rare for this to impair the ability to debride effectively. Judicious use of suction and flush allows continued visualization of the region and enhances hemostasis. A flexible endoscope should be used to examine the nasal cavity and enter the frontal sinus, when possible. In most cases, severe turbinate destruction rostrally opens the region surrounding the nasofrontal duct and allows entry to at least one compartment of the frontal sinus. Once in position, diagnosis can be confirmed, samples can be collected for biopsy and culture, and debridement can commence. Various biopsy forceps and curettes can be used for sampling and debridement, as well as suction and gentle saline flush.

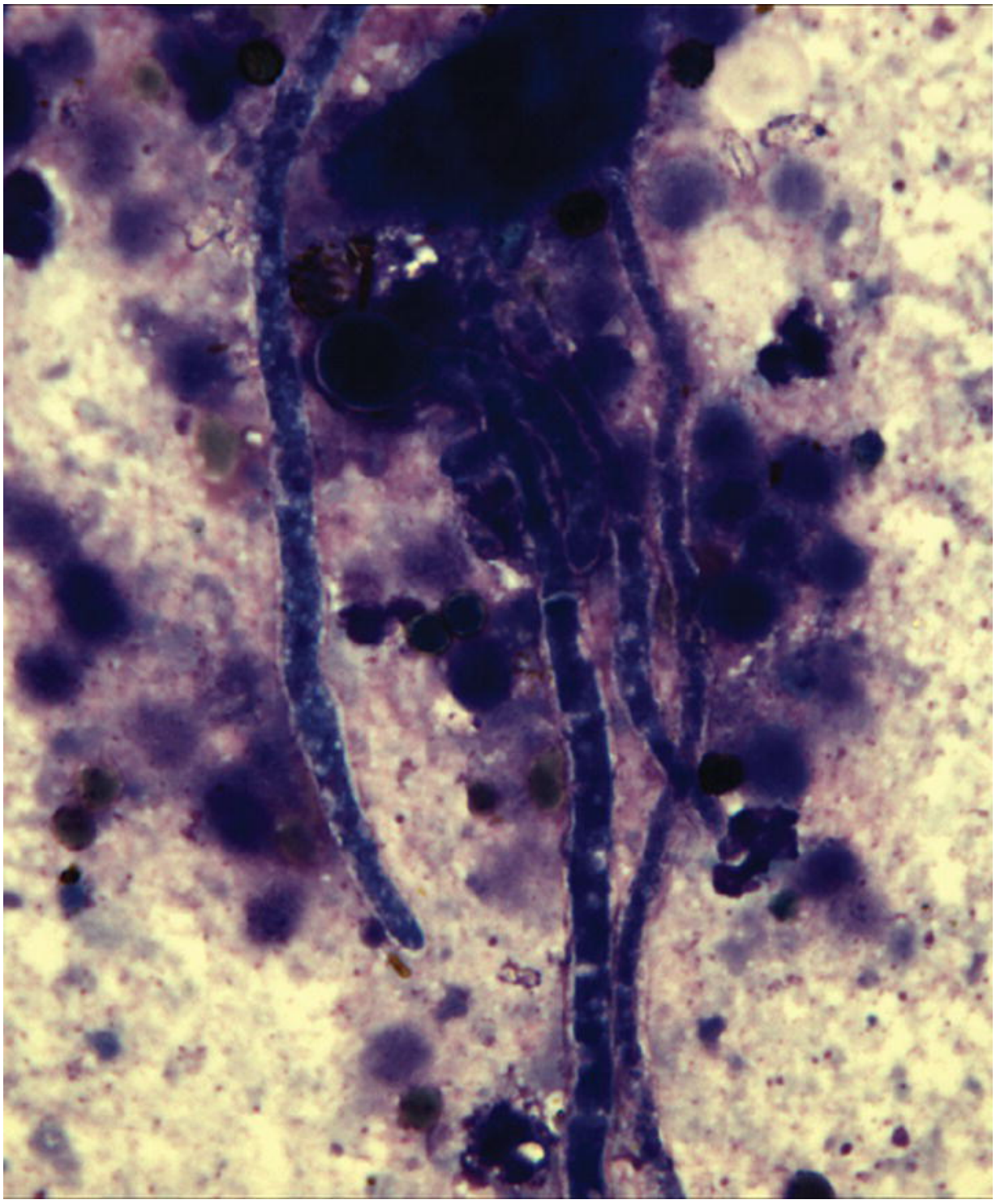


Figure 4.17 New methylene blue staining of an impression smear from the sample visualized in Figure 4.16 reveals rectangular, septate hyphae and conidia consistent with *Aspergillus* spp.

In cases lacking access to the frontal sinus endoscopically, sinus

trephination, debridement, and local treatment are required (Johnson et al. 2006). Landmarks for trephination are best obtained by review of CT images. An intramedullary (IM) bone pin (3/24 in.) and a Jacob's chuck can be used to obtain access to the frontal sinus. The site of maximal frontal sinus depth should be targeted, and no more than 1 cm of the IM pin should protrude from the chuck when performing trephination in order to avoid brain injury. Variable amounts of pressure are required to penetrate the bone over the frontal sinus, depending on whether hyperostosis or bony lysis predominates. Once the area is entered, a small (≤3 mm) rigid endoscope can be passed into the sinus to identify fungal plaques. Biopsy forceps can be used to obtain samples blindly from the frontal sinus or a suction catheter can be utilized. Periodically, the region should be visualized to ensure adequate debridement of all fungal material.

Prior to infusion of antifungal medication, the nasopharynx is occluded with a 24 French Foley catheter (Figure 4.18) and10 French drug delivery catheters are placed in the nasal cavity. In the original method described, the drug is instilled under pressure for 1 hour and the animal's head is rotated into dorsal, left lateral, right lateral, and dorsal recumbency every 15 minutes. The nares are blocked with 12 French Foley catheters to maintain the drug at the site of infection. Gauze pads are taped tightly behind the canines to prevent leakage of drug through the nasolacrimal duct. This method provides treatment of both nasal cavities and both frontal sinuses as the solution drains to fill the space. An abbreviated procedure requires occlusion of the nasopharynx only and placing the dog in dorsal recumbency with the nose pointed toward the ceiling. The nasal cavity is passively filled with antifungal medication for at least 15 minutes. Outcome is similar to the 1 hour infusion technique as long as meticulous debridement has been completed (Vangrinsven et al. 2018).

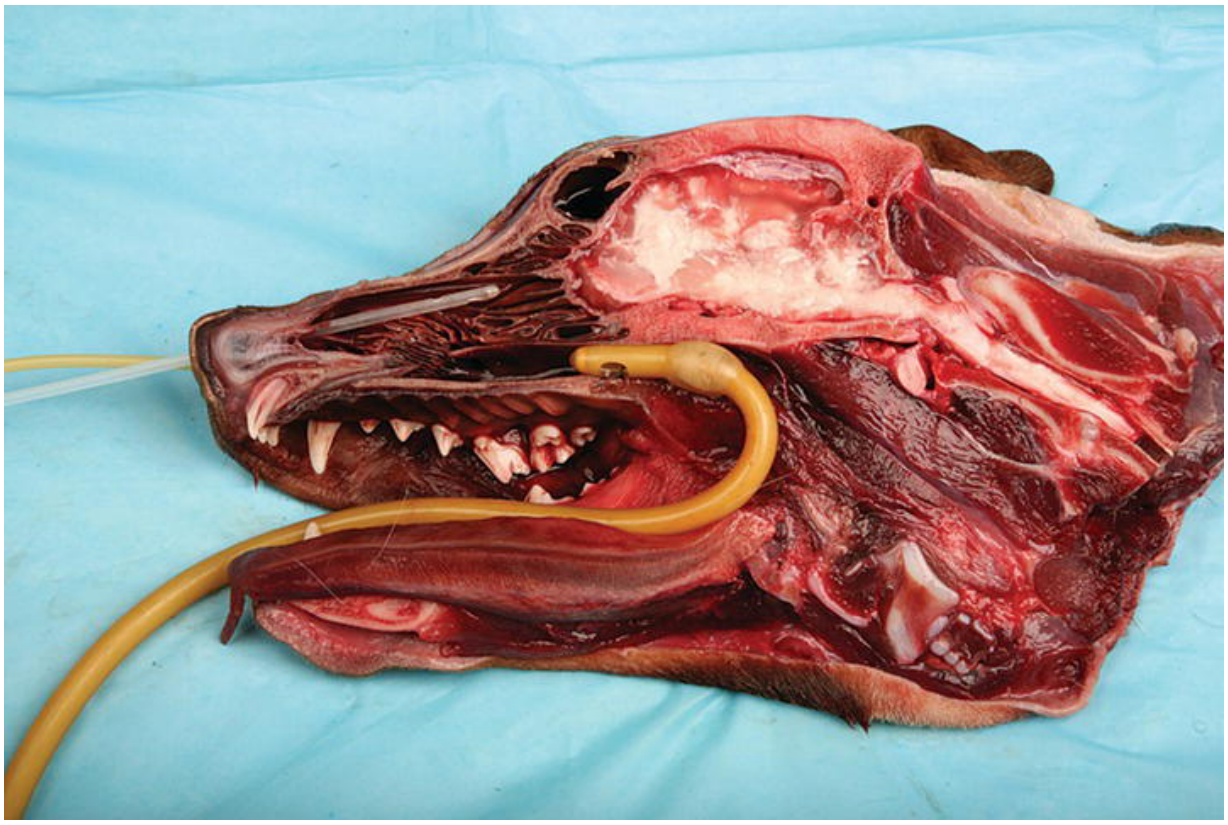


Figure 4.18 Placement of nasal catheters for treatment of sino-nasal aspergillosis. A 24 French Foley catheter is placed in the nasopharynx to prevent leakage of material into the oral cavity. For the 1-hour infusion, 10 French polypropylene catheters are used to deliver topical therapy, and 12 French Foley catheters are used to obstruct the nares and retain drug within the nasal cavity. For the modified procedure, the nose is pointed dorsally while the animal is on its back and drug is instilled directly into the nasal cavity until a meniscus forms at the nostril.

Clotrimazole is available over the counter as a 1% solution in 10 ml bottles, and 40–100 ml of solution can be required to fill the nasal cavity and sinuses of a dog. Chemical-grade powder is also available that can be diluted with polyethylene glycol to a 1% solution. Polypropylene glycol formulations should be avoided due to excessive mucosal toxicity that can lead to obstructive soft tissue swelling. Enilconazole is supplied as a concentrated commercial-grade solution (~27%), which is diluted to a 1, 2, or 5% solution prior to instillation in the nasal cavity.

After the infusion as detailed above, the dog is placed in sternal recumbency with the nose lowered to provide complete drainage of the drug from the nasal cavity. The oral cavity is rinsed clear of any medication, because exposure of the drug to the mucosa can result in excessive soft tissue swelling and airway obstruction. This appears to be of more concern with enilconazole than clotrimazole.

Rhinoscopy should be performed in 1–2 months to evaluate response to therapy and confirm lack of fungal plaques, because clinical signs and serology are not predictive of resolution of disease (Zonderland et al. 2002; Pomrantz and Johnson 2010). Repeat topical treatment should be anticipated at the follow-up visit, and if fungal plaques are again present, a second recheck should be planned in 1–2 months.

Additional treatment methods have been reported, including rhinotomy for debridement, and instillation of clotrimazole cream into the frontal sinus to provide long-acting antifungal action. While some clinicians utilize infusion of clotrimazole cream into the frontal sinus as a means of coating the region with a more viscous substance, it is not retained within the region much longer than the standard solution. Gel formulations of topical antifungals are potentially promising for prolonged antifungal therapy, (Mathews et al. 2009) although current studies are lacking. When topical therapy is contraindicated because of the presence of neurologic signs or if owners decline treatment, oral therapy with voriconazole (Bray et al. 2020) or posaconazole (fungistatic drugs) can be effective in controlling clinical signs of disease, although treatment is costly. Oral therapy with posaconazole and terbinafine proved effective in managing clinical manifestations of sino-nasal aspergillosis when signs had failed to respond to other therapy, although long-term treatment (18 months) was required (Stewart and Bianco 2017). It is unknown whether fungus was eradicated with oral treatment or if it simply controlled clinical signs because neither CT nor rhinoscopy was completed to ensure resolution of disease.

Prognosis

In the first several days after topical treatment, it is common to see an exacerbation of nasal discharge and snuffling, but this should resolve within 1–2 weeks of therapy. A 7–10-day course of a broad-

spectrum antibiotic (such as amoxicillin-clavulanate or doxycycline) can be used if discharge persists. Dogs should have monthly or bimonthly rhinoscopic evaluation and treatment until visible resolution of disease, and most dogs will require two to four treatments. Unfortunately, some dogs are never cured and others can have recurrence or reinfection months to years after apparent cure. Animals with severe destructive rhinitis often continue to have residual nasal discharge despite resolution of fungal infection because of abnormal nasal architecture and loss of normal defense mechanisms. These cases are a diagnostic and therapeutic dilemma because it is unclear whether recurrent fungal infection or turbinate destruction is responsible for clinical signs.

Feline Sino-nasal and Sino-orbital Aspergillosis

Pathophysiology

Although much less common than the canine disease, cats are increasingly recognized as being affected by aspergillosis. *Aspergillus* infection can cause predominately sino-nasal disease (caused by *A. fumigatus* most commonly) or sino-orbital disease (caused by *A. felis* or *A. udagawae*). This fungus has a worldwide distribution, although sino-orbital disease appears to be found more commonly in Australia than in other countries. Cats are systemically healthy, although the immune status of the nasal cavity is unknown. It has been hypothesized that viral destruction of turbinates or chronic antibiotic therapy for rhinosinusitis might predispose some cats to development of nasal fungal infection, likely with *A. fumigatus*.

History and Signalment

Any age cat can be affected by aspergillosis and it is possible that brachycephalic breeds are at increased risk for sino-orbital disease. Presenting complaints for cats with sino-nasal disease are similar to those seen with idiopathic rhinitis or neoplasia, with unilateral or bilateral nasal discharge, epistaxis, and sneezing commonly reported. Cats with sino-orbital disease might be noted to have facial asymmetry. Signs can be present for weeks to years.

Physical Examination

Nasal depigmentation is not a feature of aspergillosis in cats. Cats with sino-nasal disease can display obstruction of nasal airflow due to the presence of a nasal or nasopharyngeal granuloma, and cats with sino-orbital disease often have facial distortion or unilateral exophthalmos with protrusion of the third eyelid. They can also have ulceration of the hard palate or proliferative lesions behind the last molar.

Diagnostic Findings

Serology against fungal antigens by use of counterimmunoelectrophoresis, enzyme-linked immunosorbent assay (ELISA), or AGID has been positive in some cats diagnosed with aspergillosis. Galactomannan antigen testing is unreliable, similar to the situation in the dog. An immunoglobulin G (IgG) ELISA created in a research laboratory demonstrated 95% sensitivity and 93% specificity for both sino-nasal and sino-orbital aspergillosis (Barrs et al. 2015); however, currently, imaging, histopathology, and mycology are recommended for confirmation of disease.

A CT scan is helpful in determining the extent and severity of disease, although imaging findings overlap with those seen with rhinitis and neoplasia. Variable degrees of turbinate lysis and collapse can be seen (Figure 4.19), along with soft tissue mass effects in the nasal cavity or nasopharynx. Importantly, a CT scan can help define bone invasion and can determine whether both sides of the nasal cavity are involved. Invasive sino-orbital aspergillosis typically results in an irregularly contrast-enhancing retrobulbar mass, paranasal soft tissue mass effect, and bony lysis. Rhinoscopic identification of granulomatous or plaque lesions (Figure 4.20) is helpful in solidifying the diagnosis. Fungal culture of a visually obtained sample from the plaque can be helpful in identifying the cause of disease and determining anti-fungal susceptibility (Kay et al. 2021) although specific identification of the infecting species can require PCR and sequencing.



Figure 4.19 CT image of the rostral nasal cavity from a cat presented for a 2-month history of purulent nasal discharge. Cavitation and collapse of turbinates are noted on the right side of the nasal cavity. The left side is filled with soft tissue density and gas pocketing is noted. This appearance is consistent with lymphoma, severe chronic rhinitis, or granulomatous disease. Fungal hyphae consistent with *Aspergillus* spp. were found on histopathology.

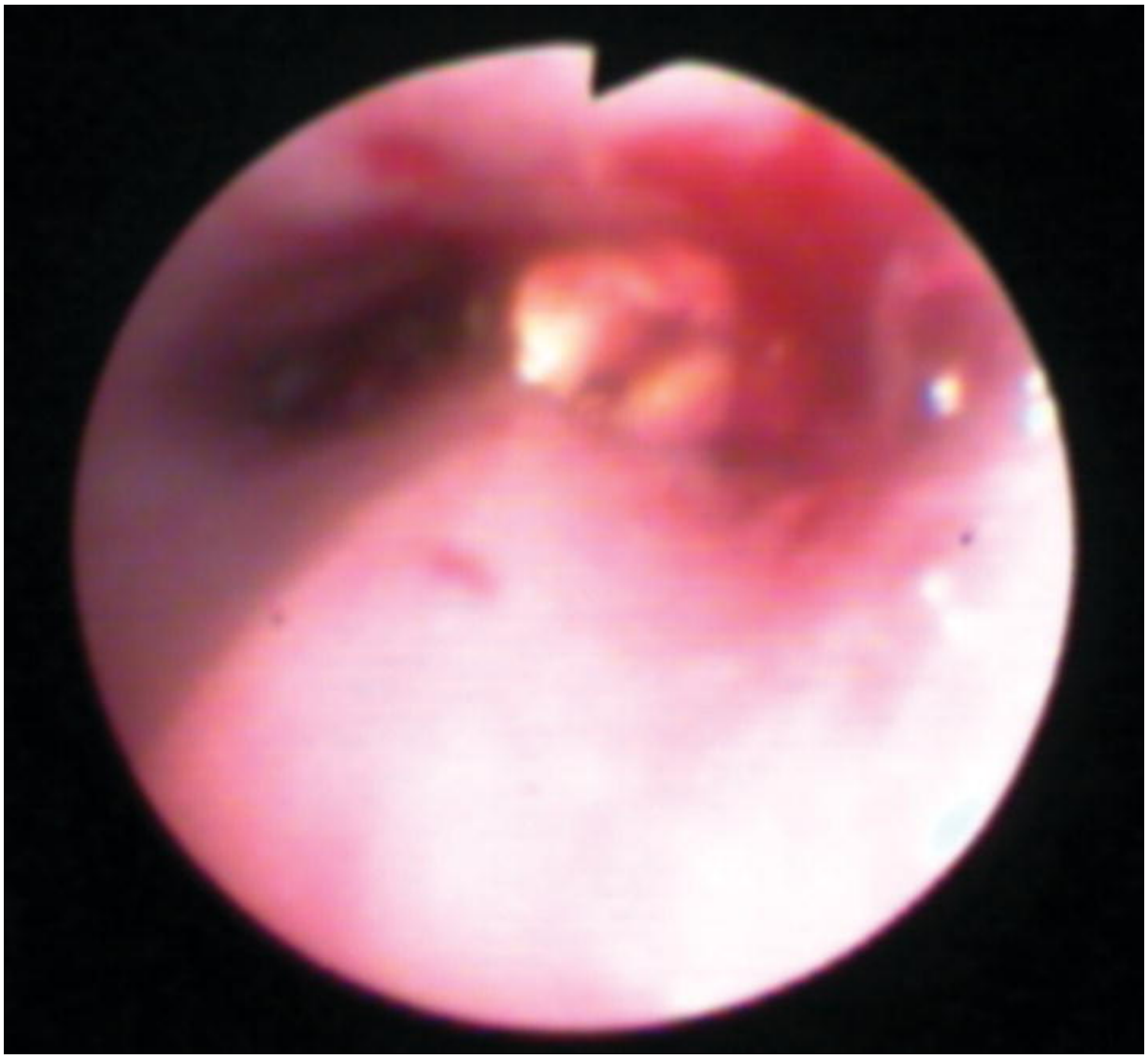


Figure 4.20 Retroflex view of the choanae in a 10-year-old spayed female (FS) Scottish Fold with a 4-year history of sneezing, epistaxis, and purulent nasal discharge. A fungal granuloma can be seen protruding into the nasopharynx. Histopathology revealed fungal hyphae.

Treatment

Optimal treatment for the cat with sino-nasal disease is unknown, although success has been reported with debridement followed by topical clotrimazole. Similar to the dog, debulking the fungal mass in cats with nasal or nasopharyngeal disease appears to be critical for success. Oral azoles can also be employed. For sino-orbital disease,

surgical exenteration and/or oral therapy with itraconazole and posaconazole have been used; posaconazole combined with terbinafine, and combinations of drugs including echinocandins have shown promise (Kay et al. 2021). Use of voriconazole is no longer recommended in cats due to neurologic side effects. Similar to aspergillosis in the dog, fluconazole lacks efficacy against *A. felis* (Barrs et al. 2013). Optimal length of therapy has not been determined and several cats have relapsed when medications have been discontinued following initial resolution of clinical signs.

Prognosis

Prognosis for feline sino-nasal aspergillosis is difficult to determine given the few cases that have been reported in the literature, but some cats will respond to therapy over 3–10 months. Sino-orbital aspergillosis in the cat carries a grave prognosis for recovery, and many cats are euthanized following diagnosis.

Rhinosporidiosis

Pathophysiology

Rhinosporidium seeberi is a rare cause of nasal fungal infection in the dog and it is even more uncommon in the cat. It has worldwide distribution but is found primarily in warm, wet environments. Little is known about the spread of disease but it might occur through contact of fungal sporangia with the nasal mucosa. Release of endospores into the nasal environment triggers an inflammatory response that generates a polypoid lesion.

History and Signalment

Similar to nasal aspergillosis, young to middle-aged dogs are affected most commonly. Unilateral clinical signs are typical, with serous nasal discharge, sneezing, epistaxis, and occasionally, the presence of a rostral nasal mass reported.

Physical Examination

Physical examination may reveal a nasal mass lesion protruding from the rostral nasal cavity in conjunction with absent nasal airflow,

but these findings are not always present and examination can be typical for any nasal condition.

Diagnostic Findings

Routine blood tests are usually normal. Rhinoscopically, hyperemic soft tissue masses in the nose display white or yellow lesions on the surface that contain rhinosporidium organisms (Cridge et al. 2021). Histopathology can reveal neutrophilic inflammation surrounding sporangia (10–500 μm wide), as well as endospores that are released after the sporangia rupture.

Treatment

Surgical removal of the mass lesion is the recommended course of action but fungal polypoid lesions can be recurrent. Use of topical povidone-iodine and systemic ketoconazole or dapsone has also been reported in a few cases (Cridge et al. 2021).

Prognosis

Due to the infrequent nature of the diagnosis, prognosis is difficult to predict.

Sporotrichosis

Pathophysiology

Sporothrix spp. can cause cutaneous disease in cats, dogs, horses, and humans and can occasionally be responsible for nasal signs or rhinitis. Infection occurs through inoculation of fungal organisms through the skin with bite wounds or scratches (from other cats or thorns). Skin lesions occur most commonly on areas exposed to fighting, such as on the limbs. The organism appears to have worldwide distribution but is most prominent in tropical and sub-tropical countries.

History and Signalment

Cats with nasal sporotrichosis typically present with nasal signs (sneezing, nasal discharge) that can resemble chronic rhinitis.

Systemic signs of illness can be found including anorexia and weight loss. Male cats that roam appear to be affected more commonly than female cats (Santos et al. 2024) and dogs are affected much less often than cats.

Physical Examination

Cats can have widening of the nasal bridge similar to that found in cats with cryptococcosis, or they might display ulcerated lesions on the nasal planum. Cats may or may not have concurrent ulcerated papular or nodular cutaneous lesions. Generalized lymphadenopathy is common.

Diagnostic Findings

Diagnosis is confirmed by finding 3–5 by 5–9 µm cigar-shaped yeast organisms in tissue samples, lymph node aspirations, or from cutaneous lesions. Organisms are typically surrounded by pyogranulomatous inflammation. Infection can also be documented by fungal culture of a deep tissue sample.

Treatment

Like most systemic mycosis, azole therapy remains the mainstay of treatment for sporotrichosis, with itraconazole being used most commonly, alone or in combination with terbinafine or fluconazole (Lloret et al. 2013). Cats should be treated at least 1 month beyond resolution of clinical signs.

Prognosis

Many animals can be cured of disease but diligence is required in administration of medication for an appropriate amount of time to ensure a complete response. Zoonotic concerns must be discussed with owners.

Inflammatory Diseases

Nasal and Nasopharyngeal Polyps

Pathophysiology

Nasal, nasopharyngeal, pharyngeal, or aural polyps are made up of fibrous inflammatory tissue that is suspected to originate from the Eustachian tube. A polyp can extend into the inner or middle ear, pharynx, or nasal cavity. Although an infectious etiology had been proposed in the cat, organisms have not been identified using culture or PCR.

History and Signalment

Nasopharyngeal polyps are usually discovered in young animals, with the majority of affected animals under the age of 12 months. They are found much more commonly in kittens than in puppies and are occasionally identified in older animals because clinical signs have been mild throughout life or not recognized as abnormal. In young to middle-aged dogs, nasal polyps predominate over nasopharyngeal. Nasal, pharyngeal, or nasopharyngeal polyps result in stertorous breathing, nasal discharge, dysphagia or dysphonia, gagging, and intermittent upper airway obstruction. Polyps in the ear canal lead to chronic aural discharge or head shaking. If otitis media is present, presenting complaints can include a head tilt, ataxia, nystagmus, facial nerve paralysis, or Horner's syndrome.

Physical Examination

Nasal or nasopharyngeal polyps lead to unilateral or bilateral loss of nasal airflow. A mass is sometimes palpable in the nasopharynx above the soft palate during an oral exam or the nasopharynx resists indentation during palpation. For animals with aural polyps, there may be evidence of otitis externa, a fluctuant polypoid mass in the ear canal, or a bulging tympanic membrane if middle ear disease is present.

Diagnostic Findings

In cases that are suspicious for a nasopharyngeal polyp, a lateral radiograph of the cervical region should be obtained. Typically it will reveal a soft tissue density within the nasopharynx, with loss of the dorsal nasal air column from the oropharynx to the back of the nasal cavity (Figure 4.21). The top differential diagnoses for this finding

would be a neoplastic process or fungal granuloma. A density filling the bulla might also be visualized, although this could represent either bullous effusion or soft tissue filling the middle ear. CT scan could be considered prior to treatment, because involvement of the tympanic bulla has been reported in 50–80% of cases in cats and impacts the treatment most likely to be effective. If neurologic testing is performed, some cats can be found to be deaf at the time of diagnosis and owners should be aware that deafness will persist after surgery (Anders et al. 2008).



Figure 4.21 Cervical radiograph from a 4-year-old spayed female domestic short hair (FS DSH) presented for a life-long history of snoring. Nasal airflow was absent bilaterally, and the lateral radiograph reveals a soft tissue density within the nasopharynx just ventral to the bulla. Gas dilation of the nasopharynx and esophageal dilation are also evident.

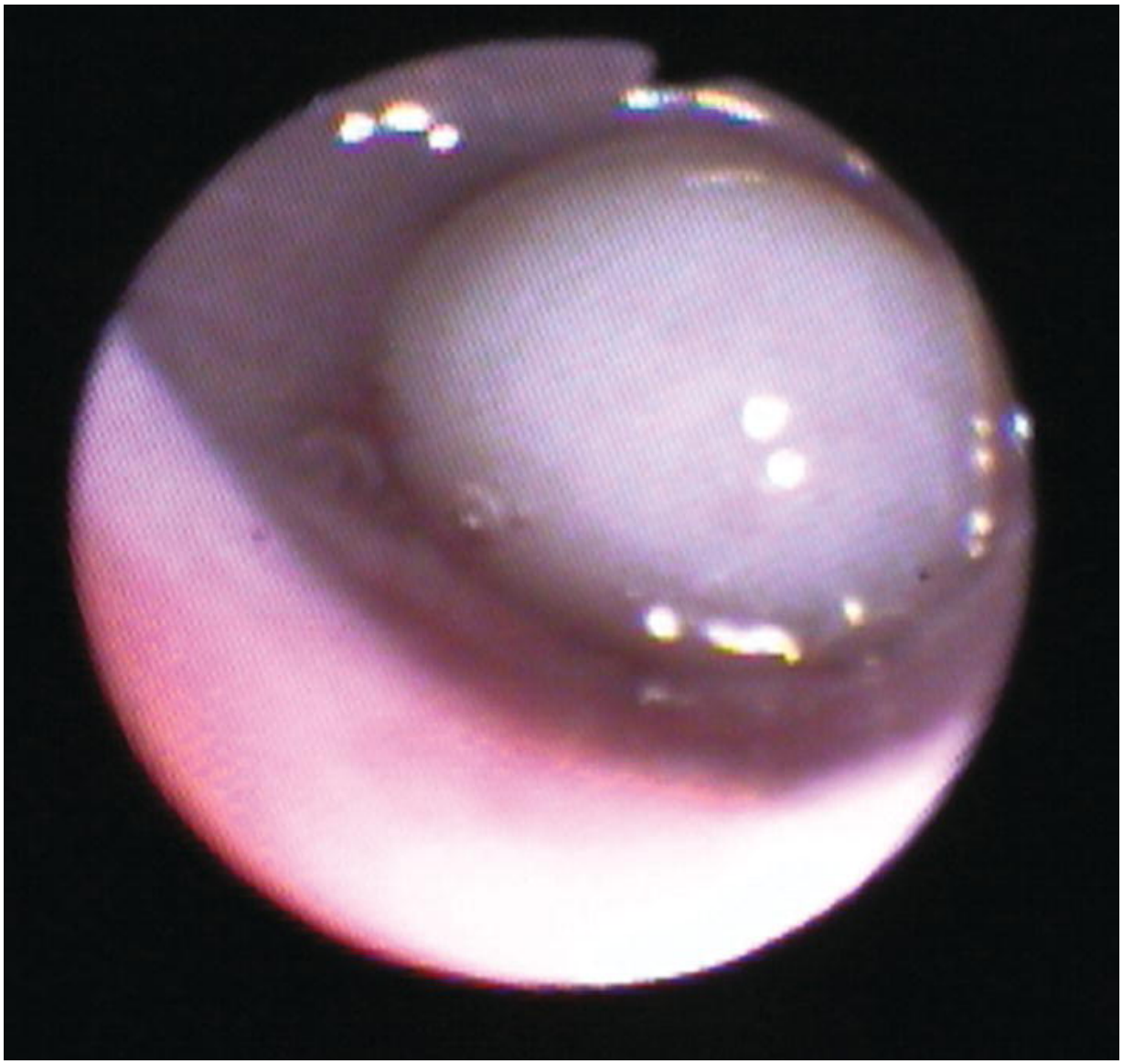


Figure 4.22 Endoscopic view of the choanae reveals a nasopharyngeal polyp.

Visual examination of the aural canal, pharynx, nasopharynx, or nasal cavity will often reveal the presence of a polyp; however, anesthesia is required. Evaluation of the nasopharynx area is most easily obtained with flexible endoscopy (Figure 4.22), although rostral retraction of the soft palate and use of a dental mirror can provide an appropriate view, especially with the animal positioned in dorsal recumbency. In dogs, nasal masses can be seen in the rostral nasal cavity as well as in the nasopharynx.

Treatment

Traction and avulsion of a nasopharyngeal or aural polyp from the stalk can be considered as an initial treatment option. This can be done in sternal or dorsal recumbency, depending on the size of the polyp and the size of the animal. A mouth gag is placed and the palate is retracted rostrally. Right-angle grasping forceps or towel clamps are placed above the palate and the tips are manipulated around the bulk of the mass. If possible, the stalk should be firmly grasped prior to extraction to avoid removing the polyp in pieces. Gentle, steady traction with a slight twisting motion will facilitate removal. Some clinicians recommend use of a tapering dose of glucocorticoids for 4–6 weeks post-extraction as a means for reducing recurrence, although the efficacy of this has not been fully established.

Rarely, removal of a large nasopharyngeal polyp can require a ventral midline approach through the palate. The incision is started at the hard palate and extended to within a centimeter of the caudal edge of the soft palate. Retaining this caudal connection will facilitate repair. After removal of the mass, the palate is closed in three layers and soft food is administered during the healing period (2–3 weeks).

In dogs, laser resection of nasal polyps, cautery, and manual retraction with suction have been used to remove polypoid material from the nasal cavity and nasopharynx. Intranasal surgery or frontal sinus surgery might also be required and can be extensive. Submission for histopathology is required to rule out neoplasia or sporotricosis as a cause for polypoid lesions.

Prognosis

Complications of traction and avulsion surgery are not uncommon but are usually transient. Unilateral Horner's syndrome (miosis, enophthalmos, and protrusion of the nictitans) is observed frequently and can occur in up to 80% of animals that undergo ventral bulla osteotomy. Owners should be advised that permanent neurologic damage is possible, although unlikely. Otitis interna can also occur after ventral bulla osteotomy, with head tilt, ataxia, and nystagmus. In cats with bulla disease, a relatively high rate of recurrence (10–50%) is reported if traction avulsion is employed. If

recurrence is noted, the recommended treatment involves unilateral or bilateral ventral bulla osteotomy, with collection of samples for aerobic and anaerobic bacterial culture. Appropriate antibiotics are prescribed to treat middle ear disease. This would also be the preferred method for managing a polyp that had recurred after traction avulsion.

In dogs with nasal polyps, particularly those extending into the nasopharyxnx, extensive surgery, laser resection, and repeated polypectomy can be required for control of disease. Prognosis remains uncertain in dogs with nasal polyposis.

Feline Chronic Rhinosinusitis (CRS)

Pathophysiology

Feline CRS is one of the most common chronic upper respiratory tract disorders seen in the feline population and is characterized by nasal discharge and sneezing with excessive mucus production. While various viral agents and bacteria are implicated as causes of acute URI of cats, the underlying pathogenesis of chronic feline rhinitis is less certain. The disease is likely multi-factorial, with viral (FHV-1) infection, secondary bacterial infection, and a poorly regulated or inappropriate local immune response contributing to the pathogenesis of disease. A role for allergy in feline nasal disease has not been fully investigated or established; therefore the use of typical anti-allergy management strategies (decongestants, antihistamines) cannot be advised.

Because this disorder is so frustrating to owners and veterinarians alike, CRS should be considered a diagnosis of exclusion. At some stage, a complete work-up should be recommended in any cat with non-specific nasal signs, even if an underlying disease process is considered unlikely. Given that CRS is partially related to bacterial infection, the disorder is prone to misuse and abuse of antimicrobials, and inappropriate treatments can lead to viral or bacterial resistance. Also, delayed recognition of other diseases affecting the upper respiratory tract, such as foreign body, dental-related nasal disease, neoplasia, or fungal infection, can adversely impact morbidity and mortality.

History and Signalment

CRS affects all ages of cats, with clinical signs first apparent in cats anywhere from 6 months to 20 years of age. In general however, young to middle-aged animals are affected more often than older animals. Stertor, mucopurulent or hemorrhagic nasal discharge, and sneezing are the most common historical complaints and clinical signs. Intermittent or partial antibiotic responsiveness is common. Nasal discharge is often bilateral; however, some cases are remarkably unilateral. Ocular and systemic signs are usually absent, in comparison to the disease in kittens or cats with acute or recurrent URI. Rarely, neurologic signs such as obtundation, paresis, or a head tilt can be noted due to extension of disease (typically bacterial abscessation) through the inner ear or cribriform plate. When seen, these warrant a grim prognosis.

Physical Examination

Cats with CRS are generally healthy and the presence of systemic signs (fever, weight loss, or anorexia) should warrant investigation of diseases other than idiopathic rhinitis. Nasal discharge may not be apparent on physical examination because cats are fastidious groomers; however, intermittent sneezing can be observed. Cats with CRS generally have preservation of nasal airflow, in comparison to cats with neoplasia or fungal infection in which airflow is obstructed. Soft palate and ocular compression are normal and it is uncommon to detect regional lymphadenopathy, although this can be found occasionally. The remainder of the physical examination is usually unremarkable, and cats are systemically well.

Diagnostic Findings

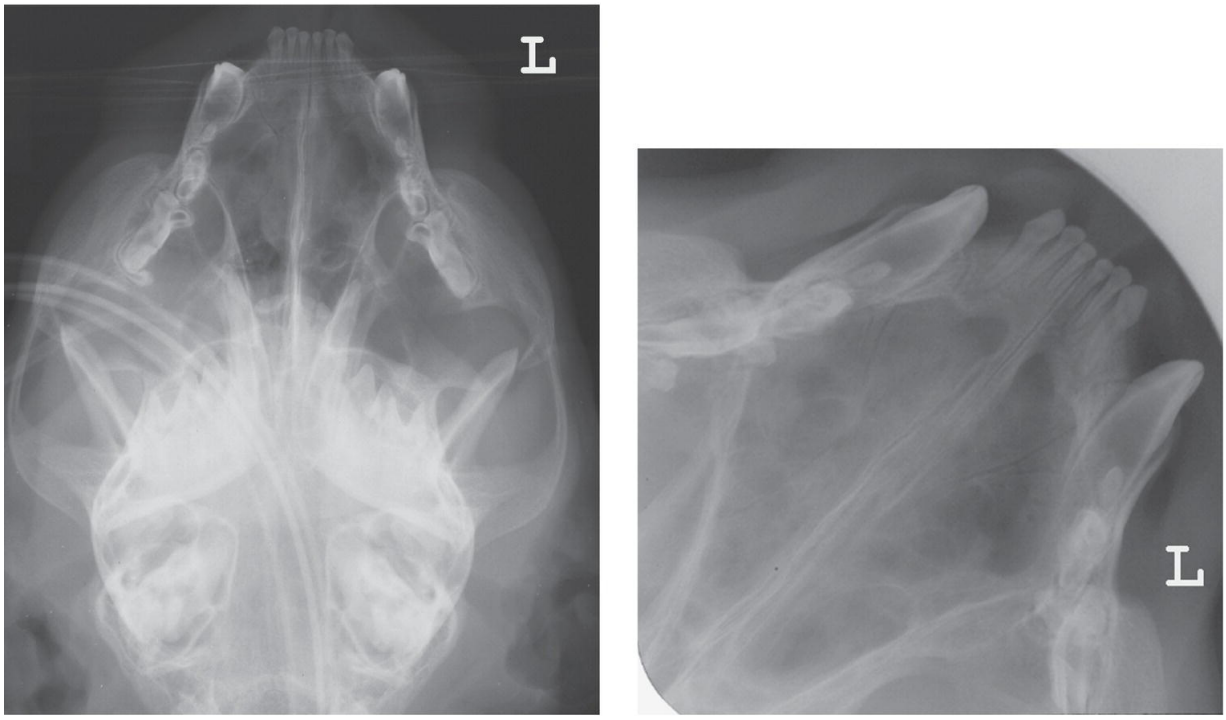
The diagnosis of CRS is one of exclusion, and owners should be made aware of this prior to initiating expensive and somewhat invasive diagnostic testing. The approach involves an assessment of the extent of systemic illness with a minimum database. Retroviral status should be assessed prior to embarking on additional diagnostic testing; however testing for *Bartonella* is not advised because it has not been associated with chronic nasal disease. No specific tests for respiratory viruses are warranted (serology, culture,

or PCR) as all cats have been exposed to these viruses and will have seroconverted, and because the presence of organisms or DNA does not correlate with disease state. Usually findings on CBC, chemistry panel, and urinalysis are unremarkable. Cytology of nasal discharge and/or a cryptococcal antigen test can be performed to rule out cryptococcosis in appropriate situations, and these tests are particularly indicated in the cat with loss of nasal airflow or regional lymphadenopathy. In the latter case, a lymph node aspirate should also be obtained. In cats with hemorrhagic nasal discharge, blood pressure evaluation and a coagulation panel should be performed.

Anesthesia is required for additional diagnostics. Skull radiographs show variable degrees of turbinate lysis and increased fluid density within the nasal cavity. The open mouth dorsoventral view (Figure 4.23a) or a dental radiograph (Figure 4.23b) provides the best visualization of the nasal cavity and a CT scan provides better assessment of intranasal structures (Figure 4.24). CT also allows evaluation of multiple sinuses (Figure 4.25) and the middle ears, which are frequently involved in the disease process and filled with soft tissue or fluid density. The severity of radiographic or tomographic changes overlap with those typically found in nasal neoplasia, making biopsy differentiation crucial.

Rhinoscopy with biopsy is performed after imaging has been completed to avoid causing hemorrhage that would alter the imaging appearance of the nasal cavity. First, nasopharyngoscopy is accomplished by retroflexing a flexible endoscope above the soft palate to rule out NPS or a mass lesion. Rostral rhinoscopy of the nasal cavity typically reveals hyperemic mucosa, variable amounts of mucoid to purulent discharge, and irregular turbinate structures (Figure 4.26). Turbinate destruction is common, although some affected cats will have minimal visual changes despite histologically abnormal tissue. If desired, a sample can be obtained for bacterial culture prior to complete rhinoscopic evaluation, bearing in mind that normal flora can be cultured. Cats with chronic rhinitis have potential pathogens isolated from nasal samples more commonly than do normal cats (Johnson et al. 2005), and cats that have been on multiple courses of antimicrobials can have highly resistant organisms isolated. Thus, culture results can sometimes aid in choosing appropriate therapy. A deep nasal swab can be obtained

using a sterile Cytosoft® cytology brush (Medical Packaging Corporation, Camarillo, CA), which is approximately the same length as the nasal cavity in a cat (see Figure 2.13).



(a) (b)

Figure 4.23 Open mouth views of the nasal cavity of a cat taken under general anesthesia obtained with conventional skull radiography (a) and dental radiography (b). Skull radiographs are obtained in dorsal recumbency with the jaw retracted, while the dental radiograph is obtained in sternal recumbency with the radiographic film placed in the mouth. Mild asymmetry is seen between the two sides of the nasal cavity, with an increase in soft tissue or fluid density on the right.

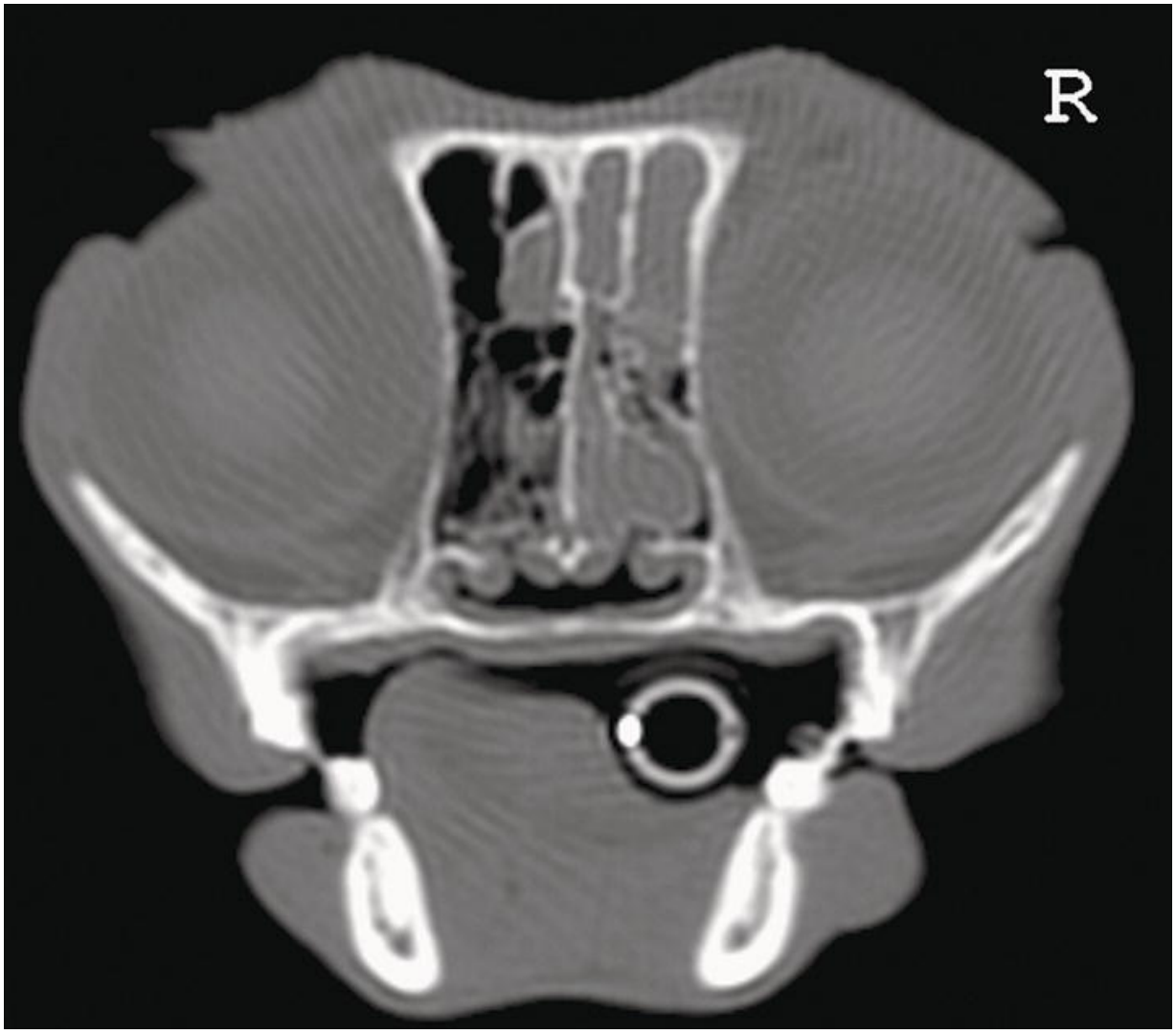


Figure 4.24 Computed tomography image of the nasal cavity in a cat with right-sided nasal discharge reveals fluid accumulation and some gas pocketing on the right side of the nasal cavity.

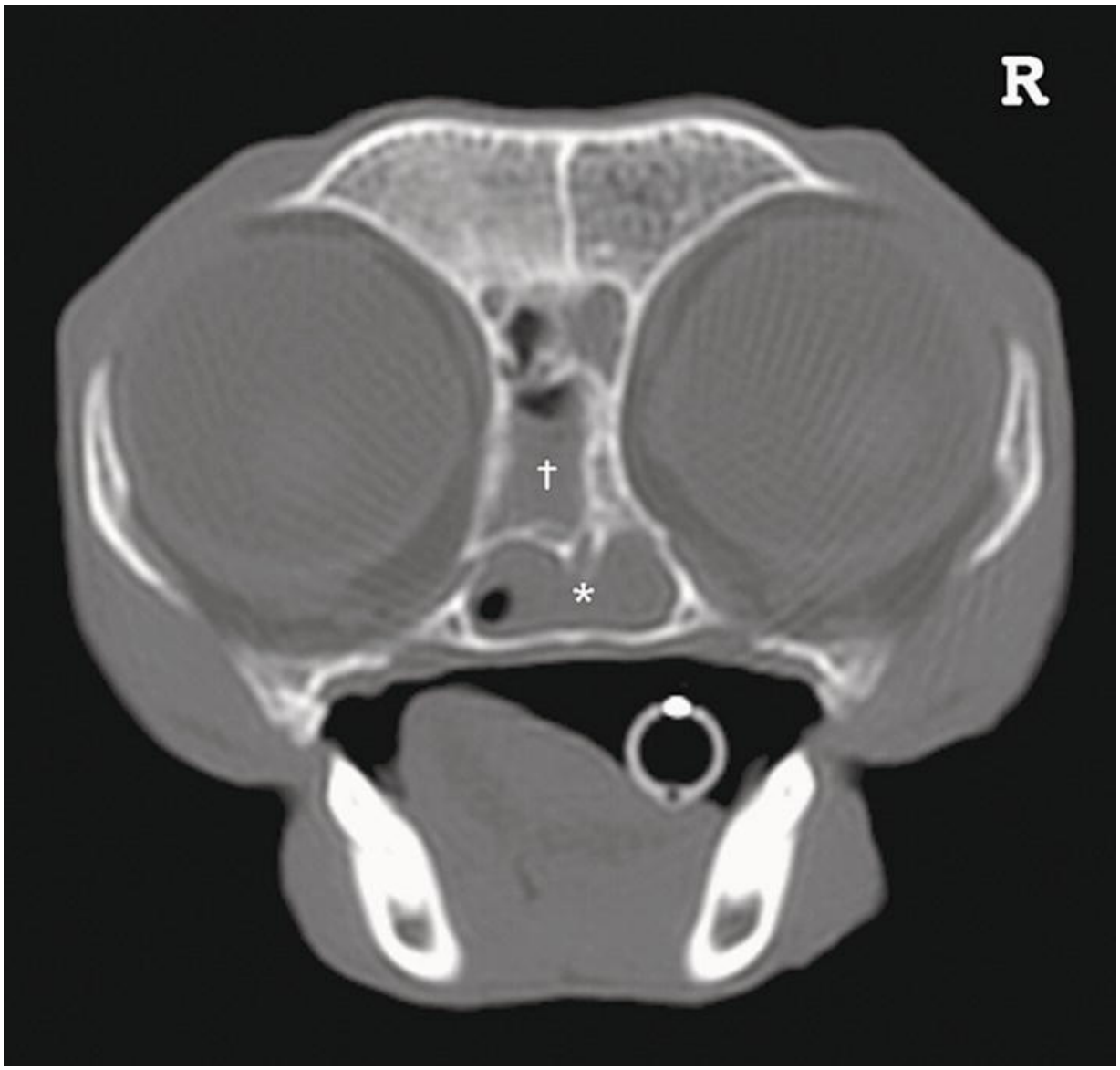


Figure 4.25 Computed tomography image through the frontal sinus and nasopharyngeal region of a 2-year-old spayed female domestic short hair (FS DSH) with life-long nasal congestion. Note the absence of air in the frontal sinuses and replacement by organizing fibrous or bony tissue. The sphenopalatine sinuses are distorted (†) and filled with soft tissue density, as is the nasopharynx (*).

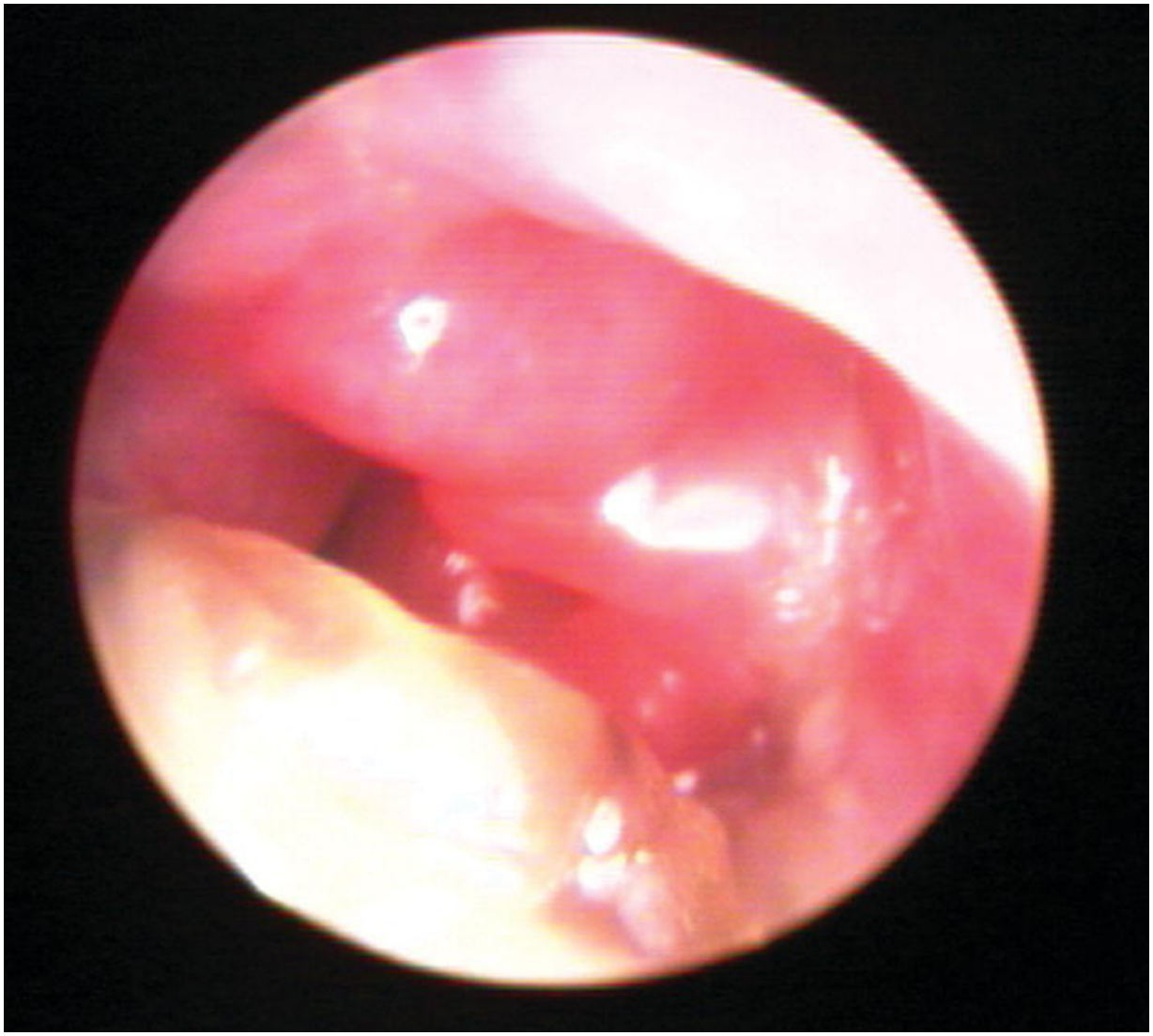


Figure 4.26 Rhinoscopic image in a cat with chronic rhinosinusitis reveals moderate mucosal hyperemia, blunting of turbinates, and destructive rhinitis (visible as increased space within the nasal cavity). Thick mucoid discharge is evident at the bottom left of the image.

Rhinoscopic appearance does not predict the presence or absence of substantial inflammation; therefore it is advisable to obtain samples for histopathology from both nasal cavities to assess the type and severity of inflammation. Cup biopsy forceps (2 or 3 mm) are recommended. Histologic evidence of nasal inflammation is virtually always present in cats with CRS, with neutrophilic inflammation indicating an acute component to the disease and lymphoplasmacytic inflammation suggesting chronicity. Eosinophilic

infiltrates could indicate FHV-1-related disease, as has been reported in facial dermatitis linked to herpesvirus infection (Hargis et al. 1999).

Extensive nasal flushing after completion of sample collection (see Chapter 2) can improve response to therapy by removing excessive mucus and inflammatory debris from the nasal cavity. After rhinoscopy, dental probing is performed to identify oronasal fistulae or large periodontal pockets that could represent an alternate diagnosis of dental-related nasal disease rather than idiopathic CRS.

Treatment

Antibiotics

Antibiotic therapy is usually employed to control secondary bacterial rhinitis. Choice of antibiotics for the individual cat is best made based on culture of a deep nasal brush sample. When collection of such a sample is not possible, antibiotic selection can be made with an understanding of potential pathogens that have been isolated previously from cats with rhinitis. Those organisms include aerobes (*Pasteurella multocida*, *Escherichia coli*, *Corynebacterium ulcerans*, *Bordetella bronchiseptica*, *Streptococcus viridans*, *Pseudomonas aeruginosa*, *Actinomyces slackii*), anaerobes (*Peptostreptococcus anaerobius*, *Bacteroides fragilis*, *Bacteroides ureolyticus*, *Prevotella*, *Fusobacterium nucleatum*), and *Mycoplasma felis* (Johnson et al. 2005). Doxycycline (approximately 50 mg/cat PO divided every 12 hours or given once daily) is an appropriate antibiotic to use because it has efficacy against many of these bacteria. In addition, doxycycline might help control clinical signs through anti-inflammatory or immunomodulatory effects. Doxycycline is well tolerated by most cats even when administered for a long period of time (4–6 weeks), and it is relatively inexpensive. The primary caution with use of this drug is the potential for development of an esophageal stricture if the pill lodges in the esophagus. Instructions on the pill vial should always contain the recommendation to moisten the pill with butter or tuna oil and to follow administration with a small volume (3–5 ml) of water or food.

Other commonly used antibiotics include azithromycin, fluoroquinolones, and amoxicillin-clavulanic acid. Azithromycin is an appealing option for long-term therapy because it accumulates in tissue. It is available as a powder for oral suspension and can be given once daily (5 mg/kg for 3–5 days), followed by administration two to three times weekly. Splitting the powder into 4–8 aliquots and creating a suspension every 10–14 days makes azithromycin a cost-effective treatment. This antibiotic is also reported to have some anti-inflammatory and tissue repair effects that could be beneficial in management of cats with marked turbinate destruction. Penicillin-like drugs are helpful in controlling signs in many cats, even though they lack efficacy against *Mycoplasma* species; however, they are frequently associated with gastrointestinal side effects. Pradofloxacin is a viable alternative with anaerobic as well as aerobic and anti-*Mycoplasma* affects. Enrofloxacin (Baytril®, Bayer, Leverkusen, Germany; 2.5 mg/kg PO every 24 hours) is generally reserved for infections that are susceptible to this antibiotic, and high doses should be avoided because of an association with development of a blinding retinopathy, particularly in cats with renal dysfunction. Clindamycin can be efficacious in cases with extensive bony involvement because of its ability to penetrate bone, but use has also led to esophageal stricture formation. Antibiotic treatment, when it is effective initially, is usually continued for 2–4 weeks based on the assumption that deep-seated infection is present. Using short courses of different antibiotics is not recommended due to the risk of inducing bacterial resistance.

In some cats, adding a topical antimicrobial to oral therapy can help control bacterial infection due to a resistant bacterium such as *E. coli* or *Pseudomonas* or due to infection with *Bordetella*. When instituted after copious flushing of the nasal cavity, topical antibiotics alone might be adequate for local control of the infectious component of disease. Gentocin® ophthalmic drops (Merck Animal Health, Madison, NJ) can be placed in the nasal cavity once to twice daily in cats that will tolerate administration.

Anti-inflammatory Agents

When histopathology supports the presence of non-specific nasal inflammation (neutrophilic or lymphoplasmacytic), treatment with piroxicam can be considered at 0.3 mg/kg PO daily or every other day. This drug is commercially available as a 10 mg tablet, therefore drug compounding is required to create ~1 mg capsules for cats. This non-steroidal anti-inflammatory agent causes subclinical gastric erosion at the recommended dose, and caution is warranted in its use in older animals or in cats with renal insufficiency. In some instances, a gastrointestinal protectant (famotidine) or prostaglandin analog (misoprostol) might be administered concurrently; however, it can be difficult giving multiple oral medications to a cat chronically. Because most cats with CRS are young to middle-aged and generally healthy, these measures are not commonly needed to avoid toxicity. Using the medication daily for 1 week then decreasing the dose to every other day will help limit side effects. Meloxicam is a tempting alternative to piroxicam because it is easier to dose and administer, although subjectively cats do not appear to respond as well to that drug. Meloxicam is licensed only for acute therapy in the USA, but it has been used long-term in Europe and Australia. There are no published reports of the efficacy of any non-steroidal agents in management of feline rhinitis.

Glucocorticoids are sometimes advocated for treatment of cats with CRS, and in some animals with excessive mucus in the nasal cavity, administration of oral glucocorticoids can reduce mucus accumulation and promote appetite. Caution is warranted if eosinophilic nasal inflammation is detected or if FHV-1-related ocular disease is present, because glucocorticoids can result in exacerbation of disease. Inhaled or topical glucocorticoids are also sometimes advocated for cats with a diagnosis of idiopathic rhinitis, although mucus must be cleared from the nasal cavity prior to use to allow absorption by the mucosal surface. Also, it is important to note that metered-dose inhaler preparations containing glucocorticoids require administration with a spacer chamber and facemask and are designed to deliver drug to the lower airways, not to the nose. Therefore, this treatment strategy is unlikely to be efficacious in the management of nasal disease. Liquid glucocorticoid medications are

available in drop formulations or as nasal sprays but are variably tolerated by cats.

Other anti-inflammatory treatments that have been suggested for use in cats with CRS include cyclosporine, oclacitinib (a janus kinase inhibitor used for management of allergic skin disease), and intranasal maropitant (an NK-1 antagonist with utility as an anti-emetic). While some of these drugs might seem appealing based on purported mechanisms of action, there are no investigations into their use in clinical nasal disease.

Antiviral Therapy

The role of FHV-1 in the induction or promotion of clinical signs in cats with CRS has not been clearly established, and specific antiviral therapy is not routinely recommended in cats with chronic disease. Trial therapy with famciclovir could be considered because it has been shown to be highly efficacious against FHV-1-related ocular disease, and there may be a role for this drug in treatment of some cats with CRS. If trial therapy is pursued, the appropriate dose of 40 mg/kg TID or 90 mg/kg TID should be employed, with continuation of treatment for 1 week beyond clinical resolution of signs. If efficacy is noted, the drug should be discontinued, not tapered, at the end of the course of treatment.

Additional Therapy

Rigorous flushing of the nasal cavity when the animal is anesthetized for diagnostic testing can improve the clinical response of cats with CRS, and intermittent nasal flush can be helpful in some cats (see Chapter 2). Animals should be fully anesthetized, intubated, and the oral cavity packed with surgical laparotomy pads to prevent aspiration, as described. Cats can also benefit from intermittent airway humidification via steam inhalation. Oral administration of *N*-acetylcysteine (150–250 mg/cat PO BID) can help some cats by reducing the viscosity of secretions, which can enhance evacuation of mucus from the nasal cavity. Antihistamines and decongestants are not routinely used in cats with CRS because nasal mucus is overly viscous in this condition and this would be worsened by these therapies.

Prognosis

Most cats with CRS that undergo advanced imaging and diagnostic testing have severe abnormalities in nasal and sinus structure and function, even when diagnosed at a young age. It is unlikely that disease can be abolished in these cats. Owners should be aware that clinical signs of disease can be controlled to a variable extent, but animals are rarely cured. Providing them with a realistic expectation for what can be achieved with medical therapy will help alleviate some of the frustrations that owners and veterinarians alike suffer when dealing with this condition. Some cats have recurrent episodes of sneezing and nasal discharge despite long-term antimicrobial and anti-inflammatory therapy, and a reasonable goal of therapy is to limit the severity and frequency of disease exacerbations.

Cats that have previously shown good response to antibiotics but become resistant to therapy should be investigated for alternate diseases. If the discharge becomes bloody, consider obtaining a blood pressure to rule out systemic hypertension, because vascular congestion can reduce antibiotic responsiveness as well as lead to blood-tinged nasal discharge. Additional consideration should be given to the development of neoplasia, aspergillosis, or acquired NPS. Each of those diseases can cause loss of nasal airflow, and that finding should trigger consideration of advanced or repeated diagnostic testing.

Canine Lymphoplasmacytic Rhinitis

Pathophysiology

Histologic evidence of lymphoplasmacytic nasal inflammation can be found in conjunction with primary neoplastic, fungal, or foreign body rhinitis. Idiopathic lymphoplasmacytic rhinitis (LPR) is a condition that lacks an identified primary source of the inflammatory infiltrate. This condition has previously been referred to as immune-mediated or allergic rhinitis, because initial reports suggested that glucocorticoid therapy was curative. Some cases have been reported to respond to hyposensitization (Lobetti 2014), which increased the interest in assigning hypersensitivity as a cause for this disorder, but the etiology remains unclear. Some dogs display a transient response

to antibiotic therapy; however, clinical signs return when the drugs are withdrawn or sometimes recur in the face of treatment. This type of response should prompt consideration of a foreign body rhinitis or tooth root disease causing nasal signs, and these are important differential diagnoses for LPR.

Increased fungal DNA was found in nasal tissue of dogs with LPR (Windsor et al. 2006), although specific fungal species have not been identified in affected dogs. Studies on the nasal immune response have demonstrated alterations in local immunity in affected dogs. In one study, a partial Th2 cytokine response was demonstrated in dogs with LPR compared to a Th1 response in dogs with aspergillosis (Peeters et al. 2007). In another study, the nasal mucosa of dogs with aspergillosis or LPR had increased gene expression for pattern recognition receptors in comparison to that of healthy control dogs (Mercier et al. 2012). Pattern recognition receptors are responsible for initiating the immune response against suspected pathogens, and therefore a common underlying immune event might predispose to both infectious and inflammatory rhinitis in the dog. Clearly, further work is required to establish an etiology for this disorder and to guide treatment regimens.

History and Signalment

Idiopathic LPR generally affects young to middle-aged, large breed mesaticephalic or dolichocephalic dogs. Males and females are equally affected. Nasal discharge (unilateral or bilateral) is the most common clinical complaint in dogs with LPR. Discharge is typically mucoid or mucopurulent in most dogs, but can be serous, and hemorrhagic or blood-tinged discharge is not uncommon. Interestingly, some dogs present with true epistaxis rather than nasal discharge. Other possible clinical signs include sneezing, coughing, reverse sneezing, stertorous breathing, ocular discharge, and pawing/rubbing at the muzzle.

Physical Examination

Nasal airflow is generally preserved in dogs with LPR and the remainder of the physical examination is often unremarkable. Some dogs with LPR have regional lymphadenopathy due to reactive

lymphoid hyperplasia. Careful thoracic auscultation and assessment of tracheal sensitivity are recommended, because some dogs with nasal signs suggestive of LPR could actually have lower airway disease (pneumonia, bronchiectasis, or eosinophilic lung disease) with regurgitation of secretions into the nasopharynx.

Diagnostic Findings

Laboratory testing is unremarkable in affected dogs, and testing for *Bartonella* has not revealed a role for these organisms in idiopathic nasal disease (Hawkins et al. 2008). Current methods to screen for allergy are imprecise and it remains unclear how results of serum or intradermal tests could relate to diseases of the respiratory tract. Imaging is required as part of the diagnostic work-up to help rule out identifiable nasal conditions. Nasal radiography has low sensitivity for differentiating inflammatory rhinitis from neoplasia or mycotic rhinitis, because soft tissue opacification, turbinate destruction, and frontal sinus disease can be seen with all three conditions. Lack of any radiographic abnormalities has also been reported (Lobetti 2014; Kaczmar et al. 2018) A CT scan provides improved definition of the extent and severity of abnormalities in the nasal cavity, although LPR can cause CT lesions that mimic those found with these other conditions (Figure 4.27). Turbinate destruction is found commonly, although it is generally mild or moderate in most cases in comparison to severe findings in sino-nasal aspergillosis. Fluid accumulation, soft tissue opacification, gas pocketing, and frontal sinus involvement are also common CT findings, and abnormalities can be unilateral or bilateral.

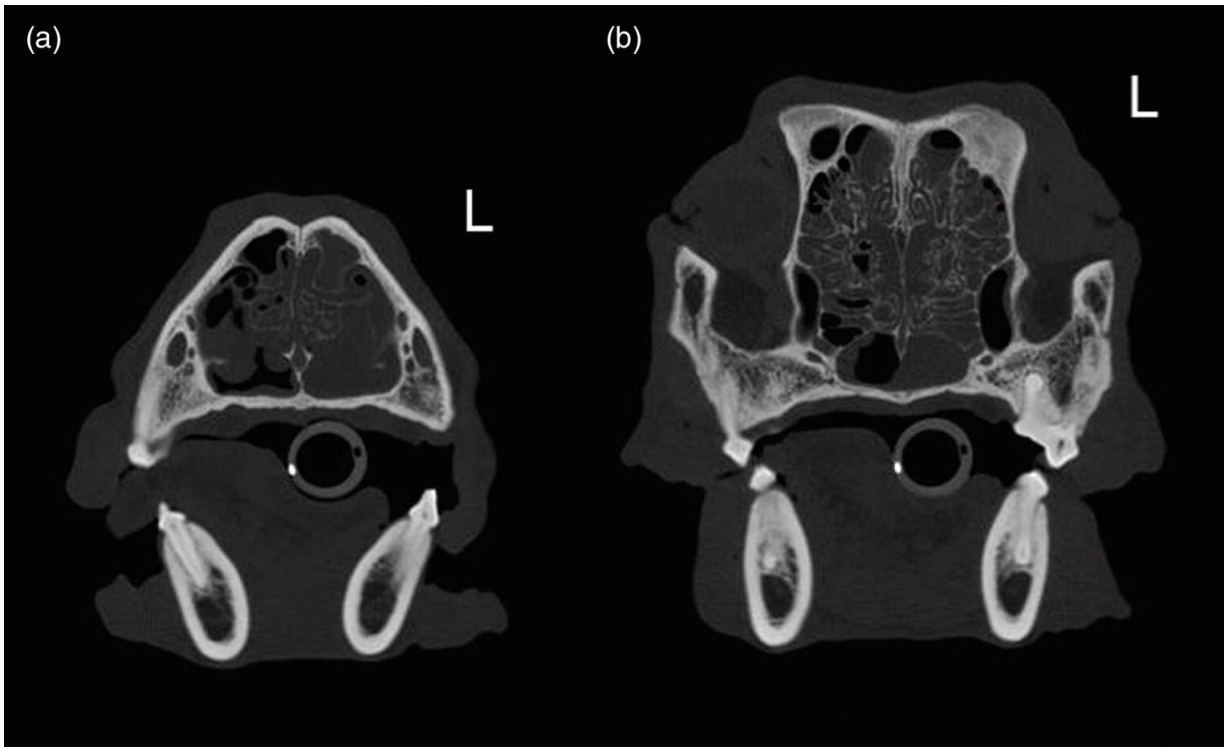


Figure 4.27 Computed tomography findings in a dog with lymphoplasmacytic rhinitis (LPR) more severe on the left side than the right. In image (a) from the rostral nasal cavity, fluid accumulation is noted and turbinate structures are indistinct on the left side. Image (b) is from more caudal in the nasal cavity and demonstrates fluid accumulation bilaterally, but worse on the left. In these images, turbinates appear to be intact.

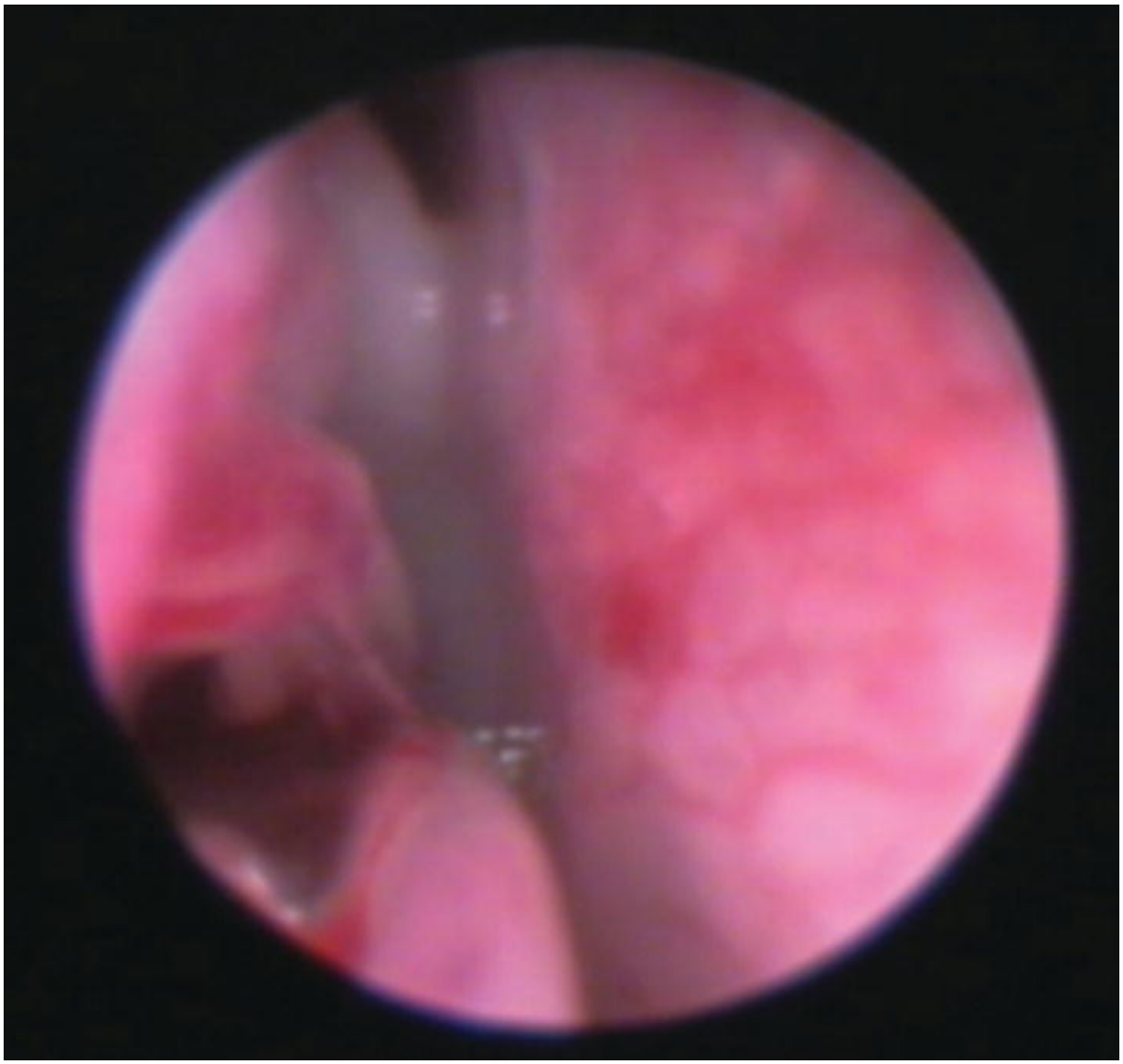


Figure 4.28 Rhinoscopic image from a dog with idiopathic LPR reveals mucosal hyperemia, mucus accumulation, and irregular turbinate structures.

Rhinoscopy typically reveals hyperemic, friable, inflamed epithelium and mucus accumulation (Figure 4.28). Mild turbinate destruction is sometimes seen. Biopsy samples indicate lymphoplasmacytic infiltrates of varying severity, mucosal edema, and bony remodeling of turbinates. Bacterial culture of a nasal swab or flush is rarely of use in determining therapy and is not recommended.

Treatment

Treatment options for idiopathic LPR are limited because the etiology of the disorder remains unclear. Modulatory antimicrobial therapy with long-term doxycycline or azithromycin or anti-inflammatory treatment with piroxicam (0.3 mg/kg PO daily) can be helpful in some dogs, although a guarded prognosis for cure must be given. Anecdotally, some response has been reported for alternate therapies (oral itraconazole; inhaled glucocorticoids). In one report, immune modulation with glucocorticoids, cyclosporine, or allergic desensitization proved effective in some dogs (Lobetti 2014). A study that used a protocol employing sequential administration of prednisone followed by a non-steroidal anti-inflammatory drug (meloxicam) reported cure for up to 6 months in some dogs (Kaczmar et al. 2018), although caution is warranted when using these two drugs in tandem due to potentiated gastrointestinal injury. Airway humidification or oral administration of the mucolytic agent *N*-acetylcysteine can help liquefy nasal secretions and may be beneficial in encouraging mucus evacuation from the nose in some cases. As with cats, antihistamines are not advised because these tend to dry secretions and potentially cause mucus impaction. Attempts can be made to decrease exposure to potential irritants in the environment, including dust in food or food storage mites. Dry food can be placed in an airtight container and moistened before feeding, or alternate food sources investigated. Using canned foods or limited ingredient diets can be considered but evidence of efficacy is lacking.

Prognosis

The etiology of LPR remains obscure, and therefore the efficacy of specific drug therapy cannot be determined. Although not life-threatening, the condition is very frustrating and owners can have difficulty tolerating clinical signs.

Nasal Neoplasia

Pathophysiology

Nasal tumors represent a small percentage of neoplasms in cats and dogs; however, the majority of cases exhibit malignant behavior through local invasion and extension. Tumor types encountered include lymphosarcoma, adenocarcinoma, squamous cell carcinoma, undifferentiated carcinoma or sarcoma, fibrosarcoma, chondrosarcoma, and osteosarcoma, as well as hemangiosarcoma. Lymphosarcoma appears to be the most common nasal neoplasm in the cat and can affect the nasopharynx, the nasal cavity, or both and can also be found as part of systemic disease. In dogs, carcinomas are approximately twice as common as sarcomas. The biologic behavior of most nasal tumors is characterized by bony destruction and local extension, which are ultimately the causes of death or euthanasia in most patients. Metastasis to regional lymph nodes is relatively common, although metastasis to the lung is rare. Nasal lymphoma in the cat can be associated with systemic disease at the time of diagnosis, or some cats can develop systemic lymphoma during or after treatment of nasal disease (Haney et al. 2009).

History and Signalment

Nasal neoplasia is primarily a disease of older dogs and cats; however, young to middle-aged animals (2–5 years) can also be affected and it seems they might often have severe and progressive disease. Clinical complaints are similar to those seen with other nasal disorders and include sneezing, epistaxis, stertorous respirations, or nasal discharge. Discharge is usually unilateral initially but becomes bilateral when the vomer bone is breached. Some animals are presented because of difficulty breathing through the nose or open mouth breathing. Neurologic abnormalities such as seizures, behavioral changes, or cerebral dysfunction can be seen alone or in conjunction with respiratory signs. The presence of these signs is highly suggestive of tumor invasion into the central nervous system and warrants a guarded prognosis.

Physical Examination

Nasal discharge (unilateral or bilateral) with loss of nasal airflow is a common finding, and facial deformity can be observed (Figure 4.29).

Unilateral epiphora or a mass protruding from the nostril seems to occur more commonly in cats than in dogs. Nasal tumors can result in differential ocular retropulsion when the tumor grows up the optic tract. When neoplasms extend caudally, they can sometimes be felt above the soft palate in the nasopharyngeal region. Regional lymphadenopathy is an important clinical finding because this is a common site for metastasis. It is important to remember, however, that metastasis can be present in the absence of palpable lymph node enlargement.



Figure 4.29 Facial asymmetry is evident in this 9-year-old male castrated domestic short hair (MC DSH) presented for evaluation of nasal discharge. The right eye is displaced laterally and dorsally by a mass effect. Tear staining is evident near the right eye and the nictitating membrane is elevated. Necropsy revealed lymphoma filling the right nasal cavity, nasopharynx, and retrobulbar space with extension into the olfactory lobe and cerebrum.

Diagnostic Findings

General laboratory tests are usually unremarkable. Fine-needle aspiration of the lymph node ipsilateral to the discharge is recommended in an animal with loss of nasal airflow, because

cytology could reveal neoplastic cells and provide a diagnosis prior to more expensive or invasive diagnostics.

Skull radiographs reveal unilateral or bilateral increased soft tissue density in the nasal cavity, destruction of turbinate structures, or vomer lysis. The frontal sinus is sometimes filled with soft tissue or fluid density, or a fluid line may be visible. This can indicate either tumor in the sinus or fluid accumulation due to obstruction of the nasofrontal ostium. A CT scan is more useful than radiography for determining tumor boundaries, assessing the integrity of the cribriform plate to investigate central nervous system involvement, and planning radiation therapy (Figure 4.30). Rhinoscopy typically reveals a mass lesion protruding between the turbinates (Figure 4.31), although in some cases only swollen or deformed turbinates are seen. Obtaining a biopsy sample while visualizing the abnormal region rhinoscopically is important for confirming the diagnosis with histopathology.



Figure 4.30 Computed tomography image from a 9-year-old spayed female (FS) Doberman with a 2-month history of left-sided epistaxis. An expansile soft tissue mass with regions of mineralization fills the rostral left nasal cavity. There is erosion of the maxilla and hard palate on the left side and erosion through the septum into the right nasal cavity. Histopathology confirmed nasal osteosarcoma.

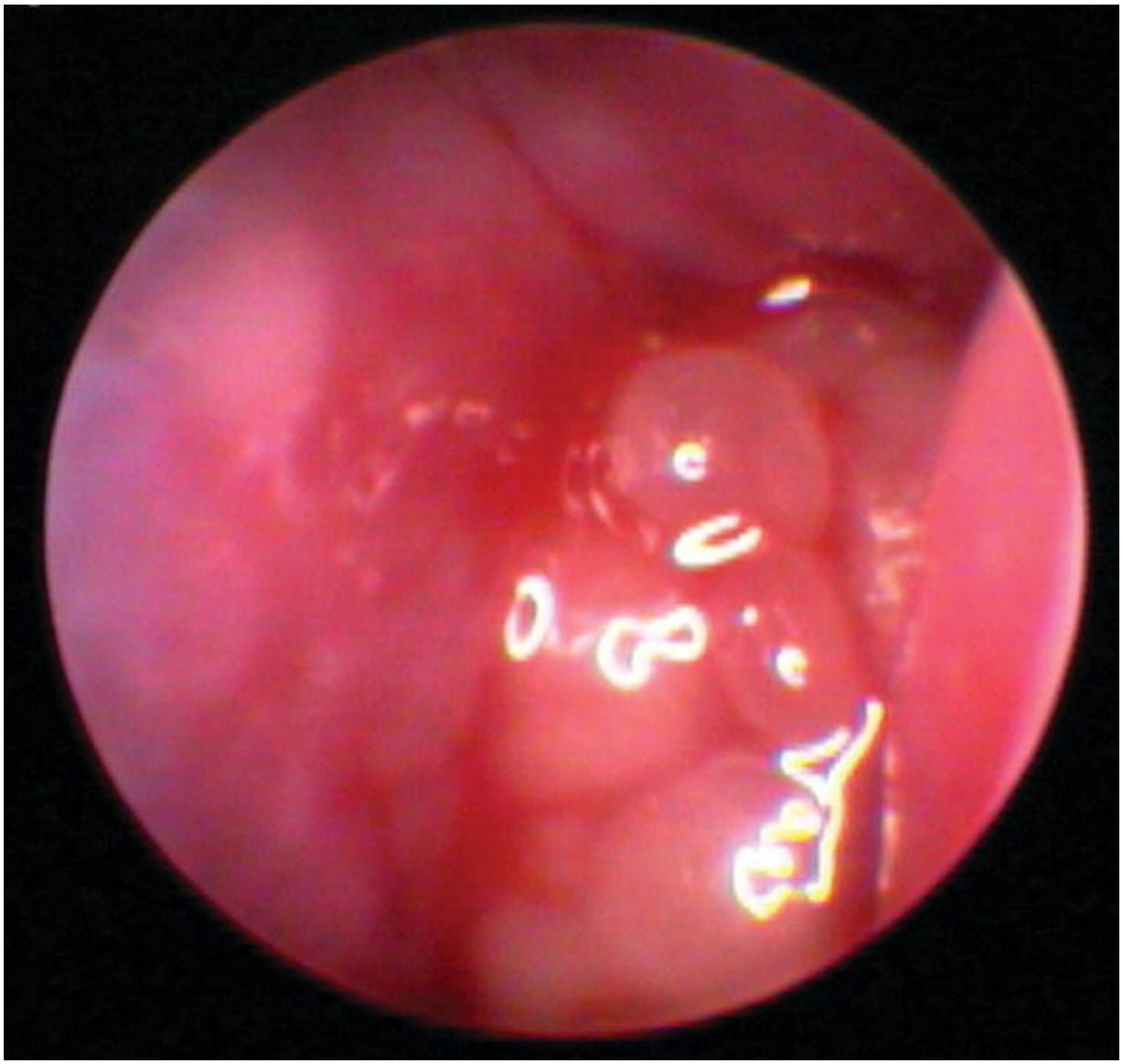


Figure 4.31 Rhinoscopic image from a dog with nasal neoplasia reveals a soft tissue mass protruding between turbinates in the nasal cavity.

When rhinoscopy and biopsy are not available, saline hydropulsion can be attempted to obtain a sample for histopathology. Ideally, CT would be performed before this to ensure the integrity of the cribriform plate, but regardless, owners should be warned of the possibility of untoward neurologic sequelae following this technique because of pressure build-up in the nasal cavity that is transmitted through the cribriform plate to the central nervous system. Prior to hydropulsion, an adequate seal on the cuff of the endotracheal tube

is ensured to prevent aspiration of the material used for the flush, and a Poole suction tip is placed in the oral cavity to collect material. A 60 ml catheter tip syringe containing room-temperature saline is inserted into one nostril, taking care to direct the tip ventrally to direct fluid into the ventral nasal meatus. The alternate nostril is occluded and firm pressure is used to eject the contents of the syringe rapidly over 1–2 seconds (Ashbaugh et al. 2011). The process is repeated in the other nostril, and two to three sequences of hydropulsion can be performed. If successful, resistance to flush will dissipate and tissue material will be found in the oral cavity. Epistaxis and tissue swelling or exophthalmos can occur after hydropulsion, but obstructed breathing can be alleviated with this technique and adequate tissue obtained for histopathology.

Treatment

The most commonly employed treatment of nasal tumors is radiation therapy, because surgery does not resolve signs or result in improved survival. Both palliative and definitive radiation therapy protocols have been reported to control clinical signs of nasal discharge and epistaxis, although stereotactic radiation therapy is preferred because it spares surrounding tissues. Novel therapeutics including cryotherapy and chemoembolization are available at some referral or university hospitals and can also provide long survival with improved quality of life. Nasal lymphosarcoma in the cat is treated with standard chemotherapeutic protocols for lymphoma, radiation therapy, or a combination of the two treatment modalities. Chemotherapeutic protocols for other nasal tumors remain under investigation, with encouraging results reported for use of alternating doxorubicin and carboplatin every 3 weeks (Woodruff et al. 2018) and for oral toceranib phosphate (~2.6 mg/kg on Monday, Wednesday, Friday), although median survival time was only 139 days (Merino-Gutierrez et al. 2023). Palliation of clinical signs can be achieved by use of piroxicam (0.3 mg/kg/day). Addition of cyclophosphamide (10 mg/m^2 daily to every other day) and doxycycline for metronomic chemotherapy might improve clinical response, but can be associated with more side effects. Yunnan baiyao can be employed to assist with control of epistaxis.

Prognosis

The goal of radiation therapy is to control or limit clinical signs, not to provide cure. In dogs, median survival times of 9–23 months have been reported for various tumors using different protocols and variable types of radiation. In some studies, dogs with nasal sarcomas have lived longer than dogs with carcinomas, and in some studies, dogs with facial distortion have poorer survival, as do cats (Giuliano and Dobson 2020). Even palliative courses of radiation (4–6 weekly or biweekly sessions) can result in median survival times of close to a year in cats with nasal carcinomas (Giuliano and Dobson 2020). Side effects of radiation therapy are predictable and expected, because the radiation dose required to kill tumor cells will kill normal cells that undergo rapid cell division, such as epithelial cells. Early side effects include mucositis, conjunctivitis, and moist desquamation of skin. Ocular lubricants can be used, but specific treatment of the skin is not recommended. If mucositis causes anorexia, cold tea mouth rinses may make the animal more comfortable. In severe cases, placement of an esophageal tube might be considered to provide nutrition. Late effects of radiation therapy are generally irreversible and include bone necrosis, cataracts, and KCS.

Cats with nasal or nasopharyngeal lymphoma can experience up to 2.5 years of progression-free disease and prolonged survival when treated with radiation and/or chemotherapy, although systemic disease can develop despite local control (Sfiligoi et al. 2007; Haney et al. 2009). It appears that inclusion of local radiation treatment improves median survival time due to better control of tumor growth, with higher doses resulting in longer local disease control (Haney et al. 2009).

Other Nasal Diseases

Xeromycteria (“Parasympathetic Nose”)

Pathophysiology

Xeromycteria or dry nose syndrome is due to loss of efferent parasympathetic innervation carried within the facial nerve to the pterygopalatine ganglion and the trigeminal nerve to the lateral nasal gland, which is responsible for the production of serous secretions that line the turbinates. The nasal mucosa responds to the loss of fluid secretions with hyperplasia of mucus-producing cells, leading to chronic thick nasal discharge that is typically unilateral.

Disruption or damage to the parasympathetic nerve supply due to trauma, infection, or neoplasia can occur anywhere along the nerve pathway or in the brainstem, and disease can be associated with Horner's syndrome or facial paralysis. Often the disease is idiopathic but it can originate from the middle or inner ear canal, and this syndrome has developed due to otitis media or vigorous ear cleaning (Matheis et al. 2012; Wegg 2019). Central nervous system neoplasia can also be associated with xeromycteria and has a more guarded prognosis than peripheral causes. Neurogenic KCS is typically found in association with xeromycteria when the site of injury is prior to the pterygopalatine ganglion.

History and Signalment

Any age or breed can be affected, although it seems to occur more often in middle-aged, female dogs. Some animals have a history of chronic ear disease or recent ear cleaning. Others might have signs consistent with central nervous system disease.

Physical Examination

Disease is typically unilateral, with crusting discharge obstructing the nasal cavity. Decreased sensation at the opening of the naris might be appreciated using palpation with a cotton tipped applicator, although this is difficult to determine. Otic examination is important for assessing the patency of the tympanic membrane as well as identifying evidence of otitis media. The ipsilateral cornea might also appear dry.

Diagnostic Findings

Other disease processes causing unilateral nasal discharge must be excluded when considering this diagnosis. CT or magnetic resonance imaging (MRI) of the skull is advisable to detect middle or inner ear disease, to exclude central nervous system disease, and to investigate local nasal disease. Schirmer tear testing often reveals an absence of tear production in the ipsilateral eye when neurogenic KCS is present.

Treatment

Oral pilocarpine (1–2%) has been used with some success in managing xeromycteria. This drug is a direct-acting parasympathomimetic with effects on the nasal lacrimal gland. Typical oral dosing starts at 1 drop of 2% pilocarpine per 10 kg body weight on a dog treat, with dose escalation until clinical signs improve or until signs of toxicity (salivation, bradycardia, urination, or diarrhea) are observed (Matheis et al. 2012; Wegg 2019). Time to improvement can be 3 months or longer and duration of treatment is unknown. If dry eye is present concurrently, ocular lubricants should be applied. If the dorsum of the nose is dry and crusted, use of a keratolytic humectant gel can be soothing.

Prognosis

Large-scale studies of this disorder are lacking. Cases associated with defined central lesions have a guarded prognosis, while those associated with aural injury or unknown causes can sometimes be cured with chronic therapy.

Pneumonyssoides caninum (Nasal Mites)

The nasal cavity and nasopharynx of dogs can be infested by nasal mites (Figure 4.32), which cause irritation and intense but intermittent reverse sneezing. Occasionally dogs will also display mild serous nasal discharge or pawing at the muzzle. The life cycle and transmission of nasal mites is unclear; however they can be a household infestation.

Definitive diagnosis requires identification of the mites in the nasopharynx on retroflex examination or in the nasal cavity; however this can be challenging because the mites rapidly move away from any light source. Occasionally mites will be found on the exterior of the dog's nose during anesthesia because inhalation anesthetics cause them to move out of the nasal cavity. A presumptive diagnosis of nasal mites can be made if reverse sneezing resolves following treatment with selamectin (6–24 mg/kg topically every 2 weeks for 3 treatments), ivermectin (200–400 μg/kg PO or SC once weekly for 3 treatments), or milbemycin (0.5–1.0 mg/kg once weekly for 3 treatments) in collie-type dogs. All in-contact dogs should be treated to avoid re-infection.

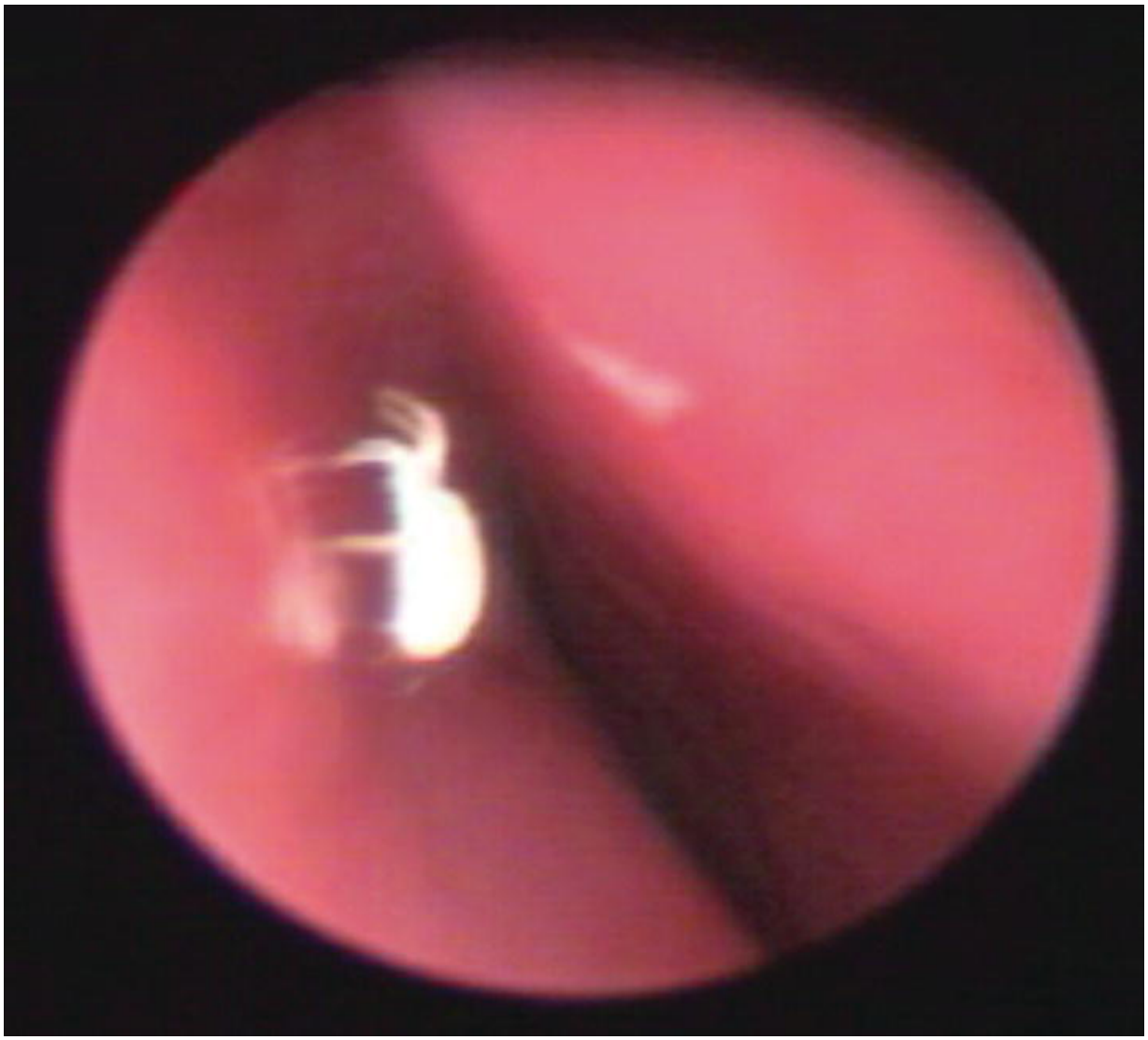


Figure 4.32 Nasal mite found in the nose of a dog presented for reverse sneezing.

Clinical Case

A 3-year-old spayed female (FS) Husky was presented for evaluation of a 15 month history of hemorrhagic nasal discharge, congestion, and difficulty breathing. On physical examination, the dog was bright and alert, euhydrated, with normal body temperature (101.7°F [38.7°C]), pulse (80), respiratory rate (panting), and a BCS of 7/9 (weight 30.9 kg). She had bilateral epistaxis with decreased nasal airflow. Regional lymph nodes

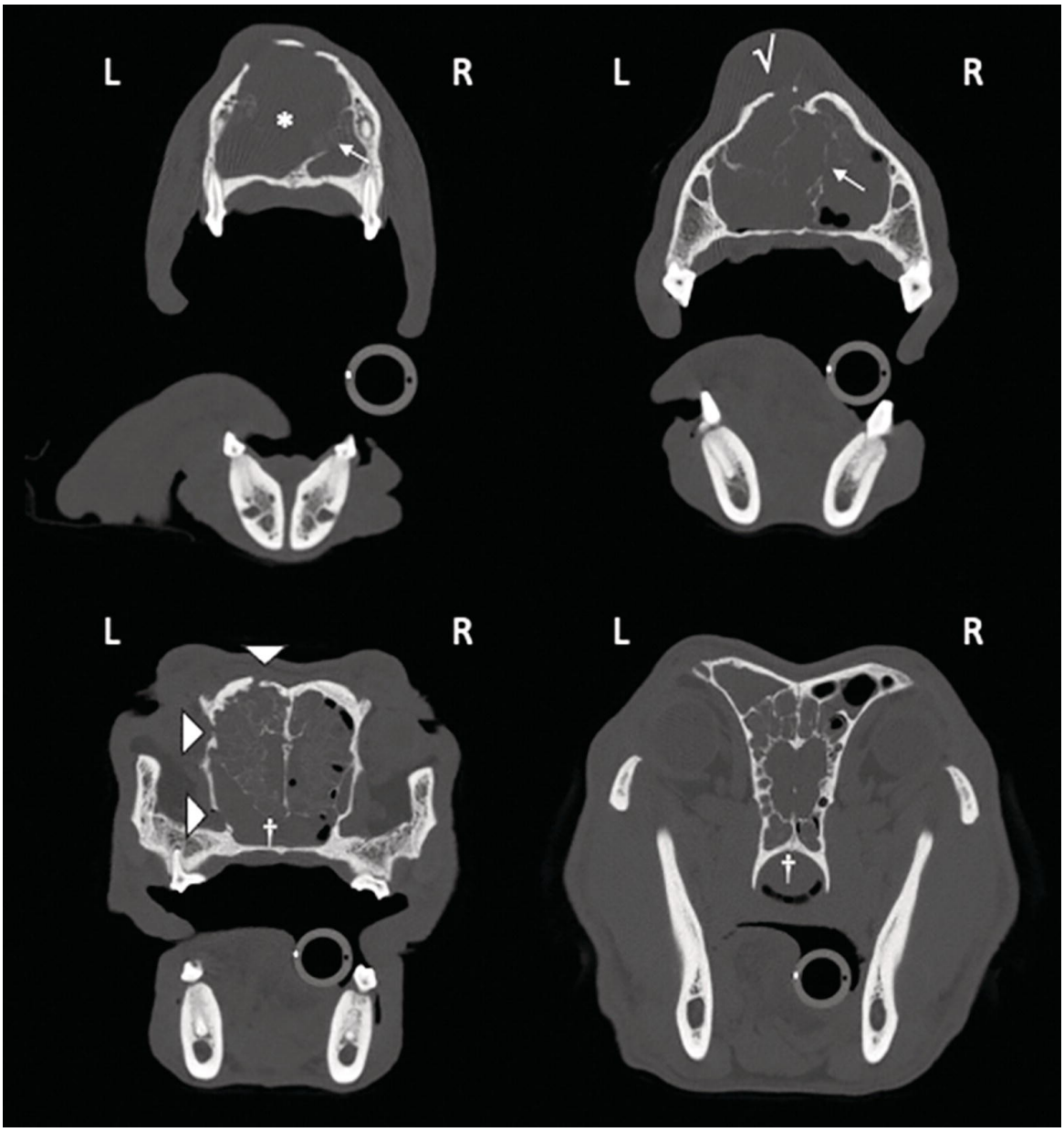
palpated within normal limits, ocular retropulsion was normal, and oral examination was not possible due to patient demeanor. There was moderate episcleral injection OS with bloody discharge and bloody crusting around the medial canthus OS.

Based on history and physical examination, a nasal obstructive lesion was considered most likely, causing blockage of both nasal cavities and the nasolacrimal duct on the left side. Differential diagnoses in this age and breed of dog included atypical fungal disease or foreign body causing a mass effect in the nose, polypoid rhinitis, and neoplasia (carcinoma versus lymphoma versus other). Baseline bloodwork, a *Cryptococcus* antigen test, ophthalmology consultation, and skull CT followed by rhinoscopy were recommended. The owner elected to pursue only the cryptococcosis IMMY lateral flow test, which was negative. [The IMMY CrAg® LFA (Cryptococcal Antigen Lateral Flow Assay) is the first and only immunochromatographic dipstick assay for the qualitative and semi-quantitative detection of the cryptococcal capsular antigen in serum, plasma, whole blood and cerebrospinal fluid (CSF).]

Two months later, the dog was re-presented due to continued epistaxis and development of a swelling on the left side of the nasal bridge, near the medial canthus OS. Other than the swelling on the nose, physical examination was unchanged and diagnostic tests were pursued. CBC showed a mild leukocytosis (17 460 cells/µl, RI 6–13 000) characterized by a mild neutrophilia (14 260/µl, RI 3–10 500). Chemistry panel showed mild hypoalbuminemia (3.1 g/dl, RI 3.4–4.3).

Computed tomography (Case Figure 1) revealed a large, heterogeneously contrast enhancing, mixed soft tissue and fluid attenuating mass (*) effacing the left nasal cavity and pushing the septum into the right nasal cavity (arrow). This mass also extended into the left maxillary recess, the left frontal sinus, the sphenoidal sinuses, the choana, and the rostral nasopharynx (†). There were multifocal osseous defects involving the hard palate, medial wall of the left infraorbital canal, and the rostral aspect of the medial wall of the left orbit (arrowhead). There was extension of cystic components of the mass through the osseous defects in

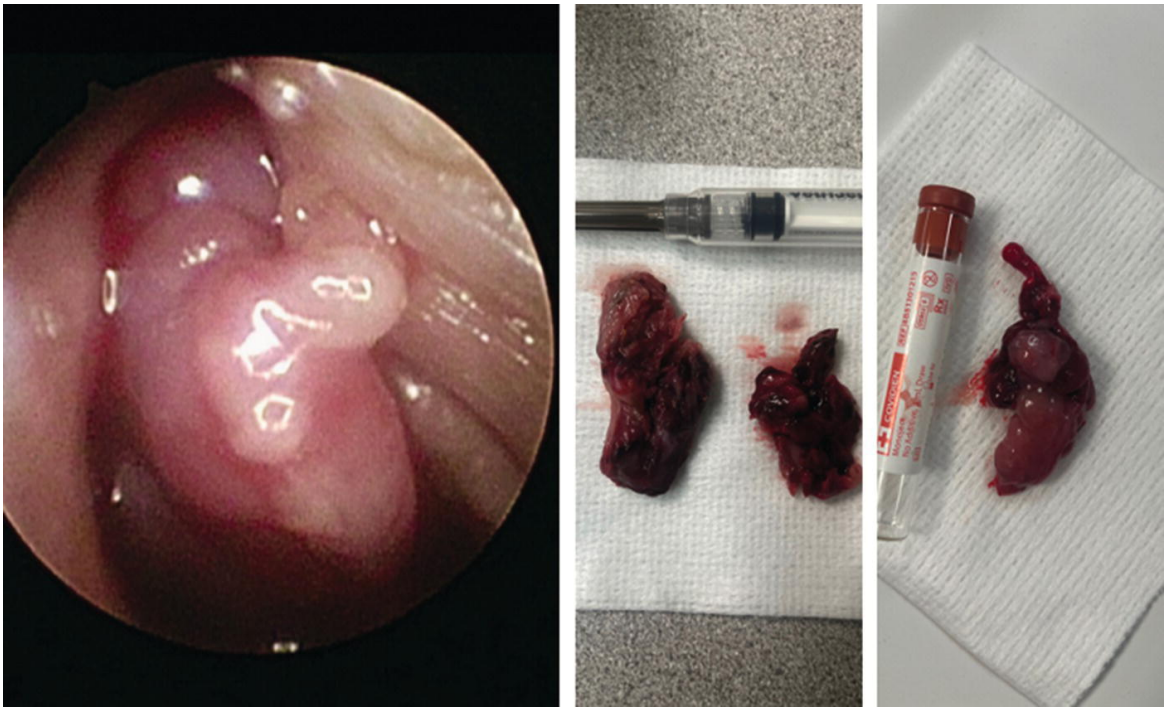
the left nasal bone and rostral frontal bone, causing marked focal bulging of the cutaneous margins (√). Multifocal permeative lysis of the osseous margins of the left frontal sinus was evident along with a defect present in the caudal aspect of the septum of the frontal sinus. Fluid attenuating, faintly peripherally contrast enhancing tissue was protruding through the septal defect into the right frontal sinus. The cribriform plate was intact.



Case Figure 1 Computed tomography.

Rhinoscopy (Case Figure 2) indicated extensive proliferation of polyploid cystic structures in the left nasal passage extending to the level of the nasopharynx. Multiple polyploid tissue structures were removed using biopsy forceps. The soft tissue structure on top of the nose could be reduced into the nasal cavity with gentle pressure, and this was also extracted via a rostral approach. An 8–10 mm circular defect was palpable on the top of the nose.

Biopsy of the removed nasal tissues revealed hemangiosarcoma, a tumor that rarely occurs intranasally and therefore, has an uncertain clinical course. Thoracic radiographs and abdominal ultrasound were recommended to investigate metastatic disease, along with consultation with radiation oncology for palliative radiation, but the owner declined. The dog was discharged on carprofen at 3.6 mg/kg/day divided BID for pain, along with Yunnan baiyao to limit nasal bleeding.



Case Figure 2 Rhinoscopy.

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5
Diseases of Airways

Structural Disorders

Laryngeal Paralysis

Pathophysiology

In normal animals, the dorsal cricoarytenoideus muscles contract to abduct the corniculate processes of the arytenoids during inspiration, causing opening of the rima glottidis. This muscle is innervated by the recurrent laryngeal nerve, a branch of the vagus that originates near the thoracic inlet and loops around the subclavian artery on the right side, or the aorta on the left side, and returns craniad to the larynx. Laryngeal paralysis is recognized as a congenital disorder or heritable disease in some breeds and as an acquired form in older, large breed dogs. Some breeds that develop congenital laryngeal paralysis are affected by a generalized polyneuropathy (Table 5.1), and in the acquired idiopathic form, several studies have now confirmed the generalized nature of the neurologic deficits. Electromyographic studies and nerve conduction velocities in peripheral limb musculature of dogs with acquired laryngeal paralysis are suggestive of axonal disease (Jeffrey et al. 2006; Thieman et al. 2010). It has been recognized that affected older, large breed dogs often display clinical signs and physical examination findings of esophageal dysfunction and decreased proprioceptive placing, supporting a more generalized neurologic defect (Stanley et al. 2010). Laryngeal sensation is also abnormal. This syndrome has been labeled geriatric-onset laryngeal paralysis–polyneuropathy (GOLPP).

Laryngeal paralysis can also result from trauma during surgery that disrupts neural transmission (thyroidectomy, repair of a patent ductus arteriosus, or tracheal ring placement), bite wounds, strangulation, or crush injuries. A mediastinal mass, granuloma, or hemorrhage compressing the recurrent laryngeal nerve can also lead to unilateral or bilateral laryngeal paralysis.

In animals with laryngeal paralysis, active contracture to open the glottis is depressed or lost, and this can be unilateral or bilateral. When unilateral, it appears that the left side is affected more commonly or earlier than the right side (Johnson 2016). Inspiration against a narrowed glottis results in a pressure drop across the larynx, and turbulent velocity of airflow causes irritation of the mucosa. This leads to mucosal edema and further obstruction of airflow. The larynx serves as an important protective mechanism against pulmonary inhalation of damaging substances. During swallowing, the palate contracts to close off the nasopharynx, the lateral walls of the pharynx propel the bolus toward the esophagus while the laryngeal folds and cartilages adduct, and the epiglottis moves caudally to block the larynx and prevent aspiration. Defects in any part of the process can lead to tracheal or lower airway injury from aspiration. It appears that some dogs with laryngeal dysfunction experience sensory as well as motor loss and this likely contributes to silent aspiration of oropharyngeal or gastroesophageal contents that leads to cough. It is common for dogs with laryngeal paralysis to accumulate secretions around the glottis, resulting in gagging or retching.

Table 5.1 Congenital forms of laryngeal paralysis.

Breed	Age of onset	Sex	Mode of inheritance	Additional findings	Reference
Dalmatian	2–6 months	Male = female	Autosomal recessive	Megaesophagus Polyneuropathy	Braund et al. (1994)
Rottweiler	9–13 weeks	Male > female	Unknown	Polyneuropathy Cataracts	Mahony et al. (1998)
Great Pyrenees	2–6 months		Autosomal recessive (postulated)	Megaesophagus Polyneuropathy	Gabriel et al. (2006)
Bouvier des Flandres	4–6 months	Male > female	Autosomal dominant	Neuronal degeneration in the recurrent laryngeal nerve	Venker van-Haagen et al. (1978)
Siberian Husky and mix	4–6 months		Unknown		O'Brien and Hendricks (1986)
White German Shepherd	9–24 months		Possibly linked to white haircoat		Ridyard et al. (2000)
Leonberger	1–3 years	Male > female	X-linked polygenic disorder	Polyneuropathy	Hultin Jaderlund et al. (2011)
Alaskan Husky	3–6 months		Suspect autosomal recessive	Phenotype: blue eyes and white facial markings	von Pfeil et al. (2018)

Cats are also affected by congenital or acquired laryngeal paralysis, but it is less commonly recognized clinically because they are less physically active and regulate activity to avoid respiratory distress associated with inspiratory obstruction of airflow.

History and Signalment

Laryngeal paralysis results in inspiratory difficulty, reduced vocalization or a change in sound of the bark/meow, excessive or loud panting, gagging, and retching. Exercise intolerance may be the first abnormality noted and can be mistaken as a sign of aging in large or Retriever breeds. Signs are worsened by heat, stress, excitement, or exercise, and severely affected animals can suffer syncope or cyanosis. Careful questioning of the owner is recommended to uncover concurrent esophageal or gastrointestinal dysfunction, because the combination of regurgitation or vomiting with laryngeal disease or laryngeal surgery enhances the risk for aspiration pneumonia.

The acquired form of laryngeal dysfunction results in clinical signs late in life (10–14 years of age), and traumatic or iatrogenic injury to the larynx during surgery can result in development of signs at any age. Purebred animals with congenital disease are young when signs are first recognized, although the disease in Shepherds and some Leonbergers has a slightly later onset (Table 5.1).

Physical Examination

In some animals with laryngeal disease, upper airway auscultation is difficult because of continual panting. Inspiratory stridor audible over the larynx is the classic finding on physical

examination; however, this can be very subtle or even non-existent in many dogs. Gently exercising the patient to increase respiratory effort might elicit stridorous sounds. Caution is warranted to avoid overheating because some dogs, particularly those that are obese, can develop life-threatening hyperthermia caused by excessive work of breathing.

Dogs with generalized neuromuscular disease can also display limb weakness exhibited by decreased proprioceptive placing, particularly in the rear limbs. Surprisingly, this finding can sometimes be lateralizing, affecting only the left or right pelvic limb. The nail beds on the rear limbs should be examined for scuff marks on the dorsal aspect consistent with dragging of the toes. Less commonly, a depressed gag or tongue reflex can be detected during oral stimulation (Jeffrey et al. 2006). A full neurologic assessment is important in dogs with idiopathic laryngeal paralysis, because dogs with signs related to a peripheral neuropathy can suffer continued weakness or exercise intolerance despite surgical treatment of laryngeal obstruction.

Diagnostic Findings

There are no specific laboratory findings associated with laryngeal paralysis. A complete blood count (CBC) should be screened for neutrophilic leukocytosis suggestive of aspiration pneumonia, and a chemistry panel and urinalysis are performed to exclude systemic disease. Several studies have ruled out an association of thyroid dysfunction with laryngeal paralysis and testing is not advocated unless concurrent clinical signs (obesity, hair coat abnormalities) or laboratory testing (non-regenerative anemia, hypercholesterolemia) suggest hypothyroidism. If an arterial blood gas is performed, mild hypoxemia might be detected, but the more obvious finding anticipated is hypercapnea associated with alveolar hypoventilation (see Chapter 2). In a dog with normal lung function, the alveolar-to-arterial oxygen gradient should be normal.

The differential diagnosis list for laryngeal paralysis includes laryngeal neoplasia, granuloma, foreign body, or inflammatory laryngitis. Cervical radiographs can be helpful in ruling out a laryngeal mass but are sometimes difficult to interpret due to overlapping structures or lack of proper alignment. Indirect evidence of upper airway obstruction can be seen as caudal retraction of the hyoid apparatus, and air in the laryngeal folds is also somewhat common, but non-specific (Figure 5.1). Thoracic radiographs are recommended to assess the esophagus and to document evidence of aspiration pneumonia. If vomiting or regurgitation is in the history, videofluoroscopic assessment of swallowing should be considered, because defective esophageal function could impact the decision to pursue anesthesia and surgery.



Figure 5.1 Right lateral cervical radiograph of a 9-year-old male castrated (MC) Labrador Retriever with stridor reveals caudal retraction of the larynx and hyoid apparatus as well as air in the laryngeal folds consistent with an upper airway obstruction.

Laryngeal ultrasound is useful in some instances to rule out a mass lesion, and an experienced examiner can document inadequate or inappropriate laryngeal motion during inspiration. It is important that an assistant distinguishes inspiration from expiration during the evaluation to ensure that the correct phase of respiration is assessed.

Diagnosis of laryngeal paralysis requires visualization of laryngeal motion under a light plane of anesthesia. The animal is placed in sternal recumbency, pre-oxygenated, and a combination of propofol–midazolam or alfaxalone–midazolam is titrated to the dose that allows the mouth to be opened safely while preserving respiratory maneuvers. An assistant identifies inspiratory effort while the examiner watches for abduction of the arytenoids. If appropriate laryngeal function is not visualized initially, doxapram hydrochloride (1.0 mg/kg) can be administered intravenously as a bolus to stimulate respiration. Additional anesthesia is usually required at this point, because doxapram is stimulatory and will arouse the animal from anesthesia. It is important that laryngeal abduction is matched with inspiratory effort, because paradoxical laryngeal motion can occur and confuse interpretation of the exam as the laryngeal cartilages are moving but are not in sync with respiration. In that situation, the cartilages of the larynx are pulled inward by inspiratory effort (rather than being abducted) and then passively open on expiration, which is mistaken for normal motion. In addition to lack of motion, signs of laryngeal inflammation are often present in animals with laryngeal paralysis, such as hyperemia and accumulation of secretions ventral or lateral to the larynx (Figure 5.2).



Figure 5.2 Endoscopic image of an 11-year-old male castrated (MC) Labrador Retriever shows dramatic hyperemia of the larynx and accumulation of mucoid secretions lateral to the larynx and ventral to the epiglottis.

While a definitive diagnosis of laryngeal paralysis is important for establishing prognosis for the patient, performing laryngoscopy simply to confirm paralysis is not always wise, because dogs with laryngeal disease are at risk for aspiration pneumonia or pneumonitis. This risk is accentuated by respiratory depression associated with anesthesia. If the dog has experienced several episodes of heat stroke and potential complications have been discussed with the owner, it is generally prudent to plan for surgical intervention at the time of diagnostic laryngoscopy.

Treatment

Laryngeal paralysis that is causing poor quality of life is treated by surgically opening one side of the larynx in a permanent fashion. Dogs with unilateral laryngeal paralysis can usually tolerate the degree of dysfunction that results from partial airway obstruction and are not candidates for surgery. Cats, however, can be severely impacted by even unilateral paralysis. Some dogs with bilateral paralysis can maintain a good quality of life when lifestyle is altered. An inflatable collar can help maintain the head in an upright position, and a harness should be used in place of a leash around the neck. Weight loss to achieve a body condition score of 4–5/9 is desirable and restricted activity during hot or humid weather should be strictly enforced. Altered feeding strategies can be helpful to alleviate the esophageal dysfunction that is common in dogs with laryngeal paralysis. Food and water should be positioned at head height to aid in passage down the esophagus. It is generally best to avoid liquid food and use soft food or meatball feedings of moistened kibble. If drinking water leads to gagging or coughing, it can be beneficial to use crushed ice or ice cubes. Addition of a product such as Thick-It® (Kent Precision Foods, Muscatine, IA) to water can create a consistency of liquid that is easier for the dog to prehend and swallow completely. Some dogs with laryngeal paralysis will also suffer from gastroesophageal reflux and the use of omeprazole and sucralfate should be considered in certain instances. Motility modifiers such as metoclopramide and cisapride are generally ineffectual and sometimes contraindicated because of the potential to increase the pressure of the lower esophageal sphincter (cisapride), which would be deleterious in a dog with esophageal dysfunction or megaesophagus. Perioperative use has not improved outcome.

Dogs that present with acute signs related to laryngeal paralysis are at risk for heat stroke. If witnessed at home, owners should be instructed to douse the animal in water prior to transporting to the veterinary clinic. In dogs that are hyperthermic, active cooling with fans and cool water should be continued until body temperature reaches 102°F (38.9°C). At that point, fans should be withdrawn to avoid an excessive drop in core body temperature that could trigger vasoconstriction. Judicious use of sedatives – acepromazine at 0.01–0.02 mg/kg intravenously (IV), butorphanol at 0.2–0.4 mg/kg IV – and oxygen should be employed, and a single dose of a short-acting glucocorticoid (dexamethasone SP at 0.05–0.2 mg/kg IV) can be used to reduce laryngeal edema. If these measures fail to alleviate distress, intubation or a temporary tracheostomy might be required, although the latter could predispose to complications. When anesthesia is administered, laryngeal motion should be assessed as the animal inspires to confirm the diagnosis of laryngeal paralysis.

For animals with bilateral laryngeal paralysis, the decision to go to surgery is based on the quality of life of the dog, the severity of clinical signs, and the time of the year. Dogs that can be maintained in a comfortable state can generally wait until spring or summer for a decision regarding surgery. Warmer weather causes dogs to breathe harder despite less physical exertion and this leads to worsened inflammation and edema, augmenting airway obstruction and necessitating surgery. Alternately, some clinicians advocate for early surgical intervention for laryngeal paralysis to prevent stiffening of the cartilage that might increase the difficulty of surgery or affect outcome. Unilateral arytenoid lateralization is currently the surgery of choice for animals with severe clinical signs related to bilateral laryngeal paralysis. Partial laryngectomy and vocal fold resection have also been employed. Use of opioids postoperatively can lead to excessive sedation and complications, therefore use of a local anesthetic line block at surgery to provide postoperative analgesia is preferred.

Prognosis

Dogs with GOLPP can have progressive neurologic signs, with rear limb weakness, hypotonia, hyporeflexia, and loss of muscle mass that worsen ambulation. Dysphagia and

megaesophagus can lead to malnutrition and further impact quality of life. Some of these complications can be managed with physical therapy and dietary modifications but some animals become very debilitated, necessitating euthanasia.

Aspiration pneumonia is the most common complication following arytenoid lateralization and can be seen in 20–30% of patients. It can occur immediately postoperatively or up to 3 years after surgery. Factors significantly associated with a higher risk of developing aspiration pneumonia include preoperative aspiration pneumonia, esophageal disease, temporary tracheostomy placement, and concurrent neoplastic disease (MacPhail and Monnet 2001). However, most dogs survive postoperative aspiration pneumonia with appropriate therapy, and owners are ultimately pleased with the clinical outcome following arytenoid lateralization. Measures to prevent aspiration should be instituted, because chronic recurrent aspiration injury can lead to bronchiectasis or persistent pneumonia that also requires management. Other complications following surgical treatment of laryngeal paralysis include suture failure leading to acute upper airway obstruction and incisional seroma.

Norwich Terrier Upper Airway Syndrome

Pathophysiology

Norwich Terrier upper airway syndrome (NTUAS) is a congenital and likely heritable condition affecting many Norwich Terriers in the USA and Europe. Although these dogs are not phenotypically brachycephalic, they have laryngeal malformation with collapse that is likely the primary defect. Narrowing of the laryngeal aditus creates a large pressure gradient across the airway opening that leads to secondary changes of laryngeal ventricular eversion, tonsillar enlargement, redundant supra-arytenoid folds, inflammation, and laryngeal collapse (Figure 5.3). A mutation in the gene for ADAMTS3 metallopeptidase enzyme, responsible for promotion of lymphangiogenesis, could make Norwich Terriers predisposed to develop this exuberant soft tissue swelling because of lymphedema (Marchant et al. 2019). Rarely, soft palate elongation or minor tracheal collapse can be observed in affected dogs. Some dogs have concurrent malformations in the nasopharynx, which might be congenital or could develop due to foreign body entrapment above the palate associated with mishandling of material in the oral cavity associated with airway obstruction.

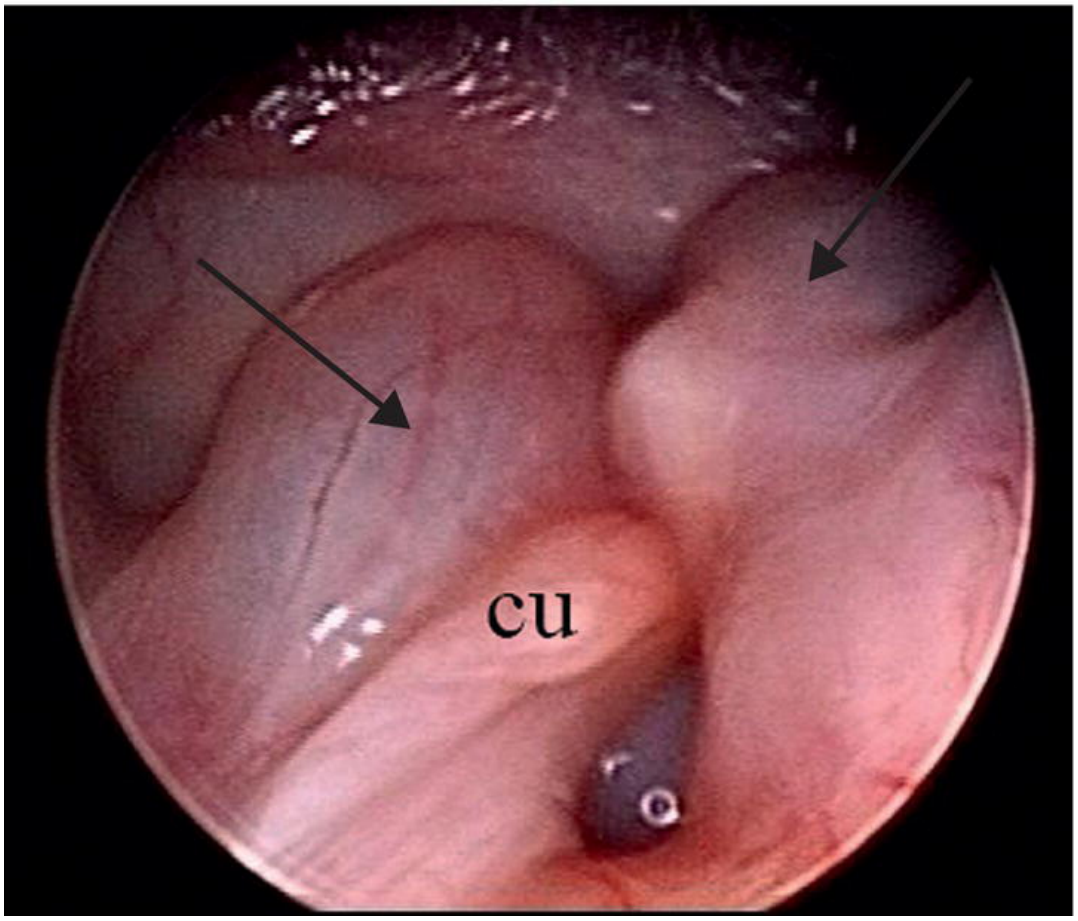


Figure 5.3 Laryngoscopic image from a 1-year-old Norwich Terrier with inspiratory stridor. Cuneiform processes of the larynx (cu) are displaced medially, indicating laryngeal collapse. Redundant supra-arytenoid tissue is indicated by the arrows. Laryngeal ventricular eversion can be seen below the cuneiform process.

History and Signalment

Affected dogs often have a history of noisy breathing, snoring, excessive panting, or exercise intolerance; however, some dogs display no clinical signs despite substantial upper airway changes. Severely affected dogs can be presented to the veterinarian for collapse or cyanosis due to airway obstruction. Cough is occasionally part of the clinical history and could be related to laryngeal irritation or low-grade aspiration injury.

Physical Examination

Upper airway auscultation can reveal stertor and stridor in some dogs, although the absence of these abnormalities does not indicate the lack of pathology. In one small study, 4 of 12 dogs with respiratory complaints had a normal physical exam, as did 4 of 4 dogs lacking respiratory complaints (Johnson et al. 2013). However, 6 of these 8 dogs without physical examination abnormalities had severe manifestations of disease identified during laryngoscopic examination.

Diagnostic Findings

Cervical radiographs can reveal an indistinct quality to the larynx suggestive of edema or inflammation, but the diagnosis and grading of laryngeal abnormalities requires laryngoscopy. Function is often preserved, except in cases where severe perilaryngeal swelling appears to impinge on abduction of the arytenoids.

Treatment

Although controversial, laryngeal ventriculectomy is often performed in severely affected Norwich Terriers as a palliative measure to increase the laryngeal opening and reduce the effects of airflow dynamics on the remainder of the larynx. Some surgeons advocate tonsillectomy for the same reason. In severely obstructive cases, resection of the dorsal periarytenoid tissue has partially alleviated clinical signs. In most cases postoperative glucocorticoids are employed; inhaled preparations are preferred and can be required for several months to years whether or not surgery is performed. The efficacy of this treatment is unknown.

Prognosis

Despite severe airway obstruction, many dogs remain overtly healthy and active throughout life. When surgical intervention has been performed, most owners indicate an improvement in respiration, although many dogs are variably clinical for disease. Clinical understanding of this affliction is important for veterinarians because it is common knowledge among breeders and owners of Norwich Terriers. Genetic investigations are ongoing. Importantly, laryngeal narrowing has critical implications for anesthesia because these dogs often require smaller endotracheal tubes than might be expected based on their size, and some dogs can require use of a stylet to secure an airway.

Epiglottic Retroversion

Pathophysiology

Normally the epiglottis sits immediately below the soft palate and is somewhat parallel to the tongue. During swallowing, it moves back to cover the larynx, and during inspiration, it moves upward to contact the palate and direct air through the nasopharynx to the larynx. In dogs with retroversion, the epiglottis is overly mobile and travels caudally to obstruct the larynx during inspiration (Figure 5.4). The cause for this is unknown, but it could represent malacic change (similar to laryngomalacia in humans), fracture of the epiglottis, or denervation to the hyoepiglottic muscles, which control movement of the epiglottis. Mild variants of this anatomic abnormality are often encountered during laryngeal exam, and it appears that additional pathology such as tracheal collapse, an elongated soft palate, airway inflammation, or obesity is required to result in clinical manifestations of upper airway obstruction.

History and Signalment

Episodic or persistent respiratory distress characterized by inspiratory difficulty is often in the history of affected dogs. Generally, animals are older (>8 years of age), females are affected more often than males, and many are over-weight. This is a disease primarily of small to medium-sized breed dogs, with Yorkshire Terriers and Cocker Spaniels represented more commonly, along with brachycephalic breeds (Skerrett et al. 2015).

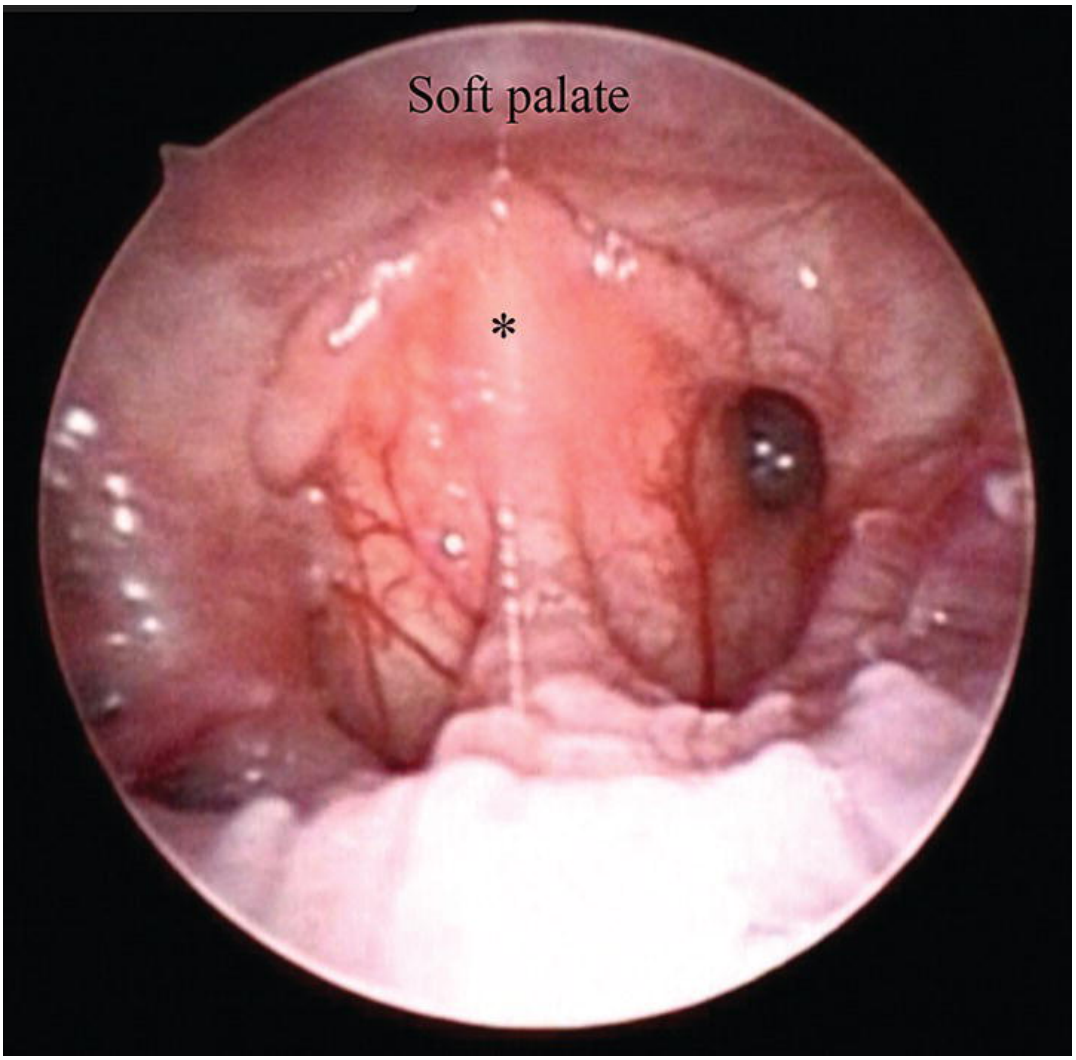


Figure 5.4 Laryngoscopic image from an 11-year-old Maltese with intermittent respiratory distress and marked upper airway obstruction. The epiglottis (*) is flipped caudally against the soft palate in a retroverted position.

Physical Examination

Intermittent or persistent stridor is the most common finding, although some dogs can appear normal at rest and only develop stridor with excitement.

Diagnostic Findings

Cervical radiographs or fluoroscopy can reveal malpositioning of the epiglottis in relation to the larynx and oropharynx. Caution is warranted in over-interpreting pharyngeal collapse, because this is common in brachycephalic breeds, even those lacking specific respiratory findings. Retroversion of the epiglottis can be visualized during laryngoscopy when the examiner has knowledge of the normal upper airway. A light plane of anesthesia is employed, and it is important that the tongue is not retracted too far cranially during the examination so that the epiglottis is allowed to rest in its normal position.

Treatment

Weight loss and environmental modifications are pivotal to reduce stress on the respiratory system. When the dog has continued airway obstruction, temporary or permanent epiglottopexy is typically performed by suturing the base of the tongue to the ventral surface of the epiglottis. Breakdown of the suture site is not uncommon. Partial or complete epiglottectomy can also be performed, but the client needs to be aware that dogs that have had surgical interventions are at risk for aspiration events post-operatively. Dogs that have persistent clinical signs require permanent tracheostomy.

Prognosis

It is unclear whether surgical intervention improves survival (Skerrett et al. 2015) and many dogs can continue to suffer from airway obstruction. Given that retroversion is often part of other upper airway obstructive diseases, further research is needed to determine optimal management strategies for these dogs.

Tracheal/Airway Collapse (Tracheobronchomalacia)

Pathophysiology

The etiology of tracheal collapse is unknown, but a study performed in a small number of dogs reported a reduction in chondrocytes and a lack of glycosaminoglycan and chondroitin sulfate in tracheal cartilage (Dallman et al. 1988). The lack of structural integrity in the cartilage is purported to result in weakening of cartilage rings, with flattening of the tracheal rings in a dorsoventral direction. An elongated dorsal tracheal membrane prolapses into the lumen of the airway, lending a dynamic component to the collapse. Repetitive contact between the membranous muscle and the ventral floor of the trachea leads to mechanical irritation of the mucosa, which enhances tracheal edema and inflammation. The cervical trachea collapses during inspiration, while the intrathoracic portion of the trachea collapses during forced expiration or cough because of the pressure gradients that develop during the respiratory cycle (Figure 5.5). Many dogs with tracheal collapse have collapse of both the cervical and intrathoracic trachea. In some dogs, the lobar bronchi also are collapsed, with the right middle and left cranial lobar bronchi affected most commonly (Johnson and Pollard 2010; Bottero et al. 2013), although it is unknown whether this is caused by the same pathology that has been described in dogs with tracheal collapse. When bronchial collapse is found in conjunction with tracheal collapse, it is termed tracheobronchomalacia. In some dogs only lobar or lower or smaller airway collapse is detected and this is termed bronchomalacia when luminal diameter is reduced by at least 50%.

Airway collapse can be static or dynamic. The most severe form of cervical tracheal collapse tends to be static in nature, often causing respiratory difficulty on both inspiration and on expiration. Lobar bronchial collapse can be static but also somewhat dynamic, with collapse evident at rest but with some degree of opening during inspiration and closure on expiration. Smaller airway or segmental lobar changes in luminal diameter tend to be dynamic. An endoscopic classification of bronchomalacia differentiated among dynamic, dynamic plus static, and static bronchial collapse to develop functional classes of airway collapse for future studies and to aid in understanding of the disease (Bottero et al. 2013), although this has not been widely applied in clinical practice.

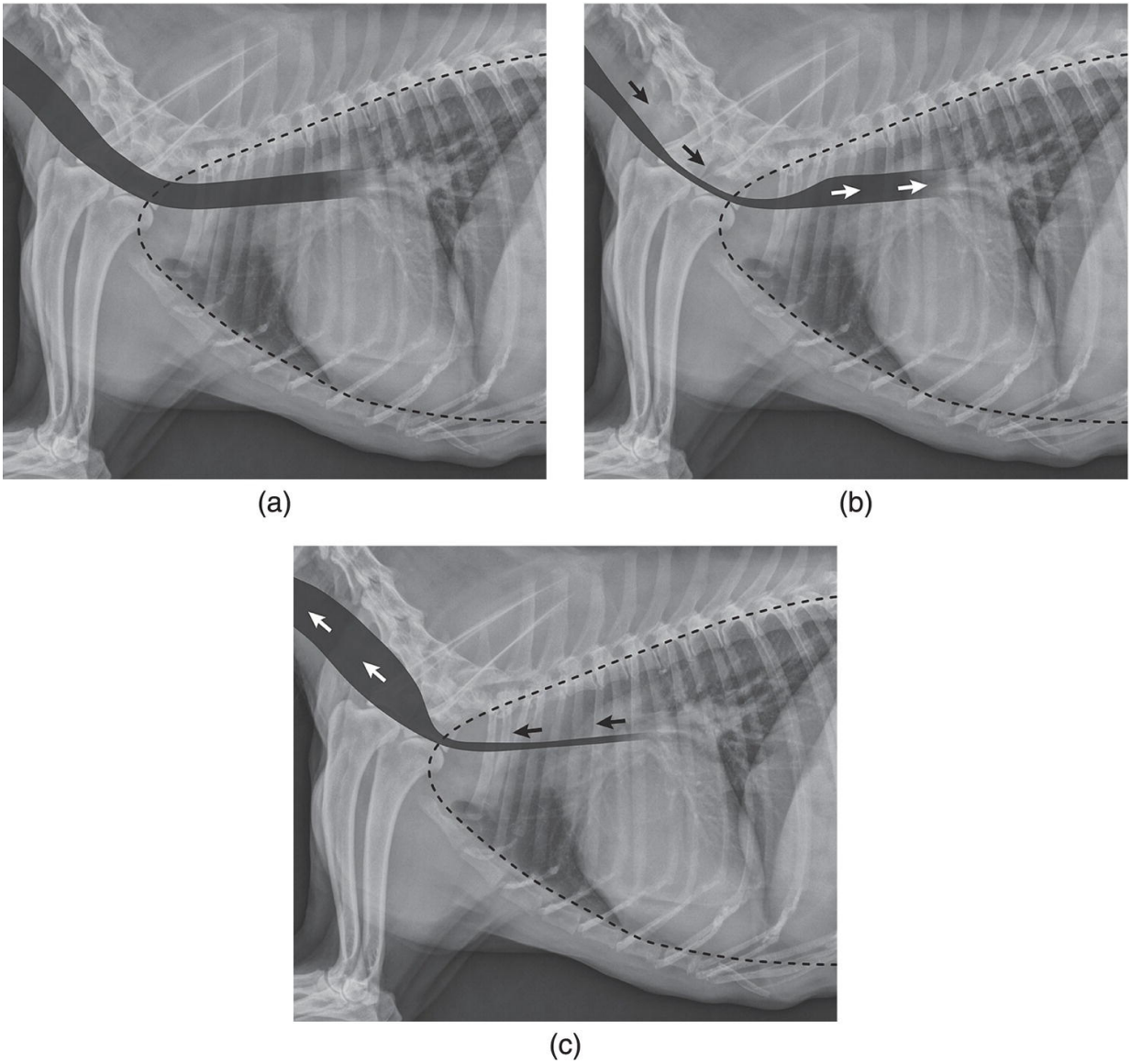


Figure 5.5 The airways are exposed to atmospheric pressure in the cervical region and intrapleural pressure in the intrathoracic region. (a) During inspiration, intrapleural pressure drops, to create a pressure gradient along the airway that results in flow of air from the mouth to the alveoli. (b) The dog with weakened cartilage rings in the cervical region (black arrows) experiences collapse on inspiration. (c) During a forced expiration or cough, intrapleural pressure becomes positive and the pressure gradient across the airways favors collapse in the intrathoracic region (black arrows) when cartilage is weak.

The role of inflammation in the development of airway collapse and in the perpetuation of clinical signs remains unclear. Mechanical trauma due to airway wall apposition can be a cause of inflammation or can result from recurrent dynamic collapse. Neutrophilic or lymphocytic inflammation is commonly found in affected dogs and likely contributes to coughing. Similarly, the role of airway infection in tracheobronchomalacia is unknown, with some studies finding a majority of dogs with intracellular bacteria or evidence of infection (Bottero et al. 2013; Lesnikowski et al. 2020) while others report an absence of infection (Singh et al. 2012). Use of different sampling methods and different definitions of infection

(intracellular bacteria, culture results, clinical features, etc.) likely play a role in these various findings.

Finally, the role of cardiomegaly and left atrial enlargement in bronchial collapse remains controversial. One case-controlled study that used bronchoscopic assessment of the severity and distribution of lobar bronchial collapse in dogs with and without left atrial enlargement concluded that airway collapse was independent of cardiomegaly and was often associated with airway inflammation (Singh et al. 2012). A study using computed tomography (CT) to define bronchial collapse based on a reduced bronchial-to-aorta ratio reported an inverse relationship between left atrial size and vertebral heart score with bronchial diameter, suggesting that the heart was involved in airway collapse (LeBastard et al. 2021). However other CT studies have demonstrated bronchial narrowing in the absence of cough in brachycephalic dogs (Yoon et al. 2020) and in other dogs lacking respiratory signs (Cote et al. 2022), raising questions about the role of various thoracic conformations and application of imaging ratios in the clinical syndrome of airway collapse.

History and Signalment

Tracheal collapse is seen most commonly in small or toy-breed dogs, such as the Yorkshire Terrier, Pomeranian, Poodle, Maltese, and Chihuahua, while bronchomalacia can be seen in any size of dog. Tracheal collapse is diagnosed rarely in large breed dogs, but bronchial collapse is relatively common. Bronchomalacia is much less common in cats than in dogs and is rarely responsible for clinical signs, although static bronchial collapse can be found in some cats with chronic bronchial disease. At the time of presentation to the veterinarian, dogs with airway collapse can range from 1 to 15 years of age, depending on the degree of airway collapse and the presence of contributing clinical conditions.

Most dogs with tracheal collapse have a chronic history of waxing and waning respiratory difficulty or cough that has grown progressively worse over time or has become refractory to treatment. This likely is the reason that several studies refer to tracheal collapse as a progressive disease. Some dogs will have both respiratory difficulty and cough. Exacerbation of cough after eating and drinking or with excitement is common in dogs with tracheal or airway collapse, and this likely reflects some degree of laryngeal dysfunction or aspiration injury. Some dogs cough excessively on waking or in the middle of the night and this could also reflect micr-aspiration. The cough is often described as paroxysmal, dry, or as a “honking” cough. Owners sometimes mistake the cough for vomiting or will report gagging or retching in association with the cough as the animal attempts to clear secretions from the airways. Worsened signs, exercise intolerance, and respiratory distress tend to occur during physical exertion, with heat stress, or in humid conditions. This could be the result of airway collapse alone, chronic bronchitis, infectious airway disease, and/or concurrent upper airway obstruction (edema, ventricular eversion, or laryngeal paralysis). Cyanosis or syncope can occur in severely affected animals due to complete airway obstruction, vagally mediated syncope, or pulmonary hypertension.

Physical Examination

Dogs with airway collapse are usually systemically healthy, they are often overweight, and they cough readily on tracheal palpation. The respiratory pattern can appear normal at rest, until coughing or stress leads to a debilitating paroxysmal event that causes air hunger or cyanosis. Caution is warranted when auscultating or palpating the trachea, because a severe paroxysm of cough could induce a crisis of coughing or cough syncope. Marked expiratory effort or an abdominal press on expiration can indicate bronchial collapse or concurrent bronchitis.

Auscultation over the trachea can reveal musical or wheezing sounds caused by turbulent airflow through the narrowed lumen. Stridor over the upper airway could represent laryngeal paralysis, but can also be heard in dogs with severe cervical tracheal collapse that results in a narrowed and fixed tracheal diameter. In dogs with cranial lung herniation or severe kinking of the cervical trachea, ballooning of the thoracic inlet can be seen during cough or forced expiration.

Lung sounds can be difficult to assess in dogs with tracheal or airway collapse due to tachypnea, obesity, or referred upper airway sounds. Inspiratory and/or expiratory crackles can be an indication that bronchomalacia is present, especially when combined with expiratory effort. An end-expiratory snap over the thorax can be an indicator that intrathoracic tracheal or bronchial collapse is present. Careful cardiac auscultation should be performed, because 20% or more of middle-aged, small breed dogs have mitral valve insufficiency in addition to airway collapse. Usually the murmur is low grade (2–3/6) and heart rate is low or a respiratory arrhythmia is present, allowing differentiation between congestive heart failure-related respiratory signs and airway collapse. Hepatomegaly is a common finding in dogs with tracheal collapse and could be related to fatty infiltration of the liver, intermittent hypoxia, or a non-specific hepatopathy.

Diagnostic Findings

Although the diagnosis of tracheal collapse can be strongly presumed based on the signalment, history, and physical examination findings, a complete diagnostic work-up should be performed to define concurrent disorders and provide appropriate therapy. Recognition of bronchial collapse is more problematic and requires advanced diagnostic capabilities, including fluoroscopy and bronchoscopy. Routine hematologic testing occasionally detects predisposing conditions or concurrent diseases in dogs with tracheal collapse, although this is rare. Increased liver enzymes are not uncommon in dogs with airway collapse, and elevations in serum bile acids have also been reported (Bauer et al. 2006). Whether this is related to transient hypoxia to the liver or fatty infiltration is unclear.

Radiographs are essential both to examine airway diameter and to detect concurrent pulmonary or cardiac disorders. Cautious interpretation of the cardiac silhouette is warranted, because the dog breeds commonly affected by airway collapse often have a larger cardiac silhouette than expected, particularly when they are small breed chondrodystrophic dogs. Also, fat around the pericardial space and reduced lung expansion from obesity can lead to the false impression of cardiomegaly. However, right-sided heart enlargement can be present in dogs with tracheobronchomalacia, concurrent pulmonary disease, or other factors that predispose to the development of pulmonary hypertension.

It is important to note that airway collapse is often a dynamic process and radiographs can give a false impression of the presence or absence of collapse. In the cervical region, overlying structures such as the esophagus and neck muscles can obscure details on airway diameter. Evaluation of left and right lateral views may improve distinction of structures; however, differences in positioning and in the phase of respiration can make it difficult to compare these views directly. Obtaining inspiratory and expiratory phases of respiration can be helpful, because the cervical region should collapse on inspiration while intrathoracic airways should collapse on expiration; however, the difficulty in timing these radiographs precisely limits the actual value. In comparison to fluoroscopy, radiographs under-estimate the severity of tracheal collapse and are less able to detect intrathoracic airway collapse, which is often more severe than cervical collapse (Macready et al. 2007) (Figure 5.6). Therefore, while radiographs are useful as a screening tool for collapsing airways, they cannot be relied on for the diagnosis and likely will provide inaccurate information regarding the location and severity of tracheobronchial collapse. Fluoroscopy, where available, is beneficial in providing

information on the degree of dynamic airway obstruction, and it also allows correlation of airway collapse with cardiac and respiratory cycles. Additional findings such as cranial lung herniation during cough can be detected (Figure 5.7).

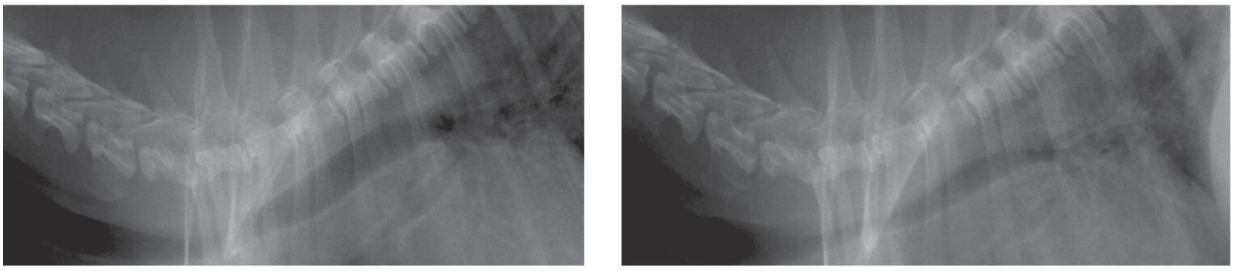


Figure 5.6 Inspiratory (a) and expiratory (b) fluoroscopic images from a 13-year-old male castrated (MC) Terrier mix with intrathoracic airway collapse. Note the dramatic reduction in the diameter of the intrathoracic trachea and carina, and the loss of air column within principal and lobar bronchi in (b).

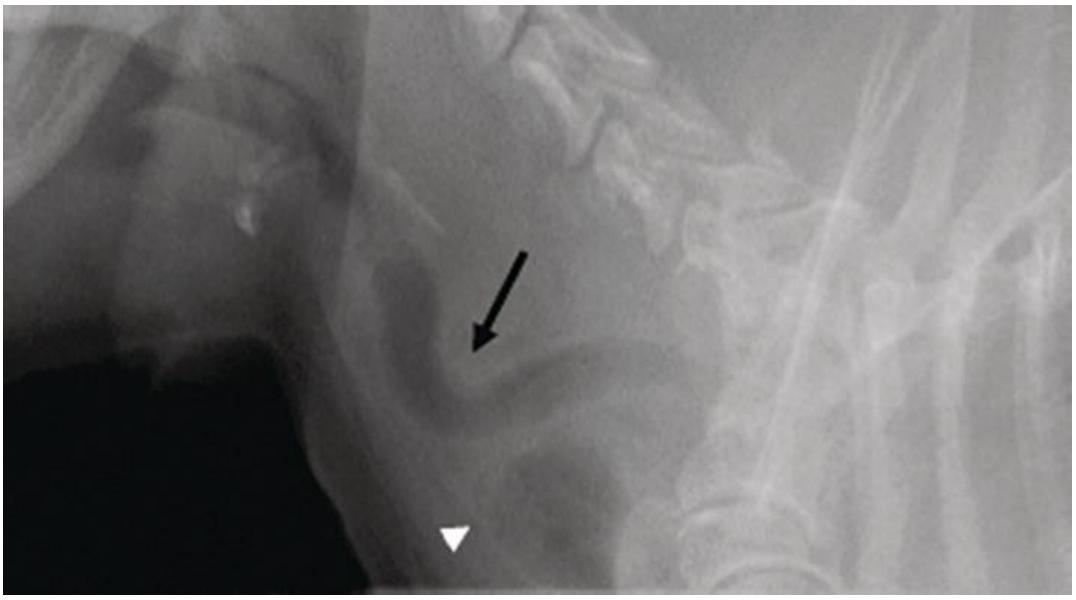


Figure 5.7 Fluoroscopic image from a 15-year-old spayed female (FS) Pug demonstrates dramatic ventral deviation of the cervical trachea (black arrow) and cranial herniation (white arrowhead) of the lung through the thoracic inlet during a cough.

Bronchoscopy can document tracheal collapse and is useful for grading the degree of collapse (Figure 5.8). In addition, bronchoscopy readily identifies bronchomalacia, which can be static or dynamic (Figure 5.9). Bronchoalveolar lavage or an endotracheal wash sample can be used to document bacterial or *Mycoplasma* infection and to detect inflammation by cytologic examination. Bronchomalacia can accompany eosinophilic or neutrophilic inflammatory disease as well as lower respiratory tract infection, therefore the importance of collecting an airway sample is readily apparent. Interestingly, airway collapse is often associated with BAL lymphocytosis, which is an unusual type of inflammatory airway disease (Johnson and Vernau 2019).

The risk of anesthesia for bronchoscopy can be significant in dogs with airway collapse, especially in obese animals with severe tracheal sensitivity or in hyperexcitable dogs. A slow

recovery from anesthesia is advisable to minimize stress, and an oxygen-enriched environment should be available. One milliliter of 1% lidocaine sprayed into the distal trachea at the end of bronchoscopy can help decrease the cough reflex.

CT with imaging during inspiration and expiration can also provide information on airway collapse, however it does not assess the presence or absence of infection or inflammation. Therefore, it provides less clinical guidance for treatment strategies.

Treatment

Animals that have marked respiratory difficulty and coughing can require emergency management. Stress should be minimized, and oxygen supplementation can be beneficial to assist in calming. Cough suppression and sedation can be achieved with butorphanol (0.2–0.4 mg/kg subcutaneously [SC] every 4–6 hours), and the addition of acepromazine (0.01–0.2 mg/kg SC) can have a synergistic effect in producing sedation. Caution should be employed when using the drugs together or when an opioid is considered, because over-sedation can require intubation, which will exacerbate airway inflammation. To decrease laryngeal or tracheal inflammation, a single dose of dexamethasone SP (0.05–0.20 mg/kg intravenously [IV]) can be administered.

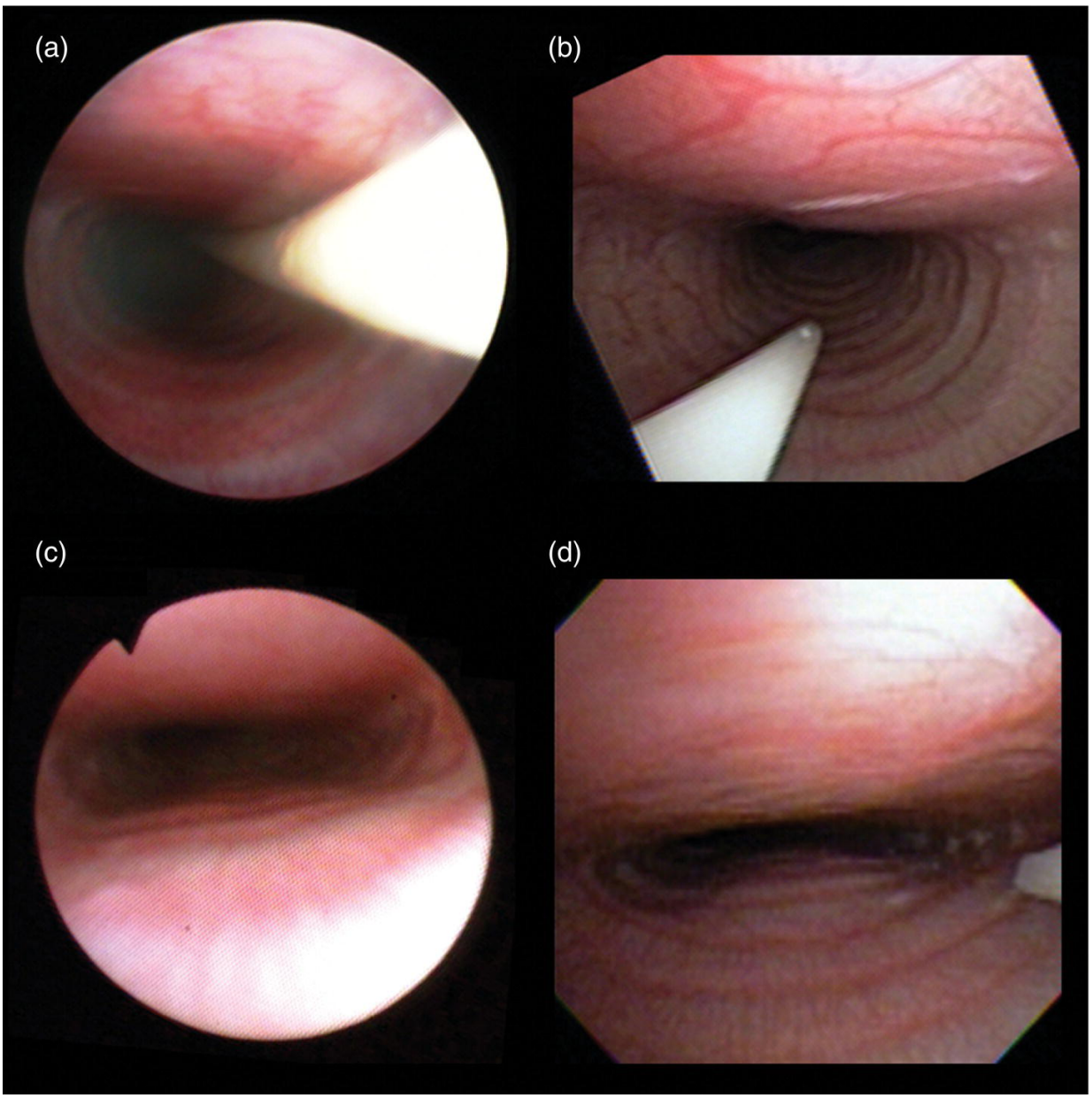


Figure 5.8 (a) Grade I: The cartilage ring structure of the trachea remains circular and is almost normal. Slight protrusion of the dorsal tracheal membrane into the lumen reduces the diameter by <25%. (b) Grade II: Flattening of the tracheal cartilage leads to lengthening of the dorsal tracheal membrane and further reduces the luminal diameter to approximately 50%. (c) Grade III: The tracheal cartilage rings are severely flattened and the trachealis muscle contacts the inner surface of the tracheal cartilage during cough. The lumen is reduced by 75%. (d) Grade IV: The trachealis muscle is collapsed onto the inner surface of the cartilage, leading to complete obstruction of the lumen. A double lumen can be seen in some cases.

Outpatient management should be designed to treat disorders identified in the diagnostic work-up whenever possible. Almost all affected dogs would benefit from weight loss (see Chapter 3). While this can be very beneficial in reducing and even eliminating cough, it can take a long time to accomplish this, and both the dog and the owner often cannot tolerate the

length of time required without using additional measures. If physical examination findings suggest bronchomalacia (crackles, expiratory effort), a trial on extended-release theophylline (5–10 mg/kg orally [PO] twice a day [BID]) can be considered to improve expiratory airflow and lessen the tendency for small airways to collapse. This drug is not indicated for use in dogs with cervical tracheal collapse, and beta-2-agonists are not beneficial. Airway infection is rarely found, but when present it should be treated with appropriate antibiotics as determined by airway sampling. If the dog is too unstable to obtain an airway sample, a trial on doxycycline (3–5 mg/kg PO BID) can be employed to treat potential *Mycoplasma* infection and to provide mild anti-inflammatory effects. If chronic bronchitis is diagnosed, glucocorticoids should be employed (see later in this chapter). These measures and appropriate client communication can generally help manage clinical signs and owner expectations.

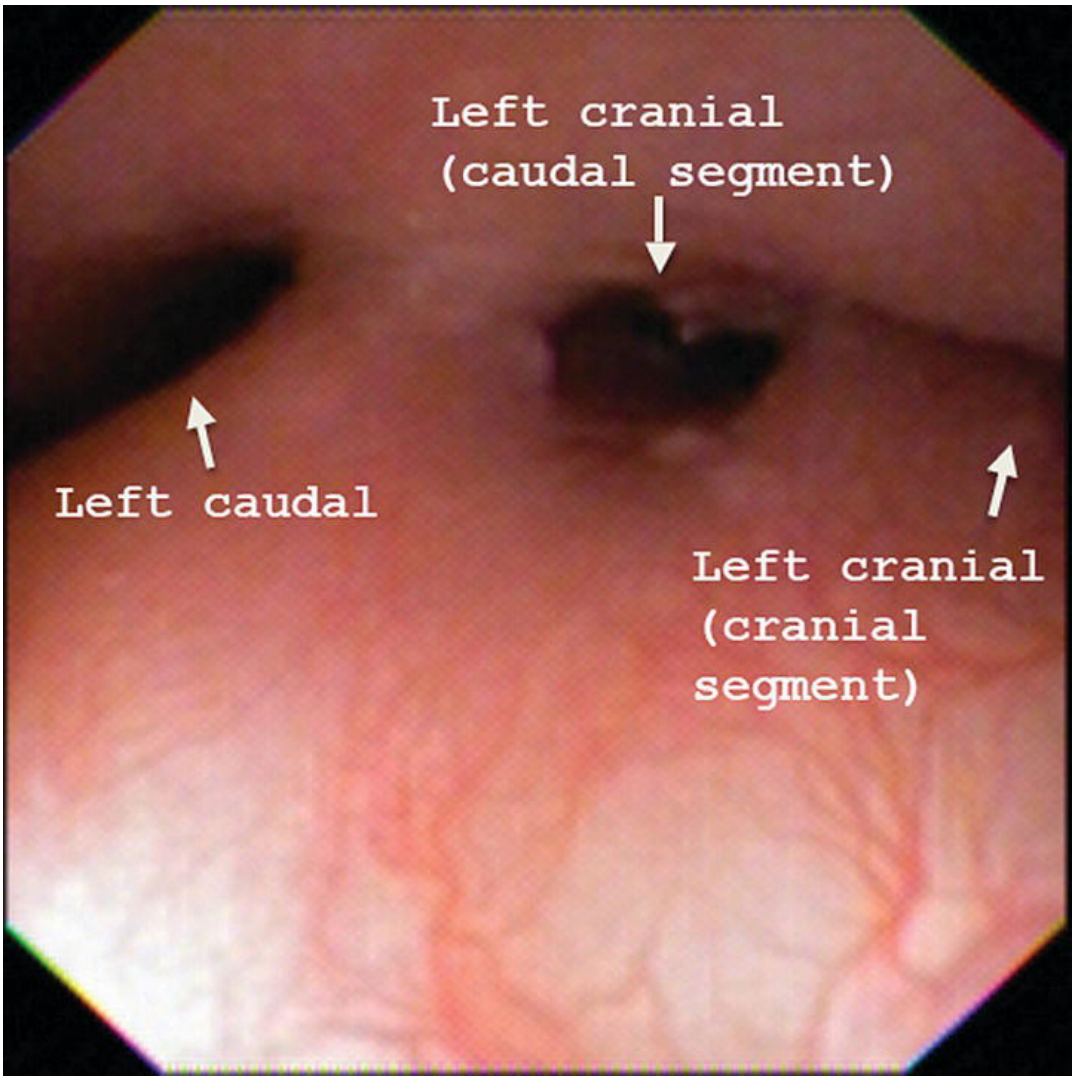


Figure 5.9 Bronchoscopic image demonstrating 70–100% collapse of lobar bronchi to the left lung lobe.

Dogs with tracheal collapse and bronchomalacia can have local airway inflammation from chronic airway injury. When this is suspected or confirmed on bronchoscopy, a short course (5–7 days) of prednisone can be beneficial, although side effects such as weight gain and panting can worsen airway collapse. If the animal responds well to oral glucocorticoids and

ongoing control of inflammation is anticipated or if oral glucocorticoids are contra-indicated due to obesity, heart disease, diabetes, or renal disease, inhaled glucocorticoids would be preferred to limit side effects. Dogs with bronchomalacia and airway inflammation can experience at least a 50% reduction in cough within 2 weeks of instituting inhaled fluticasone propionate (see Chapter 2).

Finally, narcotic cough suppressants are typically required to control cough when inflammation and infection have been managed. These drugs should be administered often enough to reduce cough without inducing severe sedation. Suggested drugs include hydrocodone (0.22 mg/kg PO two to four times a day [QID–BID]) initially or butorphanol (0.55 mg/kg PO QID–BID). Starting with a frequent dosing interval and gradually extending the time between doses and/or reducing the dose appears to be most effective in controlling signs while avoiding the development of tolerance.

Ancillary measures include avoidance of collars and decreased exposure to heat and humidity. Use of management strategies that limit aspiration injury, as described for laryngeal paralysis, can also be helpful in reducing cough. Use of omeprazole to limit acid injury to the airways has to be balanced against the tendency for some dogs to vomit when taking this drug. Upper airway surgery, if needed, can also reduce clinical signs.

Dogs that fail medical management require additional intervention. In dogs with cervical tracheal collapse, placement of tracheal ring prostheses (Figure 5.10) will result in a dramatic reduction in clinical signs (Buback et al. 1996). The primary complication of surgery is development of laryngeal paralysis from damage to the recurrent laryngeal nerve during or after surgery, and tracheostomy can be required for management. When intrathoracic tracheal collapse is detected and medical management has been exhausted, placement of an intraluminal stenting device (Figure 5.11) can be life-saving. Stents are indicated particularly for dogs that have difficulty breathing, rather than for dogs with a primary complaint of cough. It is critical that a stent of appropriate type and size is used to attain a successful outcome and that an experienced clinician places the stent (Weisse 2009). The most problematic form of tracheal collapse is grade 4 cervical collapse, where the ventral surface of the trachea bulges inward toward the dorsal surface, creating a double lumen or W-shaped trachea, sometimes referred to as a tracheal malformation (Figure 5.8d). This configuration is often encountered at the thoracic inlet and, while it can sometimes be managed with external ring prostheses, stenting is also performed in some cases. Improving stent contact with the tracheal walls through ballooning is frequently used in these cases in an attempt to improve integration of the stent with the tracheal epithelium.

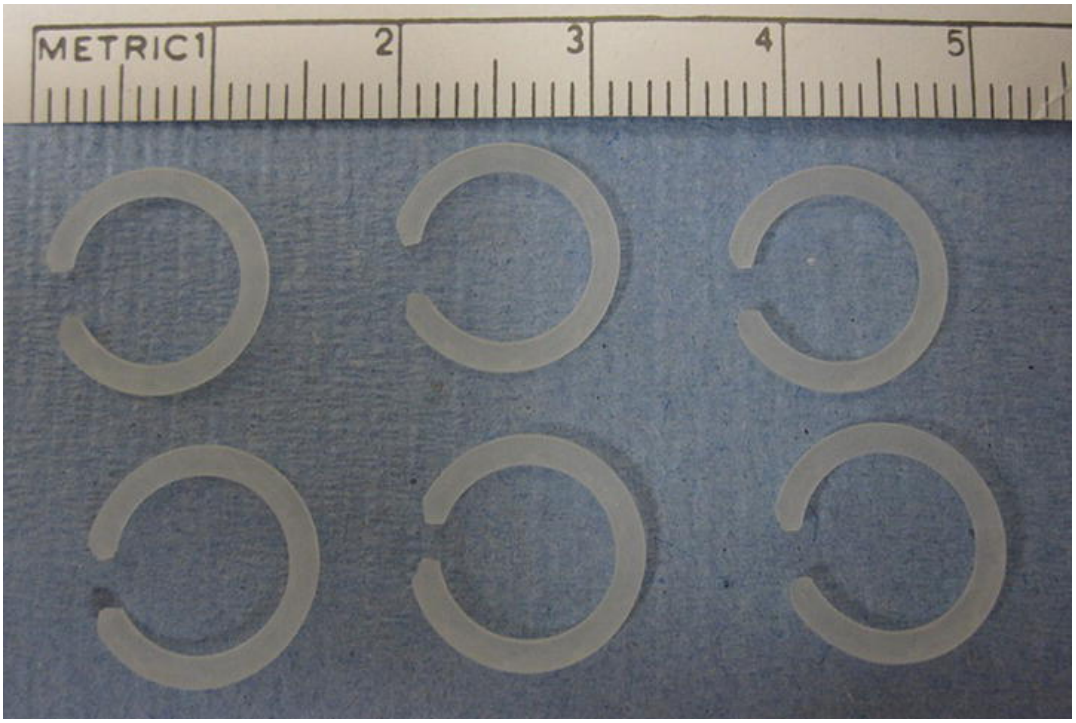


Figure 5.10 Prosthetic rings used for external support in dogs with cervical tracheal collapse.

Bronchial collapse or bronchomalacia is not necessarily a contraindication for placement of extrathoracic rings or for stent placement in the trachea, although dogs that continue to cough due to lower airway collapse are at greater risk for breaking the stent. Research into the manufacture of bronchial stents and methods to improve tracheal contact is ongoing.

Post-procedure management is typically provided in an intensive care setting. Antibiotics are often required for aspiration events, and cough suppressants can be needed to prevent damage to the stent. Longer-term complications of stent placement include migration, granuloma formation, or breakage of the stent. Owners need to be aware that multi-drug therapy and continued monitoring will be required after stent placement.

Prognosis

Tracheal collapse with or without lower airway collapse or bronchomalacia is a common cause of cough in small breed dogs. Bronchomalacia is also frequently encountered in large breed dogs with infectious or inflammatory airway disease, however, because airway collapse typically requires bronchoscopy for identification, the condition is under-diagnosed. Most dogs with tracheobronchomalacia can be managed successfully with an individualized treatment plan designed to control abnormalities noted during diagnostic testing; however, the underlying pathology of airway collapse is irreversible. Recurrent clinical signs should be anticipated and for dogs that are refractory to therapy, more aggressive interventions including stenting should be investigated.

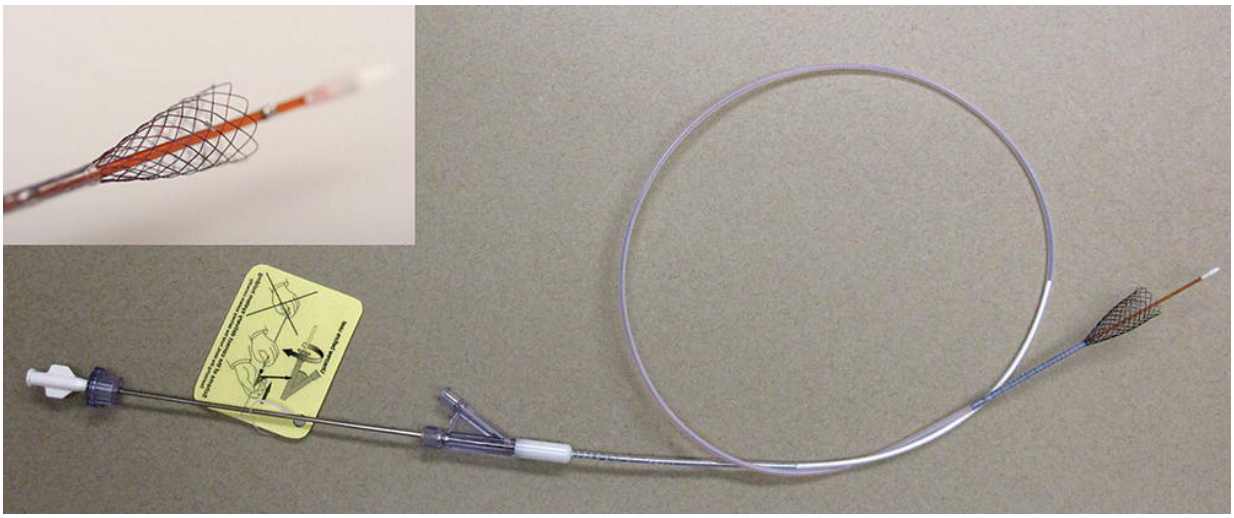


Figure 5.11 Catheter delivery system and close-up of a distal deployment stent manufactured by Infiniti Medical Corporation (Redwood City, CA) for intraluminal support of intrathoracic or complete tracheal collapse.

Bronchiectasis

Pathophysiology

Bronchiectasis is described as irreversible dilatation of the bronchi and is usually accompanied by accumulation of thick airway secretions, with or without infection. The disorder is a poorly characterized condition associated with chronic obstructive, inflammatory, or infectious airway diseases in dogs and cats. Thus, it is typically acquired but can also occur as a congenital disease in conjunction with ciliary dyskinesia. In one study, bacterial pneumonia was the most common disease process accompanying bronchiectasis in the dog, and was present in over 50% of affected dogs, while chronic bronchitis was diagnosed in over 33% of cases and eosinophilic lung disease in 12% (Johnson et al. 2016). Airway collapse was a common complicating feature of disease, found in 58% of cases regardless of an infectious or inflammatory etiology. In the cat, bronchiectasis has been recognized in association with chronic inflammatory airway disease; however, cats do not seem to develop the same suppurative and often infectious process that is seen in dogs.

History and Signalment

Dogs or cats that have bronchiectasis as part of the syndrome of primary ciliary dyskinesia are typically young on presentation and have a chronic history of serous to mucoid nasal secretions and cough that responds to antibiotics but recurs (see Chapter 6).

Animals with acquired bronchiectasis are middle-aged to older and have a chronic cough or recurrent pneumonia that is often responsive to antibiotics. Disease is clinically recognized more often in dogs than cats, and Retrievers, Cocker Spaniels, and Standard Poodles appear to be predisposed to the disorder (Johnson et al. 2016).

Physical Examination

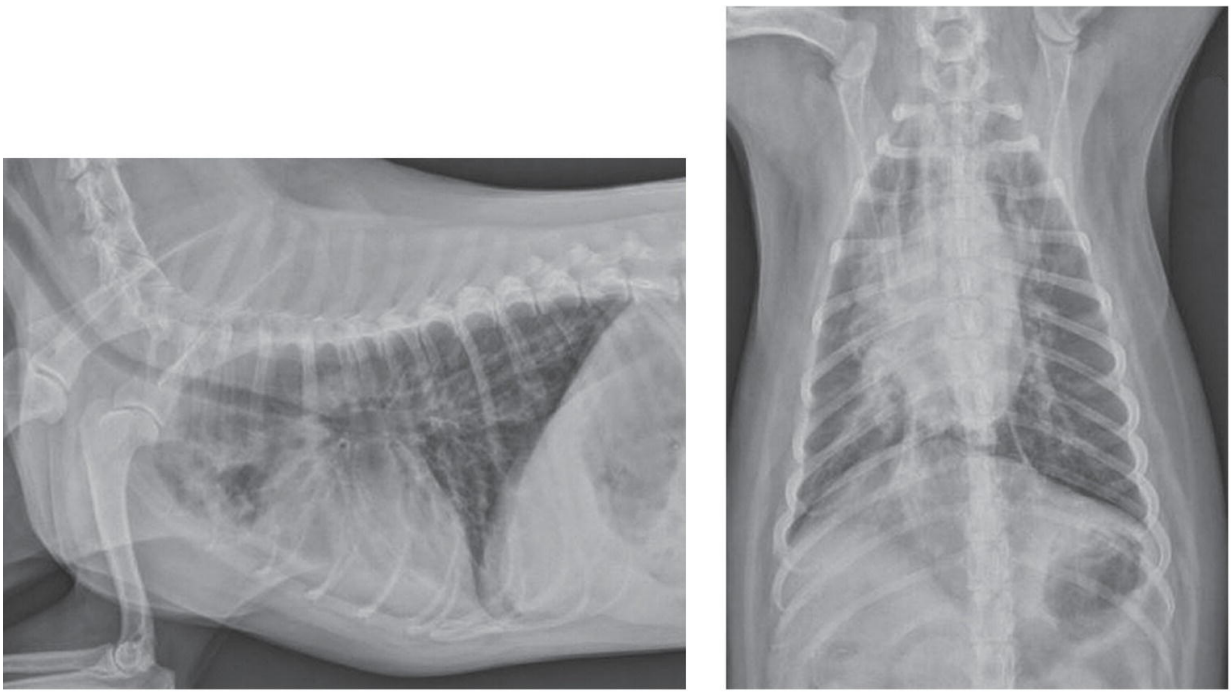
There are no specific physical examination features that characterize bronchiectasis. A rapid shallow breathing pattern and abnormal thoracic auscultation might be detected in animals with concurrent pneumonia; however, some affected dogs display only increased tracheal

sensitivity as a result of airway inflammation. A moist or retching cough is often induced as the animal attempts to mobilize secretions from the lower airways.

Diagnostic Findings

Definitive diagnosis of bronchiectasis is difficult in veterinary medicine because early radiographic lesions are subtle, and dilated, thickened airways are not readily detectable, particularly if pneumonia is not present to provide contrast on radiographs. When visible radiographically, disease should be considered advanced and irreversible (Figure 5.12). CT is preferred for visualization of dilated airways and also allows improved characterization of pulmonary infiltrates, bronchial wall thickening, and lack of peripheral airway tapering, which commonly accompany bronchiectasis (Figure 5.13). Measurement of the ratio of bronchial lumen to pulmonary artery diameter provides an objective means of recognizing bronchiectasis. Normal airways typically have a bronchoarterial (BA) ratio less than 2.0, while individual lobes in dogs with bronchiectasis can have a BA ratio exceeding 4.0 (Cannon et al. 2013). Normal cats have a smaller BA ratio (0.9), which is closer to the value reported for humans (Reid et al. 2012).

Visualization of the airways through bronchoscopy allows documentation of bronchiectasis; however, the operator must have knowledge of normal airway anatomy to recognize the abnormality. With bronchiectasis, the normal rounded bifurcations at bronchial branch points are replaced by dilated and more oval or irregular-appearing airway openings (Figure 5.14). Airway space is increased as airways are pulled open by the reduction in supporting parenchyma. In some cases, severe suppuration and mucus plugging are present and these can be related to inflammatory or infectious disease.



(a) (b)

Figure 5.12 (a) Right lateral and (b) ventrodorsal radiographs from an 8-year-old Pomeranian with diffuse bronchiectasis and a moderate bronchial pattern associated with eosinophilic lung disease.



Figure 5.13 Sagittal reconstruction of a computed tomography (CT) image from the dog depicted in Figure 5.12 reveals marked dilation of all airways with lack of normal tapering into the periphery.

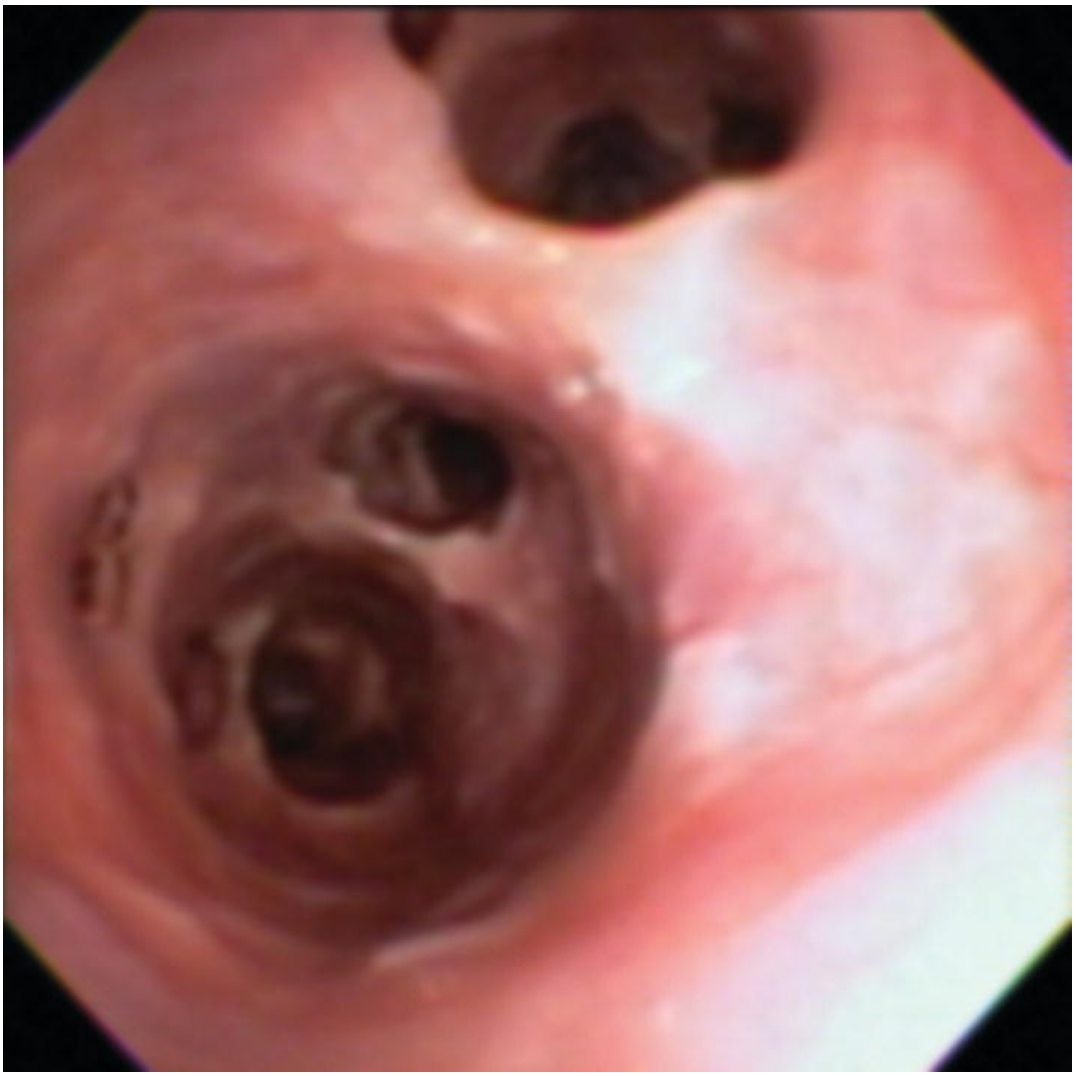


Figure 5.14 Bronchoscopic image of the lungs from a cat with bronchiectasis. Airways are dilated, the epithelial surface is hyperemic, and mucosal nodules are evident.

During bronchoscopy or by use of a tracheal wash, airway samples should be collected in affected dogs and cats for cytology and aerobic, anaerobic, and *Mycoplasma* cultures. Cytology is generally characterized by a high proportion of non-degenerate or degenerate neutrophils when bronchitis or pneumonia is present or by eosinophils in eosinophilic bronchopneumopathy or granuloma. Given the purulence of secretions and the antibiotic responsiveness of many dogs, deep-seated pulmonary infection likely contributes to the disease process, even though bacteria are not always detected on culture. In one study, bacteria were isolated in only half of the dogs with a diagnosis of pneumonia, with *Streptococcus*, *Pasteurella* spp., enteric organisms, and *Stenotrophomonas* isolated most commonly (Johnson et al. 2016). With the exception of *Stenotrophomonas*, most of the bacteria isolated often appear to be highly susceptible to antibiotics, yet animals are unable to clear the infection because of trapping of secretions and poor respiratory defense mechanisms.

Young animals diagnosed with bronchiectasis should be evaluated for primary ciliary dyskinesia (see Chapter 6).

Treatment

In dogs with neutrophilic airway cytology, broad-spectrum antibiotics are often needed for control of clinical signs, prevention of worsening airway pathology, and avoidance of systemic manifestations of chronic disease such as anemia or glomerulonephritis. Antibiotics should be based on culture and susceptibility testing whenever possible, because long-term treatment is generally required in this complicated form of pneumonia. Drugs that penetrate the pulmonary tissue well should be employed, such as doxycycline, azithromycin, enrofloxacin, trimethoprim-sulfa, chloramphenicol, and clindamycin. Six weeks to six months of treatment can be required, and in severe cases life-long antibiotics should be considered. Toxicity of the antibiotics employed should be considered before using long-term treatment. With all forms of bronchiectasis, cough suppressants must be avoided. Saline nebulization followed by coupage can help liquefy and loosen airway secretions and is an essential component in the management of bronchiectasis, although no specific studies have been performed in veterinary patients. In some cases, oral administration of *N*-acetylcysteine can be beneficial in liquefying secretions (see Chapter 3). Focal bronchiectasis is amenable to surgical resection of affected lung lobes. Dogs with bronchiectasis associated with eosinophilic lung disease are treated as described in Chapter 6.

Disease in cats is more challenging to treat because bacteria are almost never isolated and cats do not seem to respond to antibiotics as well as dogs often will. Because the underlying disease process is more likely to be chronic bronchitis in cats rather than chronic pneumonia, oral glucocorticoids are frequently employed. Inhaled glucocorticoids can be helpful in improving respirations unless inspissated airway secretions prevent penetration of the drug to the mucosa. Ancillary management with nebulization can be valuable in cats as it is in dogs.

Prognosis

Dogs with bronchiectasis can suffer recurrent bouts of life-threatening bacterial pneumonia and may develop secondary diseases such as glomerulonephritis due to immune complex formation associated with chronic antigenic stimulus. Continual antibiotic treatment and respiratory therapy are required for some dogs, while others may have periodic episodes of antibiotic-responsive pneumonia interspersed with long stages of normal health. Similarly, prognosis for dogs with bronchiectasis resulting from ciliary dyskinesia is variable. Some dogs are only mildly affected throughout life or become subclinical as they age, while others may succumb to pneumonia.

Infectious Diseases

Canine Infectious Respiratory Disease Complex ("Kennel Cough")

Pathophysiology

Canine infectious respiratory disease (CIRD) complex is associated with multiple pathogens, including parainfluenza virus (CPIV), canine adenovirus (CAV-2), and canine distemper virus (CDV), as well as newer viruses such as canine respiratory coronavirus (CRCoV), canine herpesvirus (CHV-1), and canine influenza virus (CIV). Canine pneumovirus (CnPnV) and reovirus are of questionable pathogenicity. Subtypes of influenza viruses infecting dogs include H3N8, which crossed species from horses to dogs in 2004 (Crawford et al. 2005), and H3N2, which likely originated in Southeast Asia before causing outbreaks in the midwest (Chicago, Illinois) and southern (Atlanta, Georgia) United States, with subsequent spread of the organism to multiple states. Outbreaks of viral diseases in shelters result in spillover of

pathogens into the community and vice versa. Vaccination has reduced the incidence of some viral infections; however, additional pathogens are continually added to the list of organisms involved in CIRD (Table 5.2). Lack of vaccines for CHV-1 and CRCoV results in a large population of dogs at risk for infection.

Viral infection of epithelial cells damages mucosal cells and alters local immunity, which predisposes the animal to infection with both primary respiratory pathogens (*Bordetella* and *Mycoplasma*) and other commensal and pathogenic bacteria, including *Streptococcus equi* subsp. *zooepidemicus*. Infection is prevalent in animals that are housed in shelter environments or held in close confinement, because the viruses are highly contagious and easily spread by aerosolization or fomites.

History and Signalment

Clinical signs of naso-ocular discharge, cough, and possibly anorexia or lethargy are usually seen 2–10 days post-exposure to an infected animal, and the dose of pathogens encountered might play a role in the severity of clinical disease. Young animals in shelters are quickly exposed to most organisms and will readily spread the disease to animals of any age in the general population. While infection with viral organisms usually results in a mild cough, infection with *Bordetella* classically results in a dry, paroxysmal, "seal bark" cough, and involvement of aerobic bacteria (particularly *Streptococcus equi* subsp. *zooepidemicus*) or *Mycoplasma* can lead to development of pneumonia with a moister cough.

Table 5.2 List of pathogens currently identified as involved in canine infectious respiratory disease complex.

Pathogen	Characteristics	Laboratory diagnosis
Viruses		
CPIV	RNA virus (paramyxovirus)	PCR
CAV-2	DNA virus (adenovirus)	PCR
CDV	RNA virus (paramyxovirus)	qRT-PCR
CRCoV	RNA virus (alphacoronavirus)	RT-PCR
CHV-1	EnvelopedDNA virus (alpha-herpesvirus)	
CIV	Enveloped RNA virus (type A)	Seroconversion
CnPnV	RNA virus (paramyxovirus)	qRT-PCR (research tool)
Bacteria		
Bordetella bronchiseptica	Gram-negative aerobic coccobacillus	Aerobic bacterial culture, PCR
Streptococcus equi subsp. *zooepidemicus*	Aerobic coccal bacterium (beta-hemolytic Lancefield group C)	Aerobic bacterial culture
Mycoplasma cynos or *Mycoplasma canis*	Cell wall deficient organism (Mollicutes)	Aerobic bacterial culture on specific medium, PCR

CAV-2, canine adenovirus; CDV, canine distemper virus; CHV-1, canine herpesvirus; CIV, canine influenza virus; CnPnV, canine pneumonia; CPIV, parainfluenza virus; CRCoV, canine respiratory coronavirus; PCR, polymerase chain reaction; qRT-PCR, quantitative reverse transcription polymerase chain reaction; RT-PCR, reverse transcription polymerase chain reaction.

CHV-1 was initially recognized as a cause of fading puppy syndrome, neonatal death, and abortion, but more recently has been associated with both ocular and disseminated disease of

respiratory origin. Immunocompromise, in particular, can enhance the severity of infection. Disease associated with CHV-1 tends to result in dramatic ocular involvement with marked conjunctivitis, ulcerative keratitis, and blepharospasm, as well as nasal signs and even pneumonia.

CDV is an epitheliotropic virus that can result in respiratory, gastrointestinal, and ultimately neurologic disease, which can be fatal. Although vaccination has substantially reduced the occurrence of this infection, genetic variants of the virus can develop in regions of low vaccination prevalence and vaccine breakthrough can occur when outdated or poorly stored products are used.

In general, viral infections are typically self-limiting, with resolution of signs in 7–10 days, although *Bordetella, Mycoplasma,* and CIV infections can result in chronic cough that requires specific investigation and treatment.

Physical Examination

Most dogs with CIRD remain systemically healthy, although neonates and immuno-compromised patients are susceptible to the development of pneumonia and resultant signs of illness. Most dogs display obvious tracheal sensitivity but have a normal respiratory pattern and normal lung sounds unless bronchopneumonia develops. Increasing severity of disease is recognized by the development of tachypnea, harsh lung sounds, fever, anorexia, and lethargy. With bacterial infection, a moist and productive cough can develop, tachypnea can be observed, and crackles or wheezes are sometimes auscultated. Physical examination abnormalities are usually confined to the respiratory tract, although CHV-1 can cause surface ocular disease, and chorioretinitis can be detected in dogs with CDV.

Diagnostic Findings

In privately owned pet animals that are systemically healthy, the diagnosis of CIRD is usually based on history and clinical signs. In an outbreak situation or in an ill animal, it is important to identify the infecting organism(s) in order to limit spread of disease and provide appropriate treatment. A CBC can show lymphopenia suggestive of a viral insult, or alterations in neutrophils due to bacterial infection (leukocytosis with a left shift or neutropenia associated with acute infection). If marked conjunctivitis or blepharospasm is noted, a fluorescein stain should be applied to the eyes to detect the classic dendritic ulcer of CHV-1. Thoracic radiographs would be expected to show a diffuse interstitial infiltrate in viral pneumonia and alveolar infiltrates in the presence of bacterial infection.

In animals with primarily upper respiratory tract signs, a nasal, ocular, or pharyngeal swab can be assessed for organisms through culture or molecular assay. It is important to note that these tests can confirm the molecular presence of an organism, but do not prove causation of clinical signs of disease, and a majority of PCR positive dogs can be apparently healthy (Jaffey et al. 2021). Many of these tests can be impacted by recent vaccination and other limitations of the assays must be considered. For example, CRCoV is difficult to culture and molecular identification (reverse transcription polymerase chain reaction: RT-PCR) or paired serology 2–3 weeks apart is usually required to identify exposure to the organism. Additionally, the value of a positive test is limited because detection of this virus bears little relation to the presence or absence of clinical signs.

The timing of viral shedding in relationship to the onset of clinical signs alters the value of viral culture. Experimental CHV-1 infection in dogs results in peak ocular manifestations of disease by day 7–10, yet viral shedding peaks at day 5 and declines substantially by day 10 (Ledbetter et al. 2009). In the case of CIV, diagnosis based on virus isolation is also problematic. Clinical signs begin 2–3 days post-infection, but the virus is shed only for a

maximum of 5–7 days, making it unlikely that culture or PCR will detect virus unless the dog is presented very early in the course of disease. Documentation of CIV infection (or exposure to CIV) is best made through assessment of hemagglutination inhibition serum titers for virus-specific antibodies. When possible, acute and convalescent serum samples (preferably 14 days after clinical signs are detected) should be evaluated to detect a greater than fourfold increase in titer. Usually only convalescent serum is available, but if the dog has not been vaccinated for CIV, a positive titer indicates that the dog has been exposed to the virus and is likely infected. Acute and convalescent serum samples can also be useful in the diagnosis of CPIV and CAV-2, although testing is not usually performed because dogs fully recover from infection and vaccinal titers can confuse interpretation.

If CDV is suspected, a conjunctival or genital scrape can be evaluated for inclusion bodies using direct immunofluorescence antibody testing. This is most helpful in the acute (<3 weeks) stage of disease, although evaluation of lower respiratory secretions (BAL or tracheal wash fluid) might allow detection of virus for a longer period of time (up to 1–2 months) post-infection. While a positive test can be diagnostic, a negative test does not rule out disease.

If an animal with evidence of lower respiratory tract involvement in CIRD is stable for anesthesia and a definitive diagnosis is required, collection of airway samples would be recommended for virus isolation, bacterial cultures (aerobic, anaerobic, and *Mycoplasma*), cytology with immunocytochemistry or immunofluorescence, and PCR or quantitative RT-PCR.

Treatment

In uncomplicated cases of CIRD complex, supportive care results in resolution of signs. Physical activity is restricted, collars are avoided, and nutrition and hydration are provided. If bacterial infection is considered unlikely, cough suppressants can be used to break the cycle of repetitive airway injury; however, there is a risk for development of pneumonia if bacteria are trapped in the lungs. Many dogs are initially treated with antibiotics for presumed primary or secondary infection. Doxycycline and chloramphenicol are reasonable antibiotics to use because of their efficacy against *Mycoplasma* species. *Bordetella* has *in vitro* susceptibility to a number of antibiotics, but often the bacterium is not sensitive *in vivo* because it infects cilia lining the respiratory tract, which are not readily accessed by systemically administered agents. Nebulization of an aminoglycoside can be required to reduce bacterial numbers while the immune system assists in clearing the organism (see Chapter 3). Shelter dogs with signs of CIRD had lower vitamin D levels than healthy dogs in the shelter population (Jaffey et al. 2021); however it is unclear if this is a cause or effect of the respiratory illness. Therefore, no specific recommendations can be provided for supplementation in diseased animals. Specific antiviral therapy is not currently available or recommended for affected dogs.

Prognosis

Most dogs that become infected with organisms involved with CIRD survive, although fatalities can be seen, particularly with distemper virus and influenza virus. CIV and *Bordetella* infections can result in chronic signs in some cases. Subclinical shedders represent a source of environmental exposure for susceptible dogs, particularly in the case of *Bordetella*, which can survive in the environment. Importantly, prolonged shedding of H3N2 influenza virus can occur beyond 3 weeks, despite the fact that the dog is free of obvious clinical signs (Newbury et al. 2016).

In a dense population of dogs, appropriate infection control measures should be in place to limit the spread of respiratory disease. Reducing crowding, improving air exchanges, and using rigorous hygiene practices are all helpful. Most viruses are readily destroyed by bleach

or quaternary ammonia compounds, and workers should be alert for the possibility of spreading disease while working among animals. When disease is detected in a population, limiting contact of susceptible dogs with those showing clinical signs is important; however, dogs can spread infection in the absence of clinical signs. Ideally, sick dogs should be kept completely isolated from the rest of the population, and full clothing coverage, gloves, and booties should be used in environments containing sick animals. New dogs that enter the environment should be held in isolation until the incubation period (~7–10 days) for infectious diseases has passed.

Prevention

Vaccination against the commonly encountered pathogens reduces but does not eliminate clinical disease. The 2022 American Animal Hospital Association (aaha.org) Canine Vaccination Guidelines recommend core vaccinations against CDV, canine parvovirus, CAV-2, and possibly CPIV, as well as rabies vaccination. Given the commonality of CPIV infection, vaccination should likely be considered core. Non-core vaccines should also be considered in select instances. Use of a mucosal vaccine for *Bordetella* (some of which also include CPIV or CAV-2) can be used in susceptible dogs that will be exposed to a dense population of dogs, because it provides protection within 48–72 hours of administration. Subcutaneous vaccination also provides adequate protection, but it takes longer for the dogs to develop an immune response. Intranasal vaccination can occasionally have untoward side effects and dogs that are prone to respiratory disease might best be managed with oral or subcutaneous vaccines. Vaccination in the face of an outbreak has not appreciably lessened clinical disease.

Subcutaneous vaccines are available against H3N8 and H3N2 and a bivalent vaccine is available, although dogs can still develop a mild form of disease if exposed. The initial vaccine series is typically two injections separated by 2 weeks and must be administered 4–5 weeks prior to potential exposure to closely housed dogs. These vaccines will result in seroconversion, negating one of the diagnostic methods possible for influenza. Therefore, risk factors for disease must be considered when deciding whether to vaccinate against the influenza virus.

Parasitic Bronchitis

Pathophysiology

Parasites implicated in respiratory disease include lungworms *Filaroides hirthi* (canine), *Aelurostrongylus abstrusus* (feline), *Capillaria aerophila* (dogs and cats), *Oslerus osleri* (canine), *Crenosoma vulpis* (canine), *Paragonimus kellicotti* (dogs and cats), and larval migration of *Toxocara*, *Ancylostoma*, or *Strongyloides*. Specific features of life cycle, transmission, and diagnosis of each parasite are summarized in Table 5.2.

History and Signalment

Parasitic bronchitis occurs more commonly in young, outdoor animals and particularly those that hunt, because ingestion of an intermediate host is often involved in transmission. However, it can be encountered in any cat or large or small breed dog regardless of activity, because the mechanism for transmission of many of these parasites is incompletely understood. Most airway parasites are associated with cough; however, *O. osleri* and *Paragonimus* can lead to difficulty breathing. With infection by *Oslerus*, this is due to obstruction of the trachea by parasitic nodules, while *Paragonimus* leads to difficulty breathing when rupture of a parasitic cyst results in pneumothorax.

Physical Examination

Tracheal sensitivity is generally present with most parasitic infections, and wheezing can be heard because of airway inflammation or obstruction. Tachypnea can be the primary sign observed in young kittens infected with *Aleurostronglyus*. Infection by *Paragonimus* and resultant pneumothorax can be detected by the presence of tachypnea and an absence of breath sounds dorsally due to air accumulation. Percussion can detect hyper-resonance in the dorsal thorax.

Diagnostic Findings

Blood work can reveal eosinophilia and fecal examinations can be diagnostic (Table 5.3), although because parasites are shed intermittently, a negative fecal does not rule out infection. *Filaroides*, *Capillaria*, and *Aelurostrongylus* can result in a nodular pattern, mixed interstitial-alveolar densities, or in a bronchial pattern (Figure 5.15). *O. osleri* results in nodules within the trachea near the carina, and *C. vulpis* can rarely cause nodular proliferations. These can be seen radiographically or during bronchoscopy and appear as round, soft tissue densities (Figure 5.16). In animals with larval migration, radiographic infiltrates are often concentrated in the caudal lobes. Parasitic larvae can be found in the airways (Figure 5.17), in biopsy samples, or in bronchoalveolar lavage fluid cytology. PCR is available for some parasites.

Paragonimus forms nodular densities or either air- or fluid-filled cysts. Nodules are typically thin-walled in the dog and thick-walled in the cat. Pneumothorax is evident radiographically as loss of vascular and bronchial markings in the periphery (see Chapter 7).

Treatment (Table 5.3)

Most airway parasites can be treated medically with oral or topical anti-parasiticides, although *O. osleri* can be particularly refractory to therapy. When rupture of a *Paragonimus* cyst is identified, a chest tap is needed to alleviate respiratory difficulty and lung lobectomy is usually required.

Prognosis

Most animals will recover from parasitic bronchitis. Mortality can occur with rupture of *Paragonimus* cysts or because of airway obstruction associated with refractory infection by *O. osleri*.

Inflammatory Disorders

Inflammatory Laryngitis

Pathophysiology

Non-specific inflammation of the larynx is common secondary to any infectious or inflammatory disease of the lower airway, and it can also be encountered in animals with vomiting disorders that result in acid injury to the upper airway. Brachycephalic breeds are particularly prone to development of inflammatory lesions or vocal fold granulomas, likely associated with trauma from airflow obstruction along with gastroesophageal reflux disease. Laryngeal inflammation can also occur secondary to trauma associated with choke chain injury, an insect bite, or inhalation of noxious fumes. Less commonly, primary inflammation of the larynx is encountered. In the cat, this lesion can appear similar to a neoplasm, and

biopsy differentiation is crucial. The etiology of inflammation is usually not determined, however trauma and gastroesophageal reflux disease should be considered.

History and Signalment

Animals with primary or secondary laryngitis can be of any age or breed. Owner complaints are similar to those seen with other laryngeal diseases and include inspiratory difficulty, dysphonia, inappetence or difficulty swallowing, and retching.

Physical Examination

Stridor or loud inspiratory sounds over the larynx are signs of upper airway obstruction, and cervical palpation will sometimes reveal an unusual larynx (firm or asymmetric) in some dogs or cats.

Diagnostic Findings

Cervical radiographs can reveal caudal retraction of the hyoid apparatus (Figure 5.1), although this is a very non-specific finding that can be artifactual due to increased respiratory effort. Increased soft tissue density in the region of the larynx or a possible mass lesion should be evaluated by visual inspection and biopsy under anesthesia. Careful pre-anesthetic planning is advised in case an obstructive lesion is discovered that requires a tracheostomy. A wire or stylet should be available to facilitate intubation if necessary. Secondary laryngitis is associated with hyperemia and mucosal edema, while primary or granulomatous laryngitis is typically associated with a mass effect on the larynx. A tissue sample for histopathology can be acquired using 2 or 3 mm cup biopsy forceps (Sontec Instruments, Centennial, CO, or Karl Storz Veterinary Endoscopy, Goleta, CA) and will reveal lymphocytic or granulomatous inflammation in the absence of neoplastic change.

Table 5.3 Clinical characteristics, diagnostic methods, and treatment for parasitic bronchitis.

Parasite	Method of transmission	Special features	Clinical findings	Diagnosis	Treatment
Filaroides hirthi	Fecal–oral	Young dogs in confinement or kennels	Cough	L1 in feces (Baermann)	Ivermectin 1 mg/kg once weekly × 2 Albendazole 50 mg/kg BID for 5 days Fenbendazole 50 mg/kg/day for 3 weeks
Aelurostrongylus abstrusus	Ingestion of intermediate host (snail, bird, or rodent)	Outdoor cats or hunters	Cough	L1 in feces (Baermann) or tracheal wash cytology	Fenbendazole 50 mg/kg daily for 3–10 days Milbemycin oxime 4 mg/kg every 2 weeks for 6 weeks Topical moxidectin (1%) monthly for 3 months or a single dose of imidacloprid-moxidectin topically
Capillaria aerophila	Ingestion of eggs or intermediate host (earthworm)			Eggs in fecal float or sedimentation (whipworm-like)	Fenbendazole 50 mg/kg daily for 10 days Ivermectin 0.2–0.4 µg/kg SQ for 1–2 doses
Oslerus osleri	Regurgitative feeding	Dogs exposed to wild canids?	Obstructive respirations, cough	Nodules at carina	Unknown
Crenosoma vulpis	Ingestion of intermediate host (mollusk)		Chronic cough	L1 in feces (Baermann) or BAL fluid cytology, worms in the airways or	Fenbendazole 50 mg/kg/day for 7–10 days Milbemycin oxime 0.5 mg/kg

Parasite	Method of transmission	Special features	Clinical findings	Diagnosis	Treatment
				bronchial nodules	weekly for 4 doses Topical imidacloprid (10 mg/kg) plus moxidectin (2.5 mg/kg)
Paragonimus kellicotti	Ingestion of crayfish	Hunters	Cough, tachypnea, pneumothorax	Large operculated egg in tracheal wash cytology or feces (sedimentation or zinc sulfate centrifugation flotation)	Praziquantel 25 mg/kg PO TID for 2–3 days Fenbendazole 50 mg/kg PO for 10–14 days
Larval migration	Perinatal	Young animals	Cough, tachypnea	Fecal flotation for ascarid eggs, eosinophilic airway wash	Fenbendazole 50 mg/kg daily for 10 days

BAL, bronchoalveolar lavage; BID, twice a day; PO, orally; SQ, subcutaneously; TID, three times a day.

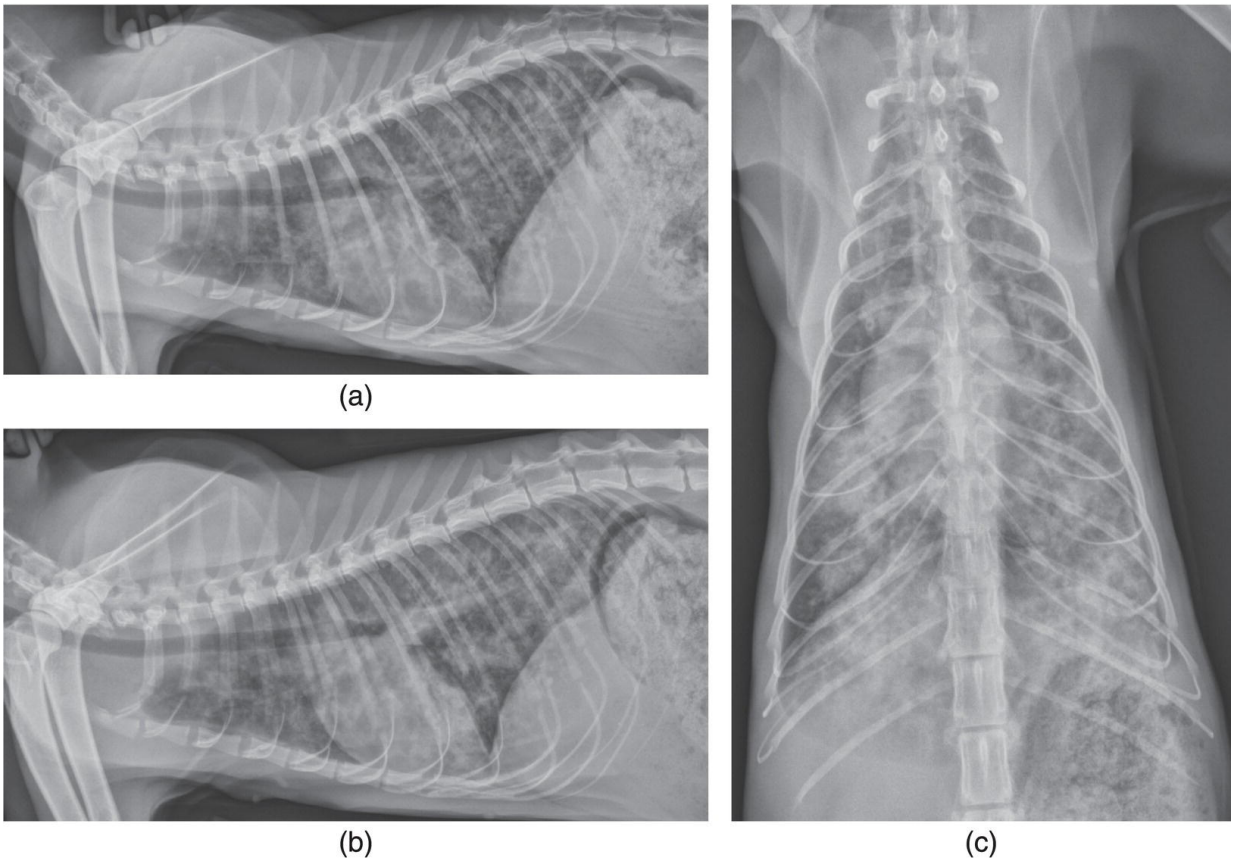


Figure 5.15 Right lateral (a), left lateral (b), and ventrodorsal (c) radiographs from a young adult intact female cat with *Aelurostrongylus* demonstrates marked alveolar-nodular infiltrates.

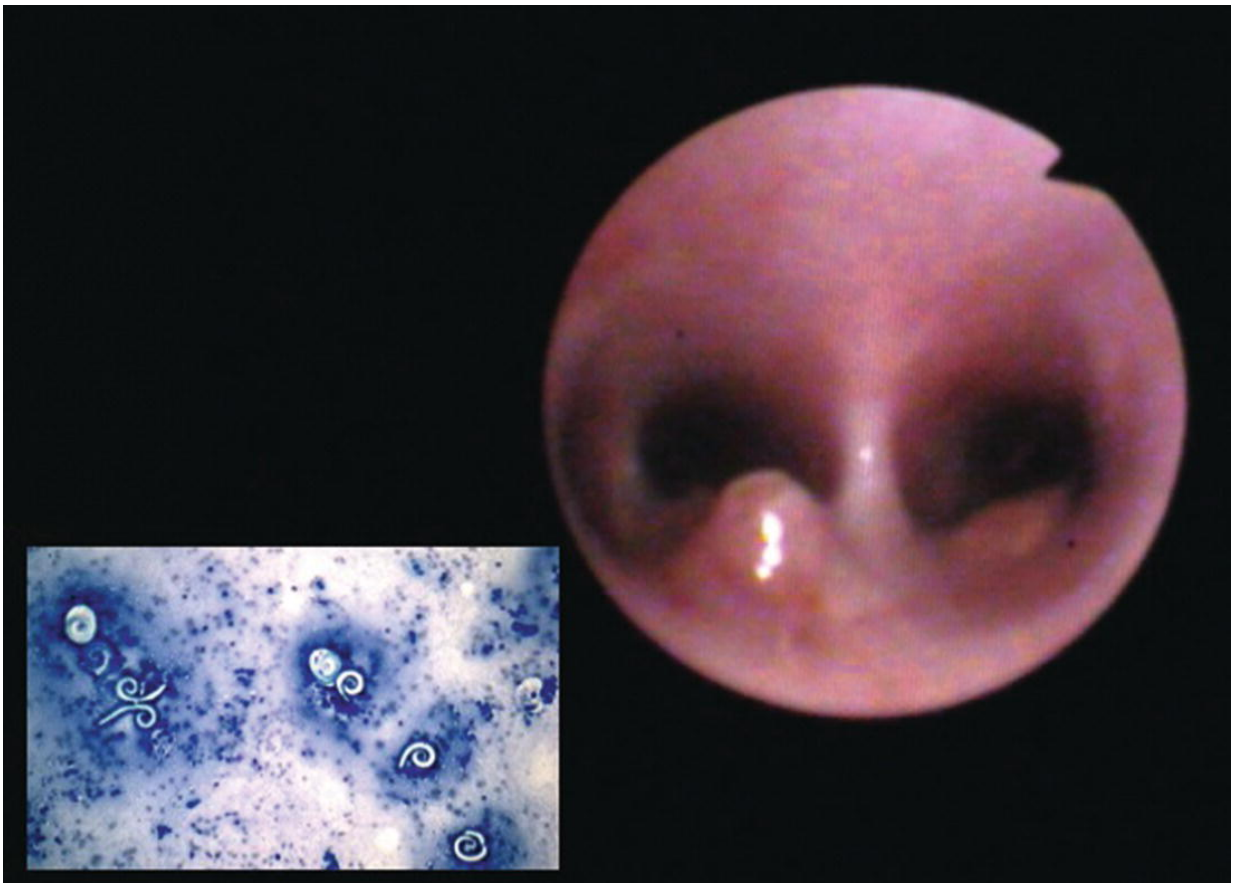


Figure 5.16 Bronchoscopic visualization of the distal airways in a 1 year old FS Toy Poodle presented for evaluation of cough shows nodular proliferations that contained *Oslerus osleri* (inset) on histopathologic examination.

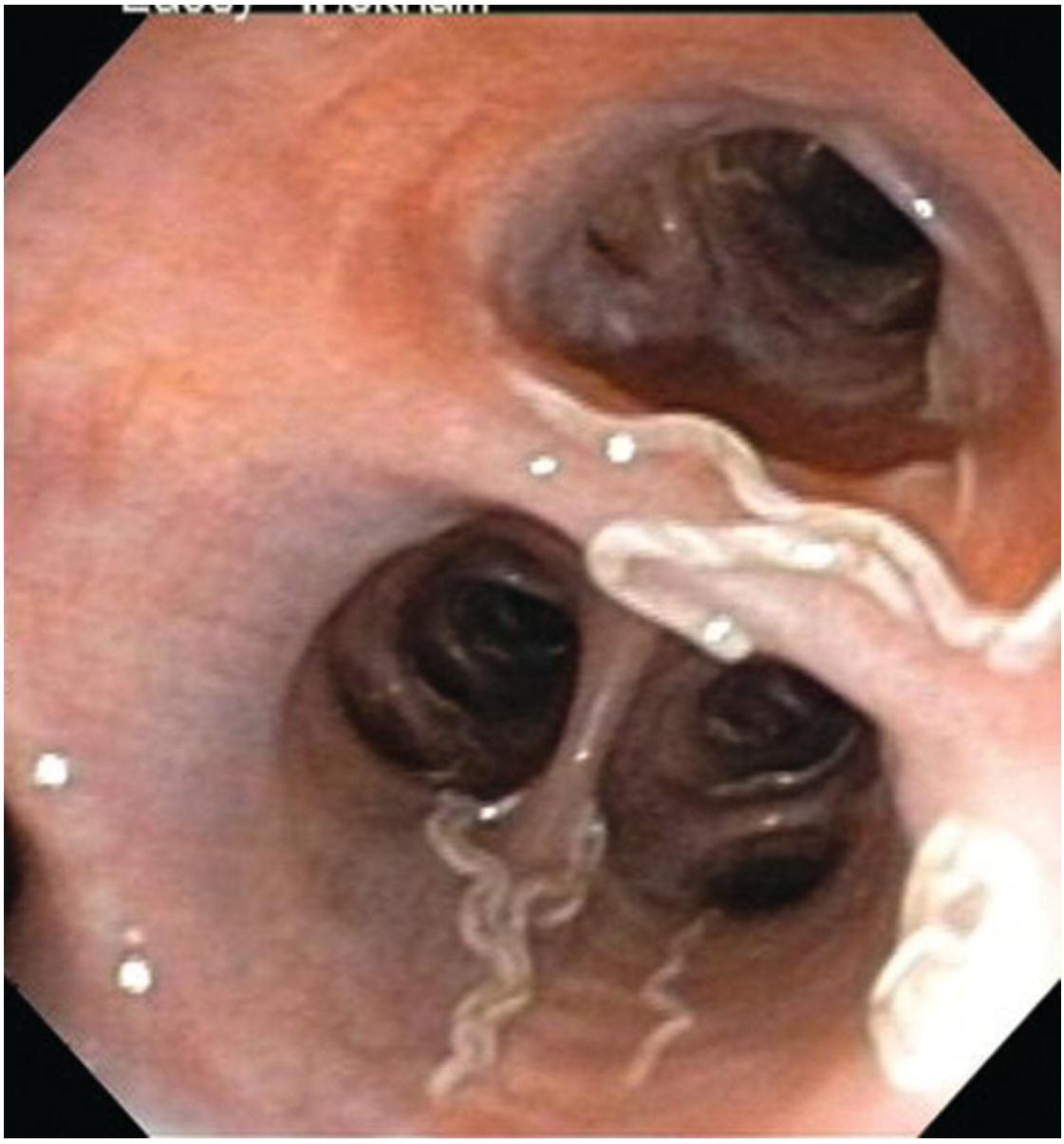


Figure 5.17 Bronchoscopy in a 6 year old Golden-Doodle with a 1 month history of cough shows parasitic larvae of *Crenosoma vulpis* in the airways.

Treatment

Secondary laryngitis will usually resolve with treatment of the underlying airway or gastrointestinal condition. Primary inflammatory laryngitis can require debulking surgery, laryngectomy, and/or tracheostomy to alleviate respiratory distress. Some cases respond adequately to glucocorticoids alone or in combination with surgery (Tasker et al. 1999).

Canine Chronic Bronchitis

Pathophysiology

Chronic bronchitis is defined by the presence of a daily cough that occurs for at least 2 months of the year and lacks a specific cause. Cough is related to activation of irritant

receptors in the airways by products of inflammatory cells and excessive airway mucus. While the specific cause is unknown, recruitment of inflammatory cells could result from exposure to environmental pollutants, second-hand smoke, or inhaled irritants. Neutrophilic infiltration of the airway results in release of proteases, elastases, and oxidizing products that perpetuate inflammation and airway damage. Histologic examination of mucosal biopsy specimens from dogs with chronic bronchitis reveals hypertrophy and hyperplasia of mucous glands and goblet cells, fibrosis of the lamina propria, and epithelial erosion with squamous metaplasia. These changes contribute to obstruction of airflow through accumulation of mucus within the airway and lead to clinical signs of cough and exercise intolerance. Bronchoconstriction is not a component of this disease in dogs.

Focal or generalized bronchomalacia can sometimes accompany chronic bronchitis and other forms of inflammatory airway disease, perhaps because inflammatory mediators lead to weakening of cartilage or have effects on airway smooth muscle tone. It is also possible that chronic airway collapse stimulates some degree of inflammation through repetitive airway injury caused by apposition of airway walls. Chronic bronchial inflammation can lead to bronchiectasis in some cases.

History and Signalment

Chronic bronchitis is a disease of middle-aged to older dogs, and both large and small breed dogs are affected. The predominant clinical complaint is persistent coughing, which can be a dry, hacking cough or moist and productive, when copious amounts of respiratory secretions are produced. A “goose honk” cough might predominate in dogs that have concurrent tracheal or airway collapse. Dogs are typically healthy and relatively active, although in the later stages of disease, exercise intolerance or heavy breathing can be reported.

Physical Examination

Dogs with chronic bronchitis are often overweight but appear otherwise healthy. Some dogs will pant excessively, while dogs severely affected by bronchitis can have prolonged expiration or an expiratory push. Tracheal sensitivity is usually present because of non-specific airway inflammation. Thoracic auscultation can be normal or sometimes will reveal coarse, diffuse crackles associated with mucus accumulation or opening and closing of small airways. These findings in conjunction with expiratory effort are difficult to differentiate from those associated with bronchomalacia. Expiratory wheezes are considered the hallmark of chronic bronchitis, although these are not commonly ausculted. Careful cardiac auscultation is advised to detect concurrent valvular insufficiency, which is a common concurrent condition in older small breed dogs.

Diagnostic Findings

The diagnosis of chronic bronchitis is one of exclusion, because infectious bronchitis (*Mycoplasma* or *Bordetella*) and airway collapse cause similar historical and physical examination findings. Clinicopathologic abnormalities are typically absent in dogs with chronic bronchitis. Arterial blood gas analysis (if performed) generally shows only mild to moderate hypoxemia, and hypercarbia is not detected until late in the disease if respiratory failure ensues.

Thoracic radiography is an important part of the diagnostic work-up to confirm the likelihood of chronic bronchitis and to rule out other conditions. Classically, a generalized increase in bronchial infiltrates is expected in dogs with chronic bronchitis. End-on bronchi (doughnuts) and airways seen in longitudinal section (tram lines) represent airway walls thickened by inflammation (Figure 5.18). However, radiographs are insensitive for detecting chronic bronchitis, and in a case-controlled evaluation using film radiography, only increased

thickness of airway walls and increased numbers of visible airway walls differed between normal dogs and dogs with bronchitis (Mantis et al. 1998). Digital radiography might be more able to detect bronchial abnormalities, however it is important to realize that normal thoracic radiographs do not rule out the diagnosis of chronic bronchitis. CT has been suggested as a means for identifying thickening of airway walls by comparing bronchial wall thickness to pulmonary artery diameter in the cranial lung lobes, with a ratio exceeding 0.6 deemed consistent with the diagnosis of chronic bronchitis (Szabo et al. 2015). However, another study reported that <15% of dogs with chronic bronchitis had a ratio greater than 0.6 and interobserver variability was relatively high, calling into question the value of CT in the diagnosis of bronchitis (Mortier et al. 2018). Different interpretations might be partly explained by the lack of pulmonary inflation during CT in the latter study. In a dog suspicious for bronchitis, the primary value of CT would be to document the sequela of bronchiectasis and airway plugging or to use inspiratory and expiratory CT to determine the presence of airway collapse.

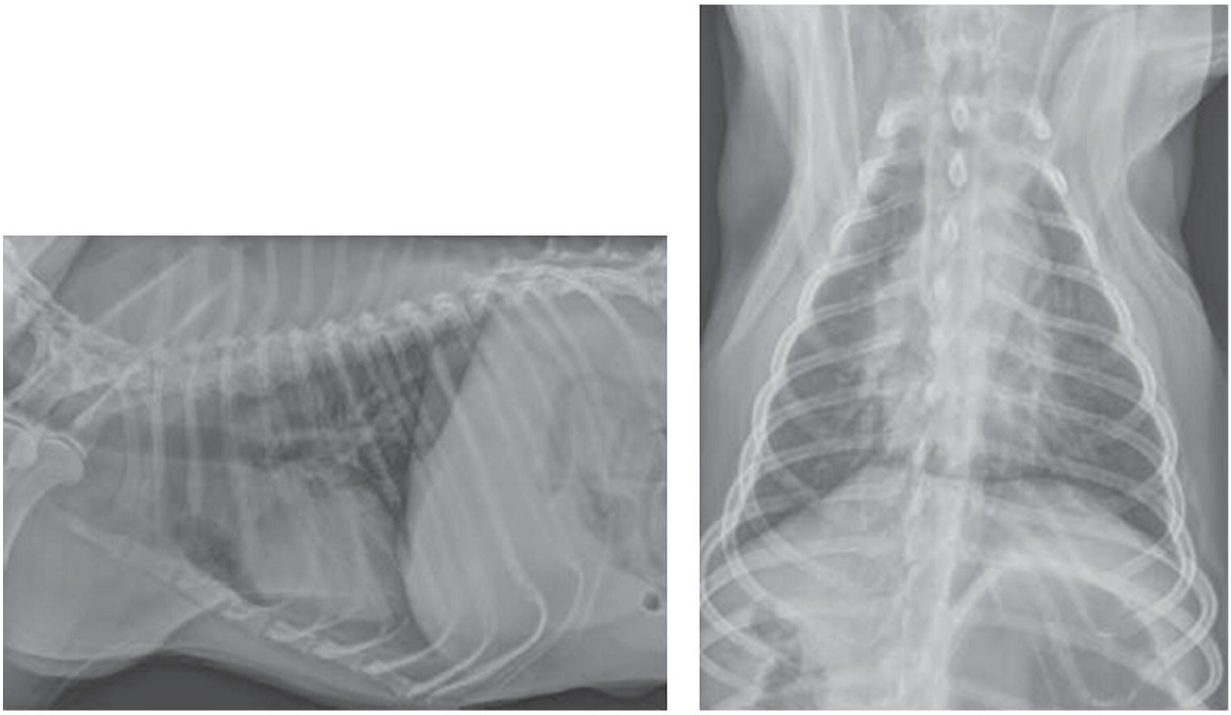


Figure 5.18 (a) Right lateral and (b) dorsoventral radiographs from a 12-year-old male castrated (MC) Basenji with a 2-year history of cough. Bronchial walls are thickened and easily visualized on both radiographic views. Spondylosis of the thoracic spine is also evident.

Collecting airway samples by tracheal wash or bronchoscopy is recommended to characterize the cellular infiltrate in the airway and to rule out infectious causes of cough prior to initiating anti-inflammatory therapy. Bronchoscopy is particularly useful when typical radiographic findings of bronchitis are lacking, because visual findings and airway cytology can be diagnostic; however, careful case selection is important to avoid complications. Obese dogs with marked expiratory effort seem more likely to have anesthetic difficulties, and judicious therapeutic trials using theophylline and weight loss might be considered for these dogs. Dogs with chronic bronchitis have airway hyperemia, the airway mucosa has a cobblestone or irregular appearance, and most dogs have increased mucus lining the airway (Figure 5.19). In

animals with long-standing bronchitis, fibrotic inflammatory nodules can be seen protruding into the bronchial lumen.

Chronic bronchitis can be confirmed with airway sampling via tracheal wash or bronchoscopy. Cytologically, chronic bronchitis is characterized by an increase in total cell numbers and a predominance of non-degenerate neutrophils (Figure 5.20). Some dogs have a high proportion of lymphocytes in airway washings, and it is unclear whether this represents a variant of chronic bronchitis or is related to bronchomalacia (Johnson and Vernau 2019). Increased mucus is present in many airway samples, and Curschmann's spirals (bronchial casts of airway mucus) are sometimes noted. Epithelial cells and squamous metaplasia can also be seen on cytologic examination.

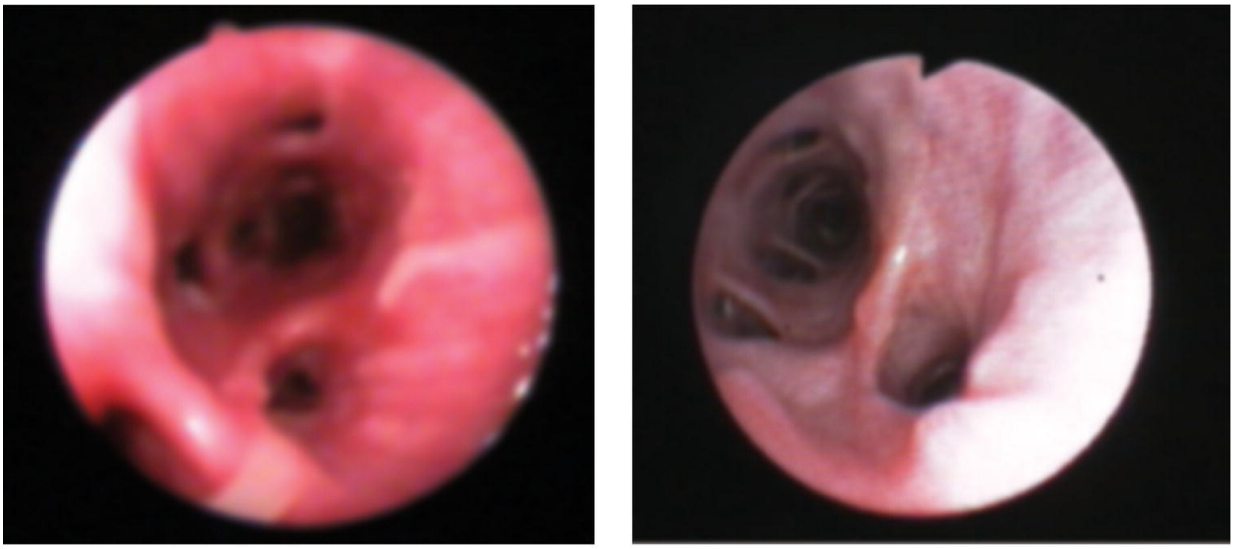


Figure 5.19 Bronchoscopic images from two dogs with chronic bronchitis. (a) The mucosa is dramatically hyperemic and thick mucus is evident streaming from the airways. (b) The mucosa is mildly hyperemic, and nodular proliferations are present that distort the epithelial surface.

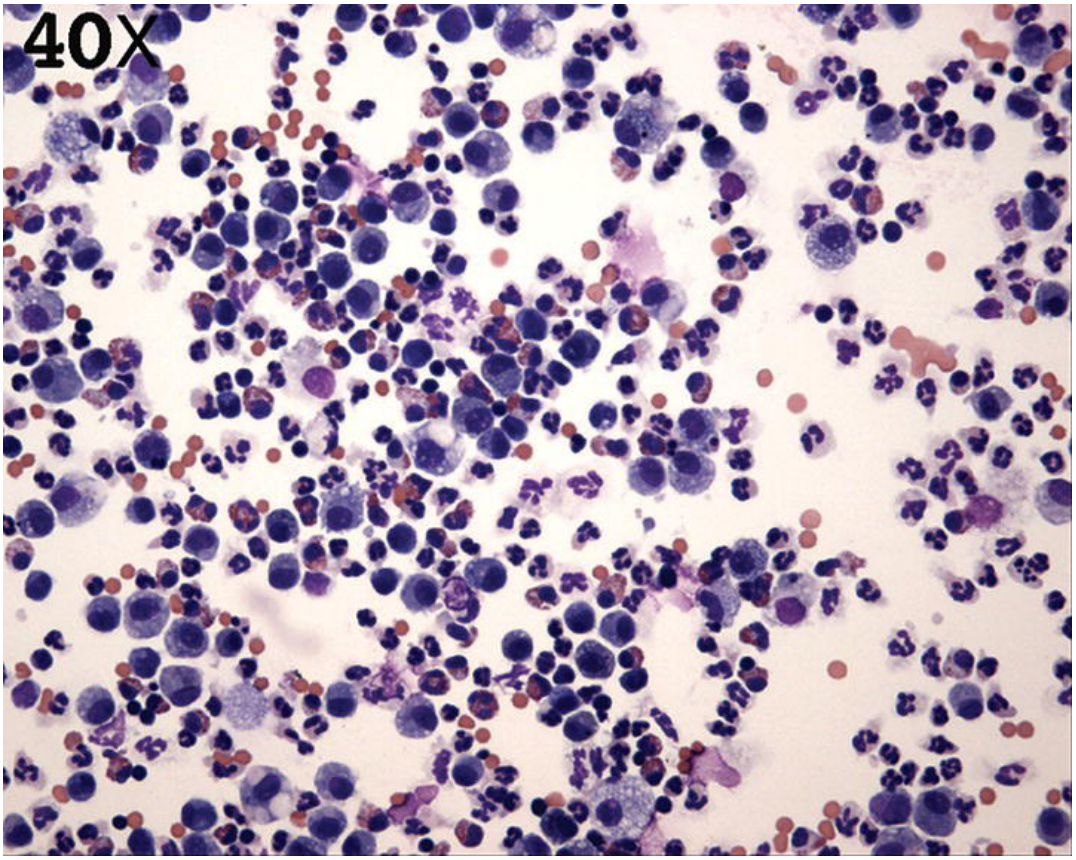


Figure 5.20 Neutrophilic airway cytology from a dog with chronic bronchitis (40×). In this cytospin preparation of bronchoalveolar lavage fluid, non-degenerate neutrophils represent 60% of the cell count, with the remainder of cells comprising alveolar macrophages. Red blood cells suggest airway hemorrhage due to increased friability of airway walls.

Although suppurative inflammation is typically present on cytologic examination, bacterial infection is not a significant problem in the majority of dogs with chronic bronchitis. A light growth of bacteria is not unexpected, because the trachea and large airways of dogs are not sterile. Because *Mycoplasma* is part of the normal oral flora but also can exacerbate lower airway injury, special culture techniques should be performed in bronchitic animals to rule out *Mycoplasma* infection.

Treatment

Anti-inflammatory Agents

Therapy with glucocorticoids is successful in resolving clinical signs in the majority of dogs. It is essential that infectious diseases are ruled out before the initiation of anti-inflammatory treatment. Dosing of glucocorticoids should be tailored to the individual, with the severity of clinical signs, chronicity of disease, and general systemic health considered in decisions regarding treatment. Short-acting glucocorticoids such as prednisone or prednisolone are generally safe and effective in dogs with uncomplicated bronchitis. Initially, dogs require dosages of glucocorticoids ranging from 0.5 to 1.0 mg/kg every 12 hours for 5–7 days to induce remission of clinical signs. As clinical signs abate, the dosage should be decreased by half every 5–10 days and, when possible, drugs should be administered on an alternate-day basis to allow normalization of the pituitary–adrenal axis. Long-term therapy (2–3 months) can be anticipated in most cases, although discontinuation of medication is often possible. When disease worsens as the drug dose is decreased, a return to the higher dose of glucocorticoid that controlled clinical signs is required. Alternatively, treatment with inhaled glucocorticoids, bronchodilators, or antitussive agents can be added (see later). Long-acting glucocorticoids such as dexamethasone, triamcinolone, and methylprednisolone acetate are not recommended as they do not have a therapeutic advantage over prednisone and are associated with more severe derangements of the pituitary–adrenal axis.

To avoid most of the systemic effects of glucocorticoids, inhaled medications can be employed in animals that will tolerate administration via a facemask. See Chapter 3 for more details. Dogs with excessive accumulation of airway mucus can sometimes require concurrent administration of oral glucocorticoids or nebulization therapy to reduce mucus and allow inhaled medications to contact the airway receptors. Some individuals require life-long or intermittent therapy with oral or inhaled glucocorticoids.

Bronchodilators

Active bronchoconstriction is not a component of canine chronic bronchitis, therefore beta-agonists (oral or inhaled) are not useful in management of this condition. However, extended-release theophylline can sometimes be clinically helpful in reducing cough or respiratory difficulty and can allow a reduction in the dosage of glucocorticoid required to control clinical signs. It might provide other beneficial effects such as enhancing cardiac performance, reducing respiratory effort, and stimulating mucociliary clearance. In dogs that fail to respond adequately to glucocorticoids, a 2-week trial on extended-release theophylline is a reasonable therapeutic option (see Chapter 3).

Antibiotics

Bacterial infection is not a component of chronic bronchitis; however, if a dog is not a good candidate for airway sampling, an antibiotic trial could be considered prior to instituting glucocorticoid therapy. Doxycycline is a reasonable antibiotic choice in this situation because of its efficacy against *Mycoplasma* and most other respiratory pathogens, as well as its anti-inflammatory effects.

Antitussive Agents

Antitussives are most commonly required in dogs with chronic bronchitis that have concurrent airway collapse. When possible, use should be delayed until clinical response to glucocorticoids has been determined and suggests that the majority of inflammation has resolved. If used too soon, antitussive agents can result in trapping of mucus in the lower airways and worsened airway injury. See Chapter 3 for further details.

Additional Therapy

Maximal efforts should be made to achieve weight loss in dogs with chronic bronchitis. Animals with concurrent tracheal or airway collapse or marked tracheal sensitivity benefit from use of a harness in place of a collar. When stresses in the environment are encountered, such as cigarette smoke, pollutants, heat, or humidity, the animal should be removed to a cool, clean area.

Some dogs benefit from intermittent airway humidification via nebulization to improve clearance of airway secretions. An ultrasonic or compressed air nebulizer is preferred for respiratory therapy because it produces sufficiently small particles of saline (2–5 μm) to penetrate deep into the airways. Sterile saline in individual unit vials is most appropriate for use in the nebulizer. Coupage of the chest or gentle exercise after nebulization facilitates clearance of secretions. For dogs with copious airway secretions, an oral mucolytic agent such as *N*-acetylcysteine might also be helpful (see Chapter 3).

Prognosis

When a diagnosis of chronic bronchitis is made, owners should understand that this is a chronic disease that can be controlled but never fully cured. Reduction in cough by 50% should be considered a successful outcome, particularly in dogs that have concurrent airway collapse or bronchiectasis. The majority of animals have residual cough and exhibit clinical signs periodically throughout life. Bronchoscopic changes and the presence of fibrosis or chronic inflammation on biopsy specimens confirm the irreversibility of airway disease. The goals of therapy are to control inflammation, thus limiting clinical signs, to diagnose and treat infection if it occurs, and to prevent worsening airway disease that might lead to debilitating sequelae such as bronchiectasis and cor pulmonale.

Feline Asthma/Bronchitis

Pathophysiology

Feline bronchial disease is a disorder associated with airway inflammation (eosinophilic or neutrophilic) in the absence of infection that results in excessive mucus production, epithelial hyperplasia, and in the asthmatic form of disease, airway smooth muscle constriction. Over time, inflammation leads to airway remodeling, which results in a physically smaller airway lumen and fixed airway obstruction, that leads to the clinical signs of cough and/or respiratory distress seen in affected cats. Acute respiratory distress is associated with bronchoconstriction of hyper-responsive airways and is considered one of the hallmarks of

the asthmatic phenotype. Chronic cough is sometimes considered more suggestive of bronchitis, although attempts to define inflammatory airway disease as two distinctive syndromes with specific etiologies have not been successful to date.

Disease prevalence has not been established in the cat population, but inflammatory airway disease is encountered frequently and is the most common cause of cough in various studies of feline lower respiratory tract disease. While etiologic factors that induce airway inflammation have not been elucidated in the naturally occurring disease, sensitization to antigen or allergen results in similar clinical and radiographic features of disease in experimental models. Studies in naturally occurring disease have produced conflicting results regarding the role of allergens in disease. In a study of 10 cats with naturally occurring respiratory signs, there were significantly more serum and intradermal responses to a wide variety of allergens (grass, weed, mold, and trees) than in cats lacking observable respiratory tract disease (Moriello et al. 2007). A non-controlled study in cats with respiratory signs suggested an allergic etiology in 15 of 18 (78%) cats based on 2+ or 3+ serum allergen-specific IgE results (van Eeden et al. 2020). Two case-controlled studies identified positive serum allergen responses in both healthy cats and those with various forms of inflammatory airway disease (Buller et al. 2020; Hörner-Schmid et al. 2023), suggesting that allergy might play a role in some but not all cats. Some studies suggest responsiveness to a mite allergen, however allergy testing in general is fraught with inconsistent results (see Chapter 2). Other factors that have been suggested to play a role in the initiation or perpetuation of airway inflammation include genetic susceptibility, exposure to environmental pollutants or irritants, oxidant-mediated damage, and gastroesophageal reflux.

History and Signalment

Any age cat can develop inflammatory airway disease, although middle-aged females (2–8 years) seem to be more frequently represented. Siamese cats may have an increased incidence of disease and might also suffer from a more chronic form of bronchial disease. Coughing and/or respiratory distress are the most frequently encountered complaints in cats with bronchial disease, and the duration of illness, severity of signs, and presence of other clinical abnormalities are variable. The cough is often described as a dry, “hacking” cough, and paroxysms of coughing with marked abdominal effort can be reported. Some cats may be observed to cough just once a day, but this low frequency does not necessarily correlate with the degree of airway inflammation present. Owners can report audible breathing sounds or wheezes that become progressively worse over time. Exercise intolerance can be evident, and the cat may limit its activity to lessen stress on the respiratory system. Cats that develop bronchoconstriction usually display acute respiratory distress, tachypnea, and occasionally cyanosis.

Environmental history is important in cats with bronchial disease, and astute owners are sometimes able to identify trigger events that result in bronchoconstriction. Coughing and respiratory difficulty can worsen in association with use of aerosol sprays, the presence of cigarette smoke, or increased dust in the environment because the airways of cats with inflammation are primed to respond to any irritant. Avoidance of recognized triggers can lessen bronchoconstrictive episodes and reduce cough.

Physical Examination

Cats with airway disease can appear normal at rest and have normal pulmonary auscultation. However, these cats will often display increased tracheal sensitivity, and post-tussive crackles can sometimes be auscultated. Harsh lung sounds, crackles, or expiratory wheezes can be heard intermittently in affected cats, and the expiratory phase of respiration may be prolonged. In cats in the midst of a bronchoconstrictive episode, air trapping can occur distal

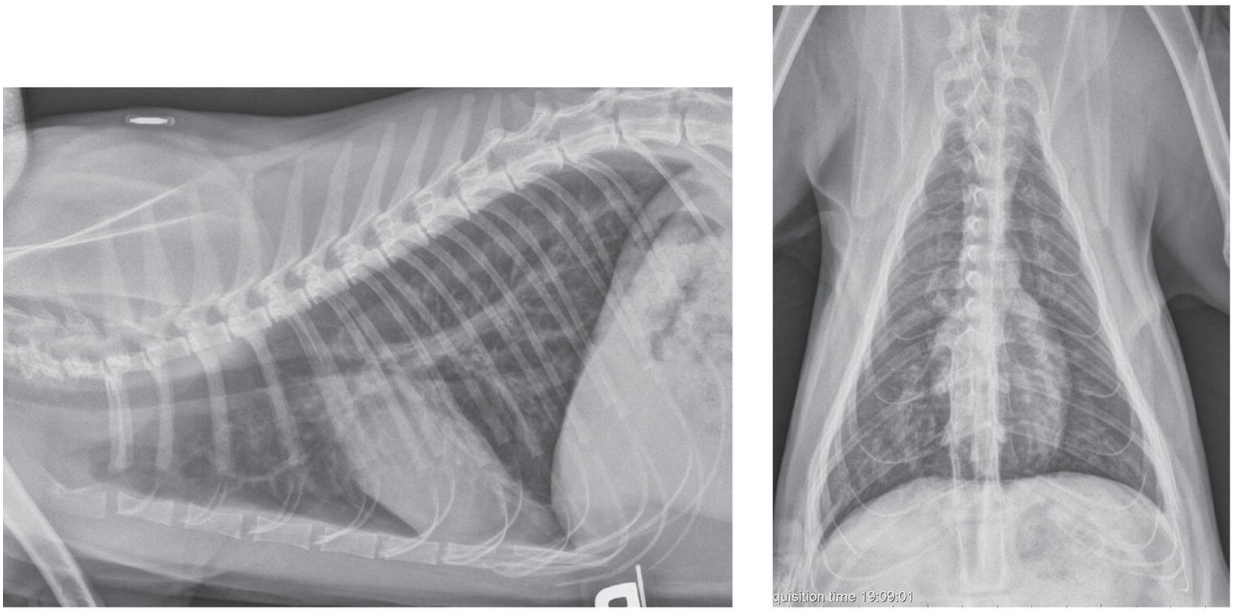
to obstructed airways, leading to a barrel-shaped chest. Auscultation in this area of the lung will be relatively quiet, and increased resonance is found on percussion. The remainder of the cat's physical examination is typically normal.

Diagnostic Findings

Cats with bronchial disease or feline asthma can have a normal leukogram or a neutrophilic leukocytosis on a CBC, and peripheral eosinophilia is a variable finding. A biochemical profile may reveal hyperproteinemia as a non-specific indicator of chronic inflammation. Specific tests are required to rule out parasitic bronchitis with *Aelurostrongylus* (see parasitic bronchitis), feline heartworm disease (see Chapter 8), and infectious bronchitis (*Mycoplasma* or *Bordetella*).

The classic radiographic finding in feline bronchial disease is thickening of airways (Figure 5.21); however, radiographs can appear relatively normal, might not match the severity of the clinical presentation, or can appear similar to those found with infectious causes of cough. Radiographic findings and severity scores of cats with eosinophilic, mixed, or neutrophilic inflammatory airway disease were similar in one study (Lee et al. 2020). Cats with acute bronchoconstriction sometimes lack pulmonary infiltrates but show other radiographic signs of airway obstruction, including flattening of the diaphragm, air trapping, or hyperlucency (Figure 5.22). An alveolar pattern (patchy or lobar involving the right middle lung lobe or other lung lobes) can be observed when a mucus plug obstructs a large airway and causes distal atelectasis (Figure 5.23).

Airway sampling through transoral tracheal wash or bronchoscopy can be used to evaluate specimens from feline airways and rule out an infectious cause of cough through culture and cytology (see Chapter 2). Pretreatment with terbutaline (orally or subcutaneously) prior to airway sampling improves the safety of the procedure, perhaps by lessening the bronchoconstrictive response to the lavage process. An eosinophilic tracheal wash specimen is supportive of the diagnosis of feline bronchial disease in a cat with cough and tends to be found in somewhat younger cats (Lee et al. 2020); however, non-degenerate neutrophils predominate in many cases of feline bronchial disease and mixed inflammation is also common (Figure 5.24). When bronchoscopy is performed and multiple lung lobes are sampled for cytology, differing types of inflammation (eosinophilic and neutrophilic) are found in a single cat in almost 50% of cases (Ybarra et al. 2012).



(a) (b)

Figure 5.21 (a) Right lateral and (b) dorsoventral radiographs from a 2-year-old male castrated domestic long hair (MC DLH) presented for chronic cough and recent respiratory distress demonstrate a marked, diffuse bronchial pattern. Bronchoalveolar lavage cytology revealed 72% eosinophils.

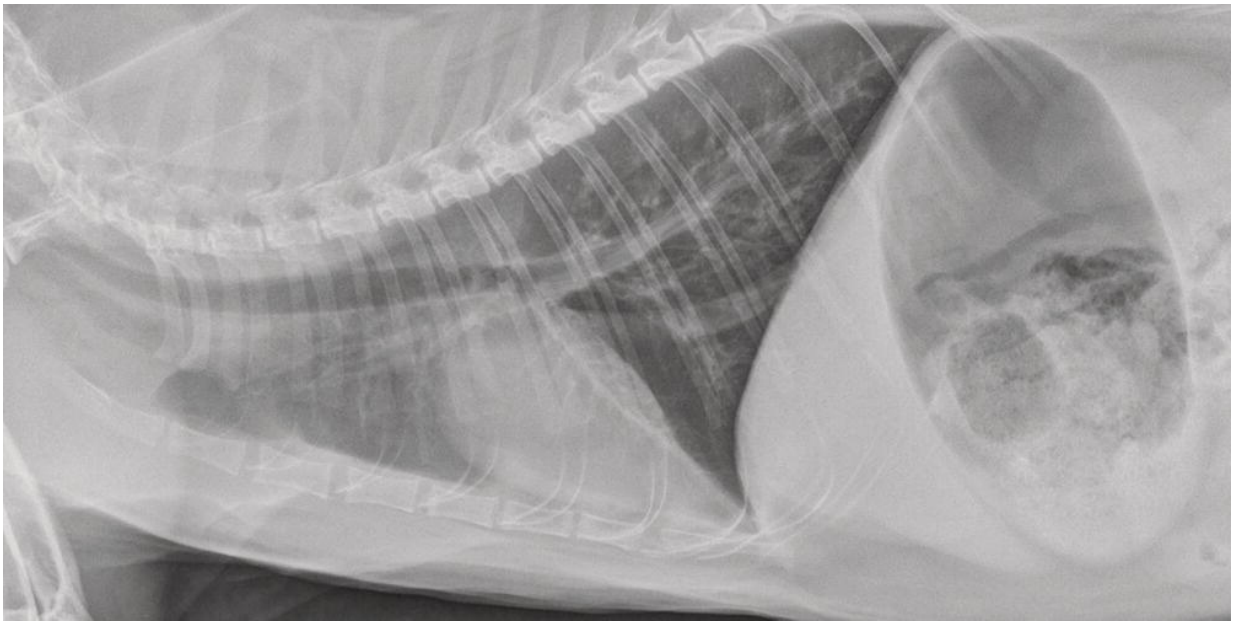


Figure 5.22 Right lateral radiograph from a 4-year-old male castrated (MC) Ragdoll cat with severe and repetitive attacks of respiratory distress. The lungs are hyperinflated and there is evidence of aerophagia. A moderate bronchial pattern is also present.

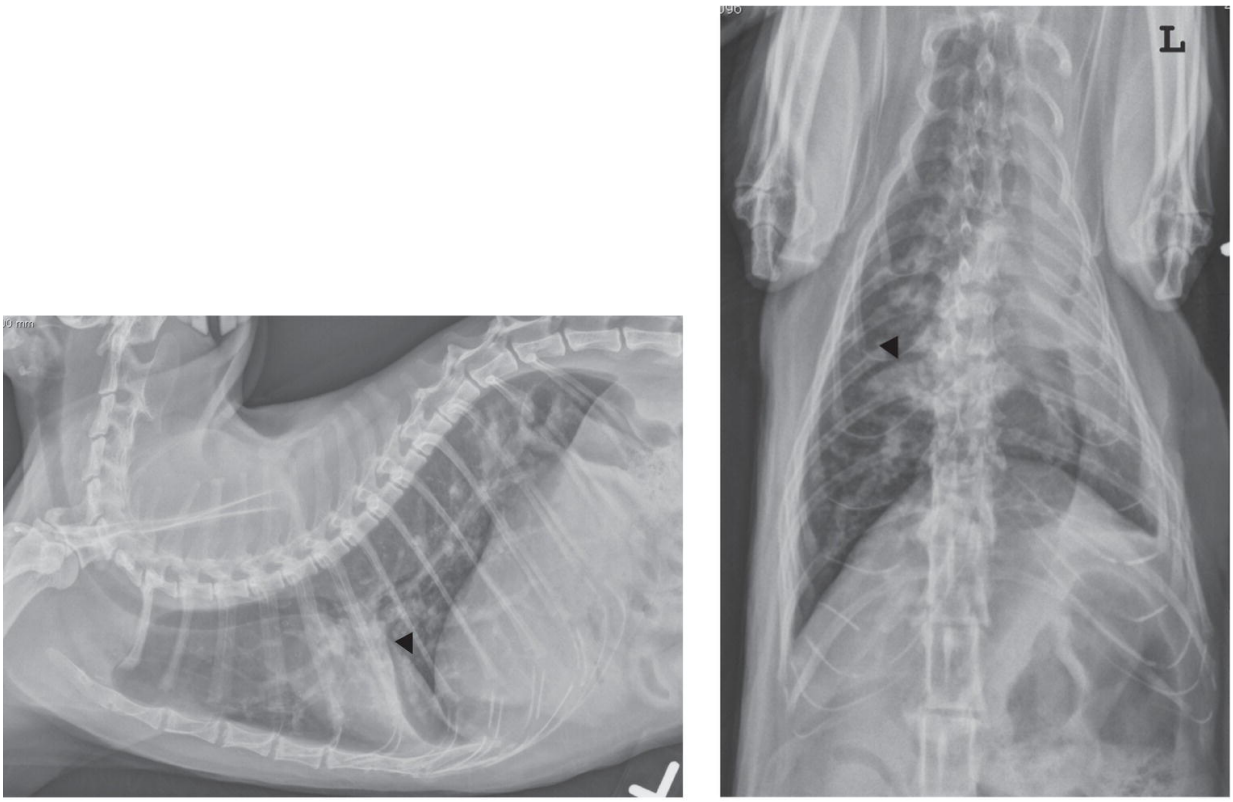


Figure 5.23 (a) Left lateral and (b) ventrodorsal radiographs from a 9-year-old male castrated (MC) Siamese with a long-term history of cough. On the lateral view, a lobar sign in the right middle lobe (to the left of the black arrowhead) is noted along with diffuse bronchial infiltrates. The ventrodorsal view reveals visible collapse of the right middle lung lobe (ventral to the black arrowhead). CT confirmed collapse of the right middle lobe and left cranial lung lobe (cranial and caudal segments) also.

Bacterial cultures should be submitted to rule out infection, although low numbers of bacteria can be isolated from the airways of both healthy and diseased cats because the airways are not sterile. The role of *Mycoplasma* as a cause for cough is somewhat controversial, but cats that have this organism isolated in conjunction with neutrophilic inflammation often respond to doxycycline, avoiding the need for long-term glucocorticoid therapy. Therefore, obtaining specific culture for *Mycoplasma* as well as aerobic bacterial culture is advised. PCR is also available for detecting *Mycoplasma* organisms, either as a general class of bacterium or for *M. felis*.

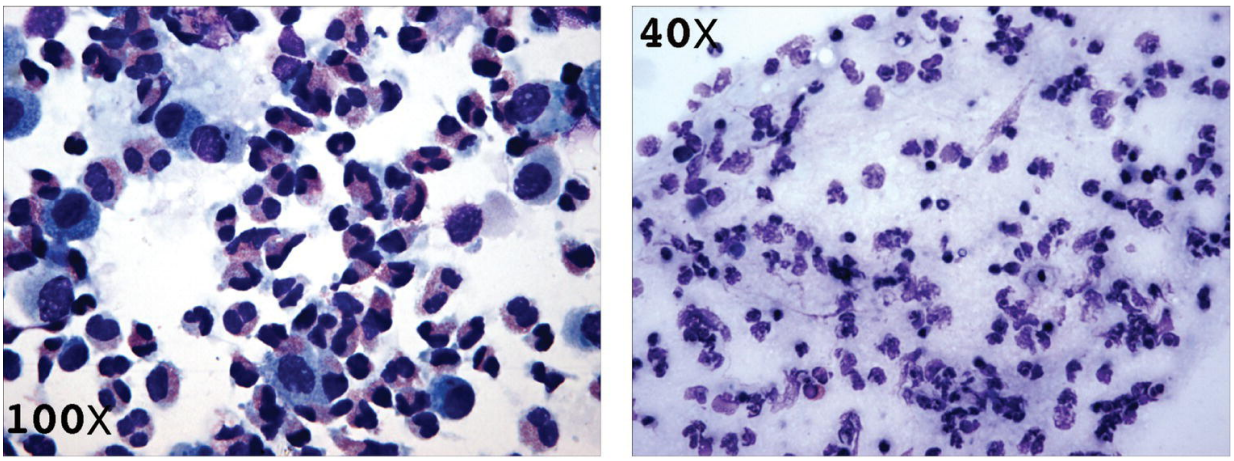


Figure 5.24 Bronchoalveolar lavage cytology from two cats with feline bronchial disease reveals (a) primarily eosinophilic inflammation and (b) neutrophilic inflammation in a mucus background.

Treatment

In the animal that presents with cyanosis and open mouth breathing, diagnostic tests should be kept to a minimum until respirations are stabilized. An oxygen-enriched environment should be provided. Terbutaline, a beta-2-agonist, is an effective bronchodilator with minimal cardiac side effects that can be administered subcutaneously or intravenously (0.01 mg/kg) and quickly relieves bronchoconstriction by functionally opposing smooth muscle contraction. Alternatively, albuterol, an inhaled beta-2-agonist, could be administered via facemask and spacing chamber. Respiratory rate and effort should be monitored visually during the first 15–30 minutes after treatment to determine therapeutic response. If the cat fails to improve, a second dose of terbutaline can be administered. If the cat remains in respiratory distress and bronchial disease remains highest on the differential list (based on a history of cough), short-acting glucocorticoids (i.e. dexamethasone) should be administered. Glucocorticoid therapy is not recommended initially because it will reduce ingress of eosinophils into the airway, thus changing the cytology of subsequent tracheal wash or bronchoalveolar lavage. If the cat fails to respond to bronchodilators and glucocorticoids, an alternate etiology of respiratory distress is likely. Because congestive heart failure can also result in tachypnea and respiratory distress, consideration should be given to administering furosemide in certain cases (see Chapter 1).

Anti-inflammatory Agents

Chronic management of feline bronchial disease relies on the judicious use of glucocorticoids to control inflammation. The duration and dose of glucocorticoid therapy are adjusted according to the severity of respiratory distress in the patient and the rapidity of response to treatment. Initially, prednisolone is administered orally at ~1 mg/kg BID for 5–14 days. The dosage can be decreased to 0.5 mg/kg BID or 1.0 mg/kg daily for 10–20 days if clinical signs are adequately reduced in severity. The dosage can be further tapered over time, but most cats appear to require life-long medication because airway inflammation can persist in the absence of clinical signs (Cocayne et al. 2011). Recurrent episodes of coughing or respiratory distress necessitate a return to the higher dosage of glucocorticoid that controlled clinical signs. Repeat diagnostic testing can also be indicated to ensure the proper diagnosis and to certify that airway infection has not developed due to immunosuppression (an unlikely

event). Cats are relatively resistant to the side effects of glucocorticoids; however, diabetes or congestive heart failure can result from oral therapy, and an attempt should be made to achieve the lowest dose of the drug that will control signs. Long-acting glucocorticoids offer no benefit in control of bronchial disease and tend to result in poor long-term control of inflammation.

Inhaled glucocorticoids are also effective in treatment of lower airway inflammatory disease (see Chapter 3). In cats with moderate-to-severe clinical manifestations of disease, oral glucocorticoids are sometimes recommended during the first 2 weeks of inhaled therapy for more rapid control of disease, however no clinical investigations have confirmed the need for this approach. It could be wise to use oral glucocorticoids initially to control airway mucus, which will then allow inhaled medications greater access to receptors lining the airways.

Bronchodilators

Cats that develop acute bronchoconstriction can require periodic treatment with a bronchodilator to alleviate smooth muscle constriction, although when inflammation is properly controlled this should not be encountered commonly. Selective beta-2-agonists such as terbutaline would be preferred and this drug is easily administered subcutaneously in an emergency situation or at home. Albuterol inhalers are also available for use with the pediatric spacing chamber and facemask, although regular use of specific isoforms of albuterol could potentially worsen airway inflammation (see Chapter 3). Beta-2-agonists are not recommended as the sole treatment for cats with asthma or bronchitis.

Sustained-release theophylline (~15–20 mg/kg orally once daily in the evening) can also be used in the cat, although it has weak to non-existent bronchodilatory properties. Sometimes it can allow a reduction in the dose of glucocorticoid required to control signs or it could have other beneficial effects on the respiratory tract (see Chapter 3).

Adjunct Therapy

Weight loss should be encouraged in obese cats, although this is much more challenging to achieve in the cat than in the dog. Similar to treatment of dogs with chronic bronchitis, sterile saline nebulization and use of mucolytic agents to encourage evacuation of mucus from the lower airways can be beneficial in some animals. Therapies used in humans such as leukotriene antagonists are not indicated for treatment of cats with bronchial disease. Allergen-specific rush immunotherapy resolved airway eosinophilia in cats with experimentally-induced allergic asthma (Lee-Fowler et al. 2009), although clinical application has not been evaluated.

Prognosis

Feline bronchial disease is associated with substantial morbidity and occasional mortality in the feline population. Cats with poorly controlled inflammation are at risk for airway remodeling, emphysema, bronchiectasis, and pneumothorax. Clinical signs of many cats are well controlled with medication; however, it must be given life-long in most cats. Cats that experience bronchoconstrictive attacks appear to be most likely to die from the disease or from euthanasia due to the cost of repeated veterinary visits.

Neoplastic Disorders

Pathophysiology

Multiple tumor types can affect the larynx and airways and include lymphosarcoma, squamous cell carcinoma, adenocarcinoma, plasmacytoma, melanoma, chondrosarcoma, and osteochondroma (a benign neoplasm). Most of these neoplasms cause clinical signs due to airway obstruction or compression rather than systemic manifestations of cancer such as hyporexia and weight loss.

History and Signalment

Lymphoma and osteochrondroma tend to affect younger animals, and other tumors are typically found in middle-aged to older animals. Owners will often report clinical complaints associated with airway obstruction, including dysphonia and loud or difficult breathing. Dysphagia is sometimes encountered with laryngeal masses that occlude the pharyngeal opening. Cough or collapse associated with airway obstruction can also be encountered.

Physical Examination

Obstruction of airways dominates the clinical picture. When a large airway is affected (larynx or trachea), inspiratory prolongation and auscultation of loud inspiratory sounds or stridor over the larger airways would be expected. An occlusive mass in a large or central airway anywhere from the larynx to the carina could result in expiratory obstruction also and expiratory sounds on auscultation. Stridor might be detected on inspiration and loud wheezes on expiration. Obstruction of more distal airways can result in variable auscultatory findings and an abnormal respiratory pattern may or may not be present.

Diagnostic Findings

Cervical and thoracic radiography can reveal a mass lesion obstructing the air column in the laryngeal, cervical, or intrathoracic region (Figure 5.25). In the laryngeal area, it can be difficult to differentiate a mass lesion from other structures, and ultrasonography could be considered to investigate the region and to obtain an aspirate if possible. However, in most cases, laryngoscopy or bronchoscopy will be required to define a mass lesion and obtain a biopsy sample for diagnosis (Figure 5.26). If a laryngeal or cervical tracheal mass is suspected, plans should be made to perform a temporary tracheostomy if required in order to secure the airway during analysis of the sample and recovery from anesthesia. For lower airway masses, an oxygen delivery catheter can be passed below the lesion while preparations are made for surgical resection and anastomosis where possible. Caution is warranted to ensure that gases can exit around the mass during expiration to avoid build-up of gas pressure and subsequent barotrauma to the lung with potential airway rupture. Obtaining a CT prior to intervention can be helpful in defining the site and extent of the lesion for surgical planning. If laryngeal or intra-airway lymphoma is diagnosed, full staging should be performed with abdominal ultrasound.

Treatment

Debulking of an obstructive lesion can provide some palliation of signs and allow a smoother recovery from anesthesia. Lymphosarcoma is treated with radiation and/or chemotherapy, and the availability of chemotherapy for other types of neoplasms depends on the cell of origin. Squamous cell carcinoma of the larynx or trachea warrants a particularly guarded prognosis. When possible, isolated masses should be surgically resected with wide margins. However animals do not do well following laryngectomy, and tracheal resection with anastomosis is limited by the amount of trachea that can be safely removed without placing excessive tension on the suture site.

Prognosis

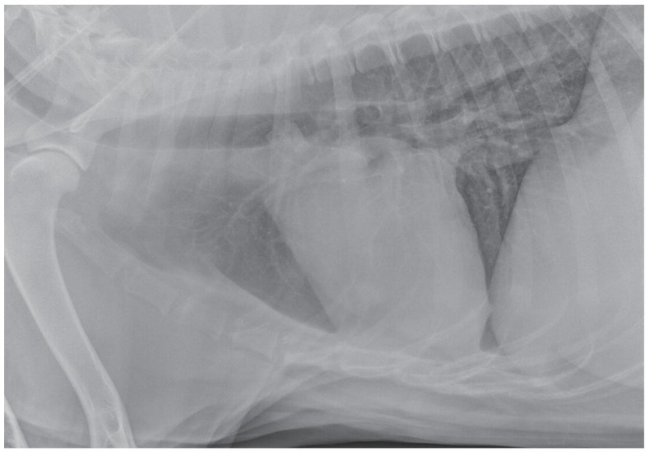
Prognosis depends on the tumor type and treatment available. Surgical resection can be curative if metastases are not present, and lymphoma in the airways responds to chemotherapy as it does at other anatomic sites. However, many affected animals are euthanized because of severe airway obstruction that cannot be adequately managed.



(a)



(b)



(c)

Figure 5.25 Right lateral radiographs from (a) an 11-year-old cat with a laryngeal mass, (b) a 9-year-old cat with a cervical tracheal mass beneath the third to fourth cervical vertebrae, and (c) a 2-year-old dog with an intrathoracic tracheal mass just proximal to the carina.



Figure 5.26 Bronchoscopic image from a 10-year-old cat with an adenocarcinoma filling ~85% of the tracheal lumen.

Clinical Case

An 11-year-old male castrated chihuahua mix was presented for evaluation of tracheal collapse. Since 6 months of age, the dog had hacked and gagged after drinking. He then started hacking and coughing multiple times a day. He also started panting heavily, with abdominal effort during respiration.

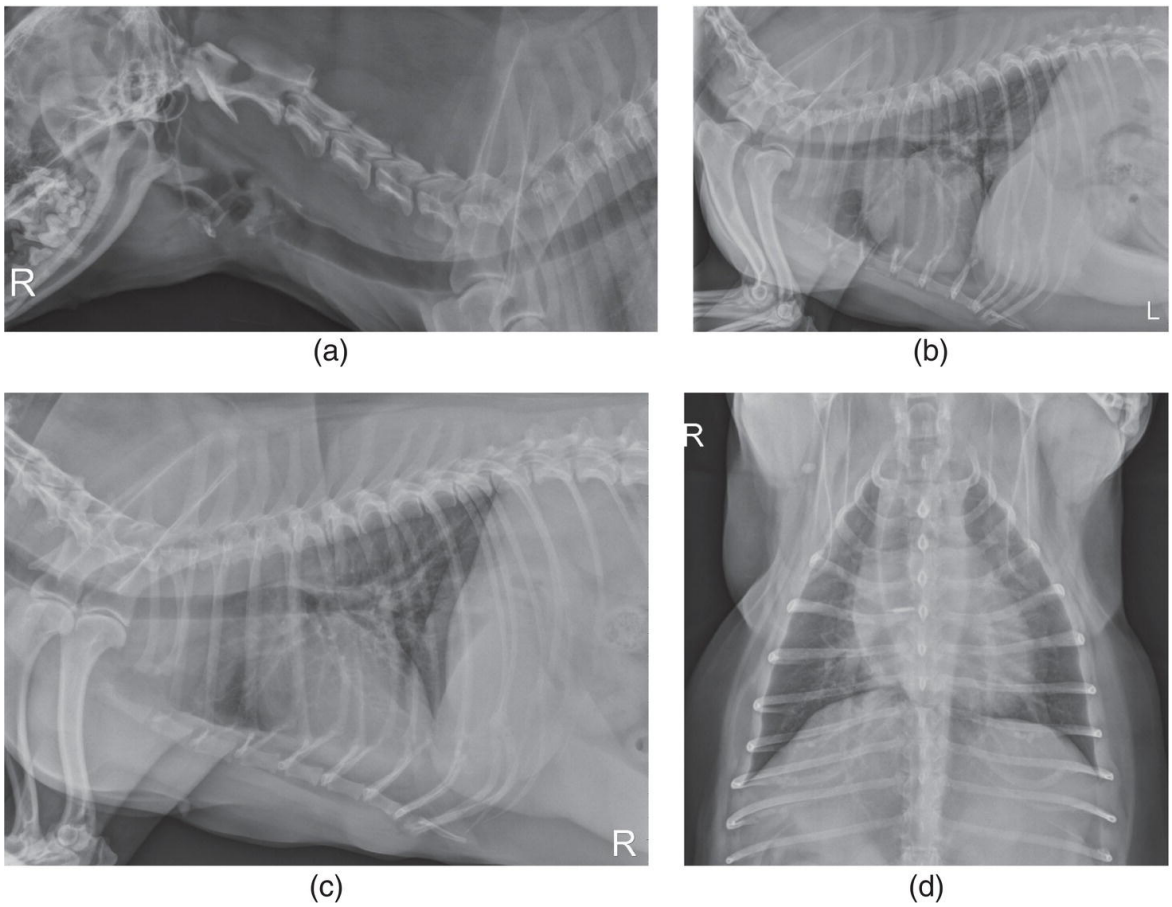
On physical examination, the dog was bright and alert with a temperature of 98.8°F (37.1°C), pulse of 134, and he was panting. Body weight was 11.25 kg with a body

condition score of 8/9. He had moderate generalized dental calculus and tartar. No oral masses or ulcerations seen. A honking cough was elicited on tracheal palpation and stridor was auscultated over the trachea. Lung sounds were clear and no heart murmur was ausculted.

Given the history and signalment, tracheal or airway collapse was considered the top differential diagnosis, with inflammatory and infectious airway disease lower on the list. Baseline bloodwork was recommended along with thoracic radiographs. Considerations would then include fluoroscopy, thoracic CT, and bronchoscopy with bronchoalveolar lavage.

A CBC and chemistry panel revealed normal values for all parameters. Cervical radiographs suggested mild elongation of the soft palate and dynamic narrowing of the nasopharyngeal gas column (Case Figure 1a). The larynx and hyoid apparatus were in their normal anatomic positions but there was mineralization of laryngeal cartilages and gas in the laryngeal ventricles. Thoracic radiographs revealed a normal cardiac silhouette (Case Figure 1b–d). There was slight dynamic narrowing of the mainstem bronchi between lateral projections and a mild diffuse bronchial pulmonary pattern. The hepatic margins extended beyond the costal arch.

Oral and laryngeal exam at anesthetic induction revealed an enlarged left tonsil that was irregular and out of the crypt. There was hyperemia of the larynx and the laryngeal ventricles were swollen but not everted. Laryngeal function was normal. Bronchoscopy revealed collapse of the dorsal tracheal membrane of the trachea during cough but no cartilaginous tracheal collapse. Severe bronchial collapse was noted with 90–100% collapse at the entrance to the left cranial and caudal lobes (Case Figure 2a), 75% collapse at the right cranial lobe, and distal collapse of many smaller airways (Case Figure 2b).

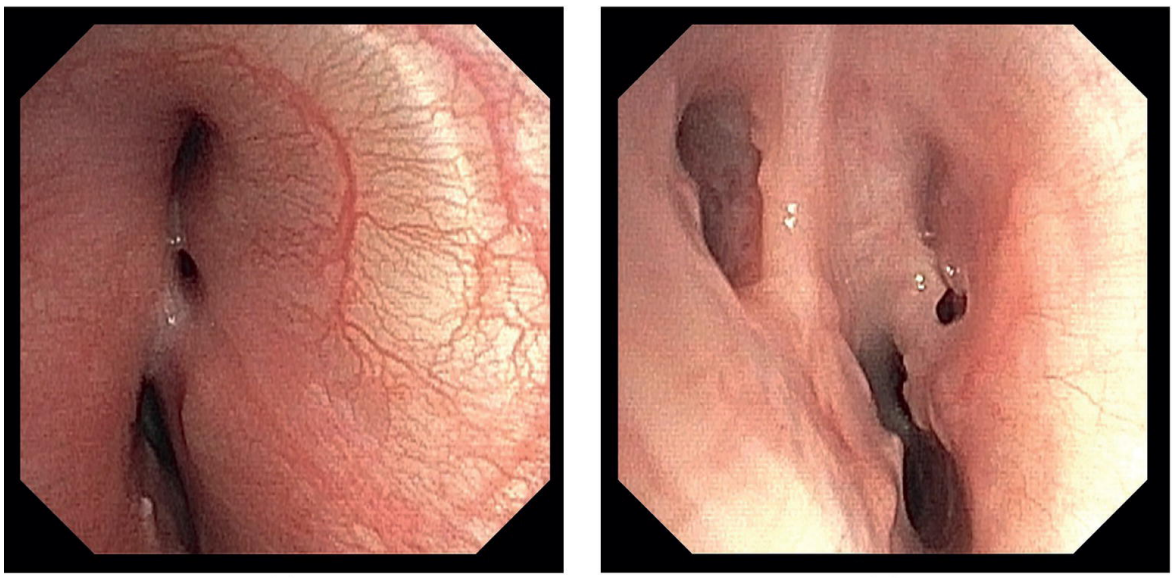


(a) (b) (c) (d)

Case Figure 1 Cervical radiograph (a). Thoracic radiographs (b–d).

Bronchoalveolar lavage cytology was hypercellular (1440–1800 cells/µl; RI 400–600) with normal differential cytology (4–6% neutrophils, RI 5–8%, 8% lymphocytes, RI 5–8%, and 75–85% macrophages). Cytologically, the fluid was characterized as mild, primarily histiocytic inflammation based on the appearance of vacuolated macrophages. Aerobic and mycoplasma cultures were negative.

Final diagnoses included bronchomalacia and inflammatory airway disease. The dog was discharged with a fluticasone propionate metered dose inhaler (110 mcg/puff) dosed at 1 puff q12h via an Aerodawg spacing chamber. Although not used in this case, extended-release theophylline would have been reasonable as additional therapy. A weight loss regimen was instituted to provide a 1–2% weight loss every week over 30 weeks to achieve a body condition score of 5/9.



(a) (b)

Case Figure 2 Bronchial collapse at the left cranial and caudal lobar bronchi (a) and distally (b).

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6
Parenchymal Disease

Structural Diseases

Primary Ciliary Dyskinesia

Pathophysiology

Normal cilia are made up of nine pairs of microtubules surrounding a central pair. Inner and outer dynein arms connect the microtubules, and the protein dynein uses adenosine triphosphate (ATP) to provide energy for ciliary motility. Primary ciliary dyskinesia (PCD) is a heritable disorder that is most often associated with a defect in the dynein arms (total or partial absence) resulting in defective ciliary motion; misalignment of the central pair of microtubules is also reported (Figure 6.1). Multiple genes are involved in the morphogenesis of cilia, and various genetic mutations have been described in humans that can result in dysgenesis and immotile cilia. Several dog breeds have been reported to develop PCD, and the genetic mutation has been described in Old English Sheepdogs (OES) affecting the *CCDC39* gene, similar to the mutation in humans (Merveille et al. 2014). This is inherited as an autosomal recessive disorder, with prevalence of carriers of the defect ranging from 7 to 19% in the OES population (Merveille et al. 2014). A genetic defect has also been reported in Australian Shepherds (Christen et al. 2023) and the Alaskan Malamute (Anderegg et al. 2019). All organs that contain cilia are affected, including the respiratory tract, middle ear, and reproductive tract, leading to recurrent sinusitis and pneumonia, serous otitis, infertility, and hydrocephalus. PCD is accompanied by *situs inversus* in 50% or more of cases, and bronchiectasis can be present early in disease or develop later in life after multiple episodes of pneumonia occur. The combination of situs inversus, chronic sinusitis, and bronchiectasis has been referred to as Kartagener's syndrome.

History and Signalment

PCD has been reported in the Dachshund, Bichon Frise, English Pointer, Springer Spaniel, Newfoundland, OES, and other breeds. It is rarely found in the cat. Clinical signs can be seen in puppies as early as 5 weeks of age, but animals can be older when the severity or recurrence of signs triggers evaluation. Historical complaints include chronic or recurrent sneezing, serous to mucoid nasal discharge, chronic cough, and episodes of antibiotic-responsive pneumonia. Signs of otitis media (head tilt, aural discharge, or nystagmus) or infertility in breeding-age animals have also been reported.

Physical Examination

Bilateral serous to mucopurulent nasal discharge is common and dogs can display evidence of pneumonia with a moist cough on tracheal palpation, increased tracheal sensitivity, and increased or harsh bronchovesicular sounds on auscultation. Generally animals remain bright and active despite respiratory infection, although severely affected animals can be febrile and cyanotic. Non-respiratory abnormalities that can be found include hydrocephalus and bullous effusion.

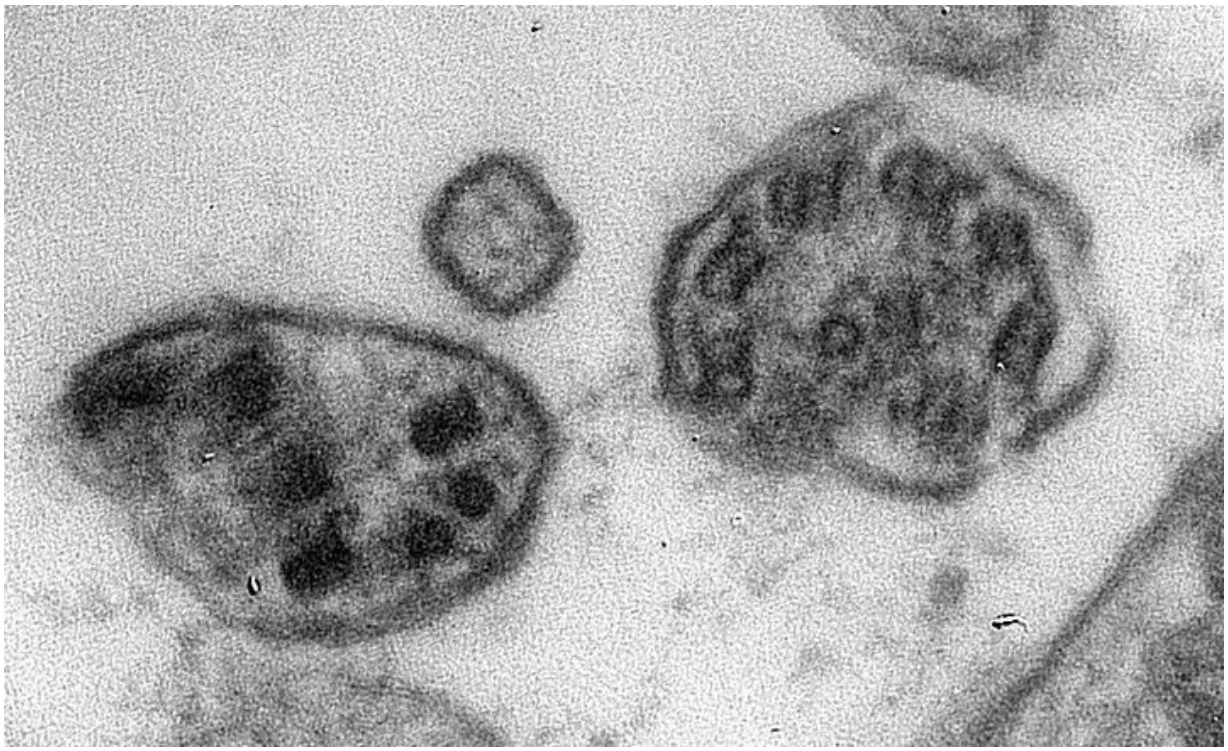


Figure 6.1 Electron microscopy image showing two abnormal cilia in cross-section. There is loss of the normal number of surrounding pairs of microtubules in both cilia, with marked misalignment of pairs on the left.

Diagnosis

A complete blood count is often suggestive of infection, with increased neutrophil numbers and a left shift is possible. Thoracic radiographs reveal alveolar infiltrates during bouts of pneumonia. Repeated bouts of infection lead to bronchiectasis, although this can be a congenital defect in some animals. Airway sampling typically reveals a septic suppurative response and isolation of *Mycoplasma* and aerobic bacteria (*Pasteurella*, *Streptococcus*, and *Staphylococcus*) is common. Diagnosis of PCD requires documentation of functional and structural defects of cilia. In an intact male dog with the appropriate clinical history, lack of purposeful sperm motility is consistent with a diagnosis of PCD, although semen samples can be difficult to obtain in young animals. Respiratory ciliary function is assessed through tracheal scintigraphy using 99-technetium-labeled macroaggregated albumin deposited at the carina. Ciliary movement of the radiolabel is followed with a

gamma camera, and animals with ciliary dyskinesia have no motion detected. *Mycoplasma* and *Bordetella* infections should be appropriately treated prior to performing tracheal scintigraphy, because infection with these organisms causes ciliostasis and can result in a false-positive scintigraphic study.

Nasal or tracheal biopsies or a semen sample fixed in glutaraldehyde can be submitted for transmission electron microscopy to identify the characteristic ultrastructural abnormalities seen in PCD; however, electron microscopy is not widely available and a properly sectioned sample is critical to assess ciliary structures. A pathologist should be consulted prior to obtaining a biopsy to ensure that an adequate sample is obtained and that a proper interpretation can be provided. Dogs with PCD will have multiple defects in cilia (loss or shortening of dynein arms, loss of the central pair of microtubules, triplets in place of doublets, etc.) and will have >5–20% of cilia affected. Findings must be distinguished from those of acquired or secondary ciliary abnormalities, which can be found with a variety of chronic respiratory tract diseases. These secondary defects typically affect <5% of the affected cilia; however, compound cilia (multiple cilia contained within a single membranous layer) are often prominent. In human patients, PCD can occur in the absence of specific electron microscopy abnormalities and it is likely that this occurs in veterinary patients also, although it has not been specifically documented. Genetic screening is available for the mutations reported in certain breeds.

Treatment

Aggressive therapy for pneumonia with appropriate antibiotics is required and owners should be taught to recognize recurrence of disease so that treatment can be instituted immediately. Respiratory therapy with nebulization and coupage can be used to encourage clearance of respiratory secretions. Cough suppressants should never be used because of the risk for trapping infected secretions in the lower airways and promoting the development of secondary bronchiectasis.

Prognosis

Many dogs with PCD are able to survive multiple bouts of pneumonia and these episodes lessen as the dog matures; however, they remain at risk for recurrent infection. Even when pneumonia is properly treated, bronchiectasis can develop later in life. Contact with animals that might serve as a source of infection, such as those in dog parks or recently obtained from a shelter environment, should be limited. Affected dogs should not be used in the breeding pool and genetic counseling is recommended.

Lung Lobe Torsion

Pathophysiology

Lung lobe torsion results when a lobar bronchus twists on its axis at the hilum of the lung, resulting in venous compression, congestion within the tissue, and swelling of the lung lobe. The lobes most commonly affected by torsion are the right middle lung lobe (particularly in large breed dogs) and the left cranial lung lobe (in Pugs and other small breed dogs). In cats, the left and right cranial lobes are affected most commonly, followed by the right middle lung lobe (Tinsdale et al. 2022), although torsion is much less common in cats than in dogs. Lung lobe torsion is often found in conjunction with pleural effusion that is exudative in character, although lobar torsion can be found in the absence of effusion.

The precise etiology of lung lobe torsion is unknown. In deep-chested dogs and Pugs, it has been suggested that the conformation of the thorax plays a role in allowing the bronchus to rotate on its axis. Brachycephalic dogs also commonly have collapse of the bronchus to the left cranial lung lobe and this could play a role in the development of torsion. This has been referred to as primary lung lobe torsion (Rossanese et al. 2020) and is the most common cause of torsion in the dog. Torsion could possibly be associated with atelectasis of a lobe from bronchial obstruction caused by mucus impaction or a neoplasm with subsequent twisting of the lobar bronchus. Lobar consolidation due to infection might predispose to torsion, and a torsed lung lobe can develop a secondary infection due to loss of blood supply. Previous anesthesia and surgery have been

implicated in some cases. Finally, it is possible that pleural effusion precedes lung lobe torsion, causing floatation or collapse of a lung lobe and an environment that allows the lobe to twist along the bronchial axis. These types of cases have been proposed to reflect secondary lung lobe torsion (Rossanese et al. 2020).

History and Signalment

There is an increased incidence of lung lobe torsion in deep-chested dog breeds such as the Afghan hound and in Pugs. Dogs, particularly Pugs, as young as 3 months can be affected (Latimer et al. 2017), but it is most common in middle-aged dogs (Park et al. 2018). Torsion is uncommon in the cat, but it has been found in cats with chronic, poorly treated lower airway inflammatory disease (likely preceded by lobar collapse associated with mucus obstruction), pulmonary carcinoma, or with pleural effusions, including chylothorax and pyothorax (Tinsdale et al. 2022). Clinical complaints can be acute (within 24 hours of torsion) or chronic (present for 2–3 months) in nature and include tachypnea or difficulty breathing, lethargy, anorexia, and coughing. Hemoptysis can be observed. In chronic cases, weight loss can be noted, likely in association with ill health due to the torsion.

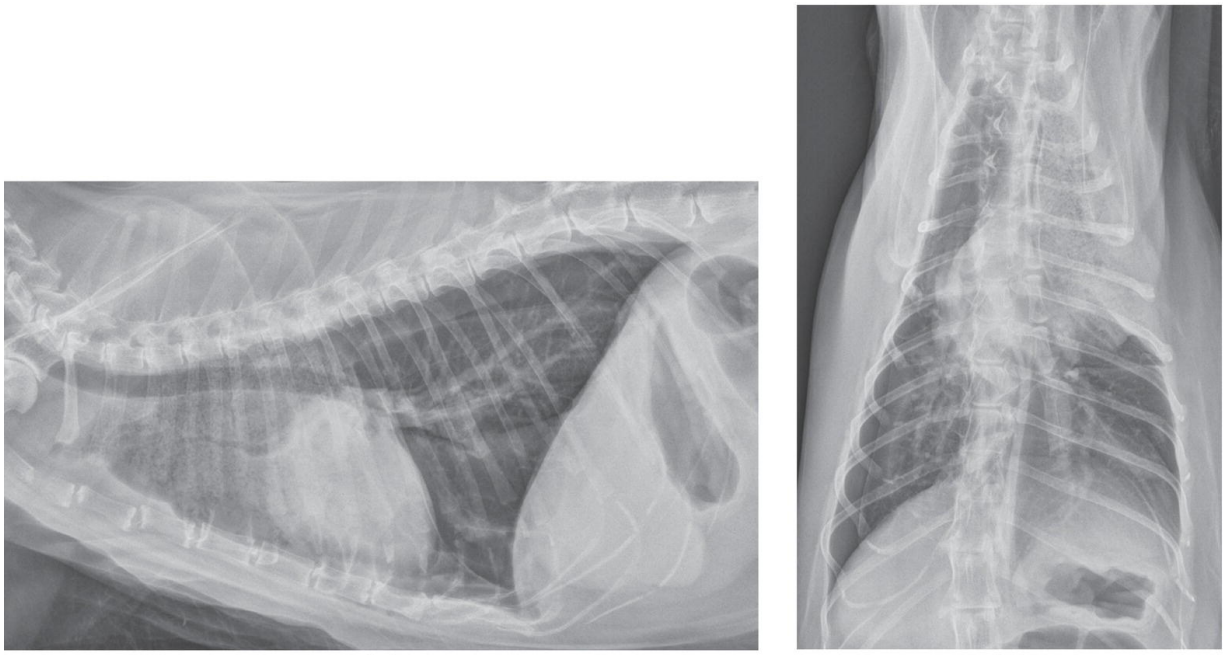
Physical Examination

Tachypnea is a common finding, which could be a result of pleural effusion, lung consolidation, or a pain response. Heart and lung sounds can be muffled or absent focally in the region of the torsion or ventrally in the thorax due to the presence of pleural effusion. Elevated body temperature is detected in 25–50% of cases.

Diagnostic Findings

Affected animals usually display a neutrophilic leukocytosis due to stress, inflammation, necrosis, or infection. Radiographs reveal consolidation or atelectasis of the affected lung lobe. Lobar opacity is a common radiographic finding and a vesicular lung pattern is considered pathognomonic for torsion (Figure 6.2). Abnormal bronchial position is visualized in some cases and detection is likely enhanced by the use of digital radiography and image adjustments.

Pleural effusion can be found in over 80% of cases, either diffusely or in the region of the torsed lobe. Thoracocentesis is often indicated to alleviate respiratory distress and improve visualization of thoracic contents. Thoracic ultrasound with evaluation of pulmonary blood flow might be helpful in some cases, although the most common finding appears to be hepatization of the lung lobe. Bronchoscopy can document lung lobe torsion as the cause for lobar consolidation through visualization of a twisted appearance to the bronchial opening (Figure 6.3), although this can sometimes appear similar to bronchial collapse or stenosis. Finally, computed tomography (CT) can be performed where available to evaluate lung lobe changes and to identify underlying or concurrent conditions. Features consistent with lung lobe torsion include abrupt termination of the bronchus to the affected lung lobe, increased size of the lobe with augmented attenuation due to consolidation and emphysema, and lack of contrast enhancement due to compression on the vasculature (Seiler et al. 2008; Rossanese et al. 2020).



(a) (b)

Figure 6.2 (a) Right lateral and (b) dorsoventral radiographs from a dog with torsion of the left cranial lung lobe demonstrate a lobar opacity in that region along with a vesicular gas pattern.

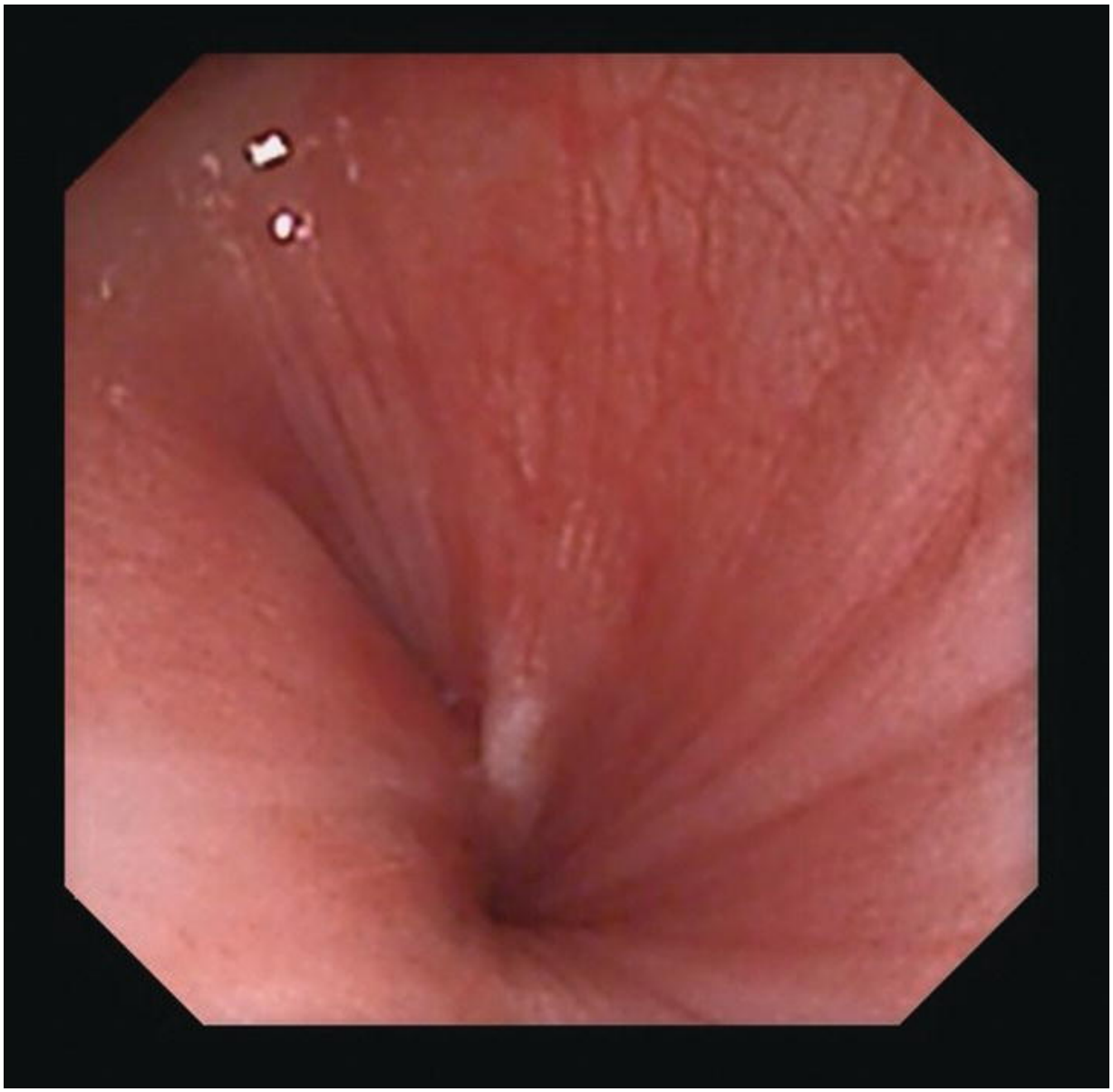


Figure 6.3 Bronchoscopic image demonstrating torsion of the right middle lung lobe.

Thoracic fluid analysis reveals chyle or an inflammatory exudate (see Chapter 7) in up to one-third of dogs, with a modified transudate or hemorrhage reported in the remaining cases (Park et al. 2018). Cytology of the fluid is indicated to rule out infectious or neoplastic disease, and samples should be evaluated by aerobic and anaerobic bacterial culture to rule out empyema. Histopathology of lung tissue usually shows pulmonary hemorrhage, inflammation, and infarction,

but can sometimes reveal a primary disease process responsible for the torsion, such as neoplasia or bronchial obstruction.

Treatment

Lung lobectomy is required for appropriate treatment. The lobe should not be de-rotated prior to removal because of the risk for ischemic injury associated with reperfusion. CT guidance is used to determine the appropriate approach, with an intercostal thoracotomy used most commonly. Video-assisted thoracostomy can also be employed, and chest drain placement is used to maintain a negative intrapleural pressure in the first day after surgery. Chylothorax can resolve after lung lobectomy, but sometimes requires additional management (see Chapter 7).

Prognosis

The majority of dogs have an uncomplicated recovery from lung lobectomy with survival to discharge of up to 99% and an excellent long-term prognosis (Rossanese et al. 2020). Cats appear to have concurrent diseases and require additional surgical procedures (Tinsdale et al. 2022); prognosis ranges from good to less favorable. Dogs that have torsion of the right cranial and right middle lung lobes concurrently, dogs with underlying neoplasia, and those with persistent effusion might have a worse prognosis (Park et al. 2018). Some dogs can develop torsion of a second lung lobe postoperatively.

Infectious Diseases

Viral Pneumonia

Pathophysiology

Etiologic agents of viral pneumonia in the dog include canine distemper virus (CDV) and canine influenza virus (CIV). Less commonly, canine parainfluenza virus-3 (CPIV), canine adenovirus-2 (CAV-2), canine herpesvirus (CHV-1), and canine respiratory coronavirus (CRCoV) can cause parenchymal infection, but these organisms more typically result in airway disease, predispose to

bacterial pneumonia, or are present as a co-infecting organism in bacterial pneumonia (Viitanen et al. 2015). In the cat, feline calicivirus (FCV) is the most common viral cause of pneumonia, although feline herpesvirus-1 (FHV-1) can cause a severe tracheitis and pneumonia.

Viruses are spread by inhalation of aerosolized viral particles that gain access to the lower respiratory tract. These viruses cause diffuse epithelial cell death and provoke an inflammatory response, primarily within the interstitium. Most viral infections are self-limiting, but they can predispose animals to bacterial bronchopneumonia and thus can lead to more severe systemic signs.

Non-effusive feline infectious peritonitis (FIP) virus (the mutated coronavirus) can be associated with a granulomatous pneumonia positive for FIP virus antigen in 76% of cases (Slaviero et al. 2024). This is due to immune-mediated vasculitis with secondary pyogranulomatous inflammation rather than to an infectious process and many cats have concurrent pleuritis and pleural effusion (see Chapter 7).

History and Signalment

Puppies and kittens are more susceptible to most viral agents than adult animals, with the exception of CIV, which tends to affect mature dogs. CHV-1 can also affect mature dogs, resulting in viremia and pneumonia, although upper respiratory signs typically predominate. Generally, clinical signs are acute in onset and associated primarily with cough, but naso-ocular discharge can also be present. Animals held in close confinement are more prone to viral infection and outbreaks are common. CDV results in more severe clinical and systemic signs of illness and is characterized by concurrent or sequential development of gastrointestinal and then neurologic signs, typically manifest as myoclonus, which warrants a guarded prognosis.

Physical Examination

Dogs or cats with viral pneumonia can have fever and/or tachypnea that ranges from mild to severe. Lung sounds may be slightly loud or

harsh and tracheal sensitivity is usually present. Dogs with CDV can have chorioretinitis or neurologic deficits that involve the cerebrum, cerebellum, or spinal cord.

Diagnostic Findings

Diagnosis of a viral pneumonia is often based on clinical suspicion, history and signalment, environmental exposure, and vaccination status. A complete blood count will sometimes reveal lymphopenia early in viral infection. Viral pneumonia is expected to result in a diffuse interstitial pattern on thoracic radiographs, although bacterial complications can lead to alveolar infiltrates.

Various methods can be used to confirm the presence of virus or exposure to a virus, including culture, polymerase chain reaction (PCR) or reverse-transcriptase PCR (RT-PCR) for RNA viruses, and serology; however, it is more difficult to determine if the virus is actually the cause of disease (see canine infectious respiratory disease, Chapter 5). Airway wash fluid or pulmonary tissue can be analyzed by fluorescent antibody staining or application of immunohistochemistry to fixed tissue to identify virus-specific antigen; however, tests are not widely available for all viruses and can be difficult to perform. Finally, electron microscopy can be used to detect viral inclusions in tissue samples.

Treatment

General supportive care measures are instituted, including subcutaneous or intravenous fluid therapy, airway humidification, and oxygen therapy as needed. Affected animals are kept segregated from other animals to avoid spread of disease. No specific antiviral therapy is generally recommended, but broad-spectrum antibiotics are often administered to treat or to prevent secondary bacterial infection. *Mycoplasma* spp. are commonly found in conjunction with suspected viral infection, thus doxycycline or azithromycin would be appropriate for use.

Prognosis

Regular vaccination protects against most of the viral infections that can cause pneumonia and results in less severe clinical

manifestations of disease. In general, viral pneumonia has a good prognosis, as most animals will respond to supportive care and treatment of secondary bacterial pneumonia. Dogs with distemper virus that develop neurologic disease have a poor prognosis in general, although some will survive.

Bacterial Pneumonia

Pathophysiology

Bacterial pneumonia occurs when large numbers of opportunistic pathogens overwhelm host defense mechanisms or when highly pathogenic organisms gain access to the airways. It can also result from failure of respiratory defense mechanisms, systemic immune compromise, or inhalation of a foreign body, oropharyngeal material, gastric contents, or a caustic substance (see later for aspiration pneumonia). Therefore, in the animal with bacterial pneumonia, a search should begin for an underlying disease or predisposing disorder that allows parenchymal infection. Enteric organisms, *Pasteurella* species, *Bordetella*, *Mycoplasma*, and anaerobes are the most common bacteria found in lower respiratory tract infections in adult dogs and in puppies (Johnson et al. 2013). In cats, *Mycoplasma*, *Pasteurella*, *Streptococcus,* and anaerobic species are found most commonly (Dear et al. 2021).

Bacterial colonization of the respiratory epithelium incites chemotaxis of neutrophils. These inflammatory cells release proteolytic enzymes and reactive oxygen species to kill the bacteria; however, this process sets up an inflammatory environment within the lung. A delicate balance develops between control of bacterial growth and restriction of worsening lung inflammation. In some cases, overwhelming inflammation perpetuates lung damage, resulting in gas exchange abnormalities that can lead to respiratory failure.

Special consideration must be given to the possibility of pneumonic plague in animals from certain regions of the western United States (Colorado, New Mexico), Asia, and Africa, and in circumstances where exposure to the organism is possible (Pennisi et al. 2013; Nichols et al. 2014). Infection is caused by *Yersinia pestis*, and the

disease is of marked zoonotic concern, particularly when an infected cat is encountered, because this species is more commonly affected by the pneumonic form of disease. Animals become infected through a bite from an infected flea or by ingestion of an infected mammalian host such as a prairie dog, squirrel, rabbit, or rodent, therefore exposure history is an important contributor to the diagnosis. While the bubonic form is more common (mandibular lymphadenopathy), the pneumonic form is more readily spread to humans through aerosolization of organisms.

History and Signalment

Pneumonia is encountered in any age of animal. Puppies are most commonly affected by primary infectious pneumonia, young hunting or sporting dogs are most commonly affected by foreign body pneumonia, and older animals develop bacterial pneumonia in association with aspiration injury or immune compromise. Certain dog breeds are predisposed to infectious pneumonia. For example, Irish Wolfhounds develop an unusual rhinitis/bronchopneumonia syndrome in young dogs (Clercx et al. 2003) as well as recurrent bacterial pneumonia in older dogs (Viitanen et al. 2019). Ciliary structural abnormalities, various forms of immunodeficiency (immunoglobulin insufficiencies or abnormal lymphocyte subpopulations), swallowing or esophageal dysfunction, and laryngeal paresis or paralysis have been ruled out in many affected dogs (Viitanen et al. 2019). Bronchiectasis was a common finding on CT along with mucosal irregularities on bronchoscopy in one study (Viitanen et al. 2019), although whether these are a cause or result of recurrent pneumonia is unclear. The reasons that Irish Wolfhounds develop recurrent bacterial pneumonia remain unclear.

Dogs or cats with bacterial pneumonia can have an acute history of a productive cough, labored breathing, and respiratory difficulty or distress However, some animals present with more chronic and vague signs of illness such as malaise, depression, anorexia, and weight loss. Importantly, even foreign body pneumonia can result in chronic clinical signs. Animals that display chronic antibiotic-responsive pneumonia are suspicious for the presence of a foreign body, bronchiectasis, broncho-esophageal fistula, or chronic recurrent aspiration injury. Nasal discharge can be found

concurrently in dogs with pneumonia due to coincident nasal infection or when animals cough respiratory secretions into the nasopharynx (Figure 6.4).



Figure 6.4 Fluoroscopic image demonstrates barium being coughed or regurgitated into the nasopharynx.

Physical Examination

Abnormalities indicative of bacterial pneumonia are sometimes but not always found in the examination of the respiratory tract. Parenchymal infection with alveolar flooding by inflammatory debris should result in restrictive lung disease, and a rapid, shallow breathing pattern is expected, but this will depend on the extent of disease. Depending on the stage and severity of disease, thoracic auscultation can reveal loud, harsh bronchovesicular sounds or adventitious lung sounds (crackles or wheezes). Absence of lung sounds in a specific region of the thorax might be suggestive of lung consolidation or rarely, pleuropneumonia. Tracheal sensitivity is usually present, and with foreign body pneumonia or pneumonia in

association with bronchiectasis, it is often dramatic. Cough followed by swallowing is suggestive of a process that is causing increased secretions in the lower airway.

A mucopurulent nasal discharge can be present in some animals. Although pneumonia is an inflammatory condition, fever is detected in <50% of affected adult dogs or puppies (Radhakrishnan et al. 2007) and the percentage of cats with pneumonia that have fever is likely <25%.

Diagnostic Findings

Peripheral leukocytosis with a left shift supports the diagnosis of bacterial pneumonia in an animal with appropriate clinical findings, although this was found in only 1/3 of cats (Dear et al. 2021) and is present in an unknown percentage of dogs. Neutropenia with a degenerative left shift can occur if acute fulminant pneumonia results in pulmonary sequestration of neutrophils. Leukogram findings likely reflect both the severity and the stage of disease, with leukopenia in the peracute stage and neutrophilia in the latter stages. Bands are present in variable percentages and likely reflect the severity of the inflammatory response. A biochemical profile and urinalysis assist in the diagnosis of underlying conditions such as diabetes mellitus and hyperadrenocorticism, which are associated with defective neutrophil function and might predispose an animal to pneumonia. Feline leukemia virus (FeLV)/feline immunodeficiency virus (FIV) serology should be performed in cats with pneumonia, although a direct association has not been made between viral status and the development of bacterial pneumonia. C-reactive protein and other acute phase proteins have been investigated for use in the diagnosis and monitoring of pneumonia in dogs but these are often elevated in a variety of inflammatory processes. Nonetheless, future studies could show a role for these biomarkers in determining the severity of disease or response to therapy.

Pulse oximetry can be employed to approximate the severity of lung dysfunction as well as the need for oxygen supplementation, although it provides only a crude estimation of lung function. Hypoxemia is common in animals with moderate to severe

parenchymal disease, and an arterial blood gas provides a more accurate assessment of oxygenation (see Chapter 2).

Thoracic radiographs obtained in the early stages of bacterial pneumonia demonstrate mild or diffuse interstitial infiltrates. Alveolar infiltrates with air bronchograms are considered the classic radiographic finding (Figure 6.5) and develop over time. In severe cases, these infiltrates can coalesce to cause lobar consolidation. A lobar or patchy segmental infiltrate can also be suggestive of underlying foreign body pneumonia, although pure interstitial infiltrates were seen in one-third of such cases (Schultz and Zwingenberger 2008). Pleuropneumonia is uncommon in small animals unless a pleural foreign body or bite wound is the cause of pneumonia. In these cases, infection with *Actinomyces* can sometimes be found.

Direct airway sampling through tracheal wash, bronchoscopy with bronchoalveolar lavage (BAL), or fine-needle aspiration of the lung is indicated to confirm the etiology of pneumonia and to obtain samples for Gram stain, aerobic and anaerobic bacterial culture with antibiotic sensitivity testing, *Mycoplasma* culture, and cytology. Of these techniques, tracheal wash is most suited for radiographically diffuse disease, while bronchoscopy (Figure 6.6) or fine-needle lung aspiration would be preferred for focal disease (see Chapter 2). Bronchoscopy is particularly indicated for animals suspected of foreign body pneumonia because of the high success rate in providing resolution of disease. When either tracheal wash or bronchoscopy is performed, completion of a thorough laryngeal exam is warranted at the onset of anesthesia to rule out laryngeal dysfunction as a contributor to pneumonia. Gram staining characteristics and cytology can be useful for identifying the most likely infecting organism and initiating early antibiotic therapy.

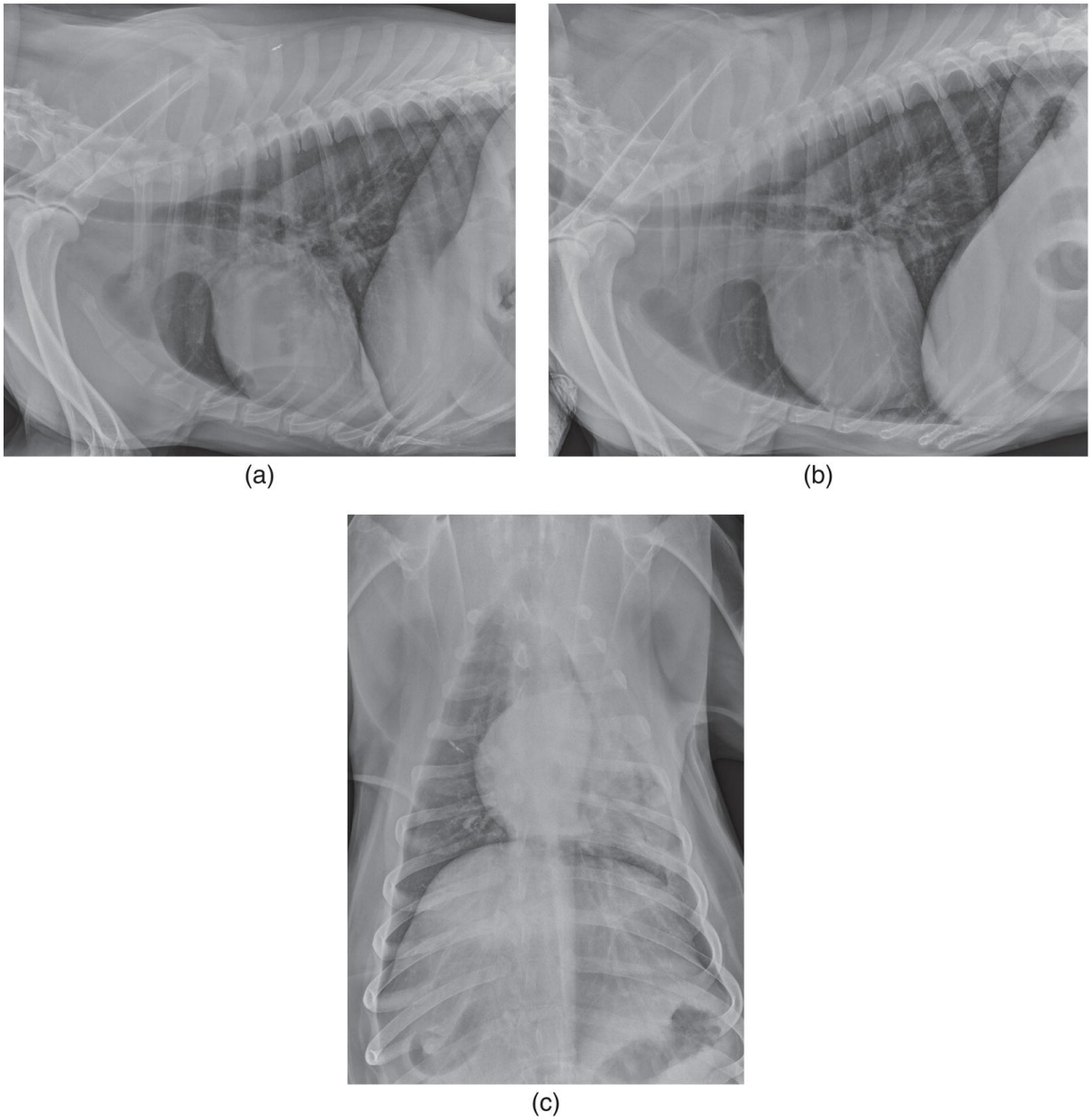


Figure 6.5 (a) Right lateral, (b) left lateral, and (c) dorsoventral radiographs from a 10-year-old male castrated (MC) Weimeraner with bronchopneumonia affecting primarily the left lung lobe. Air bronchograms are visible in the left lung lobe in the right lateral and dorsoventral views but not in the left lateral projection.

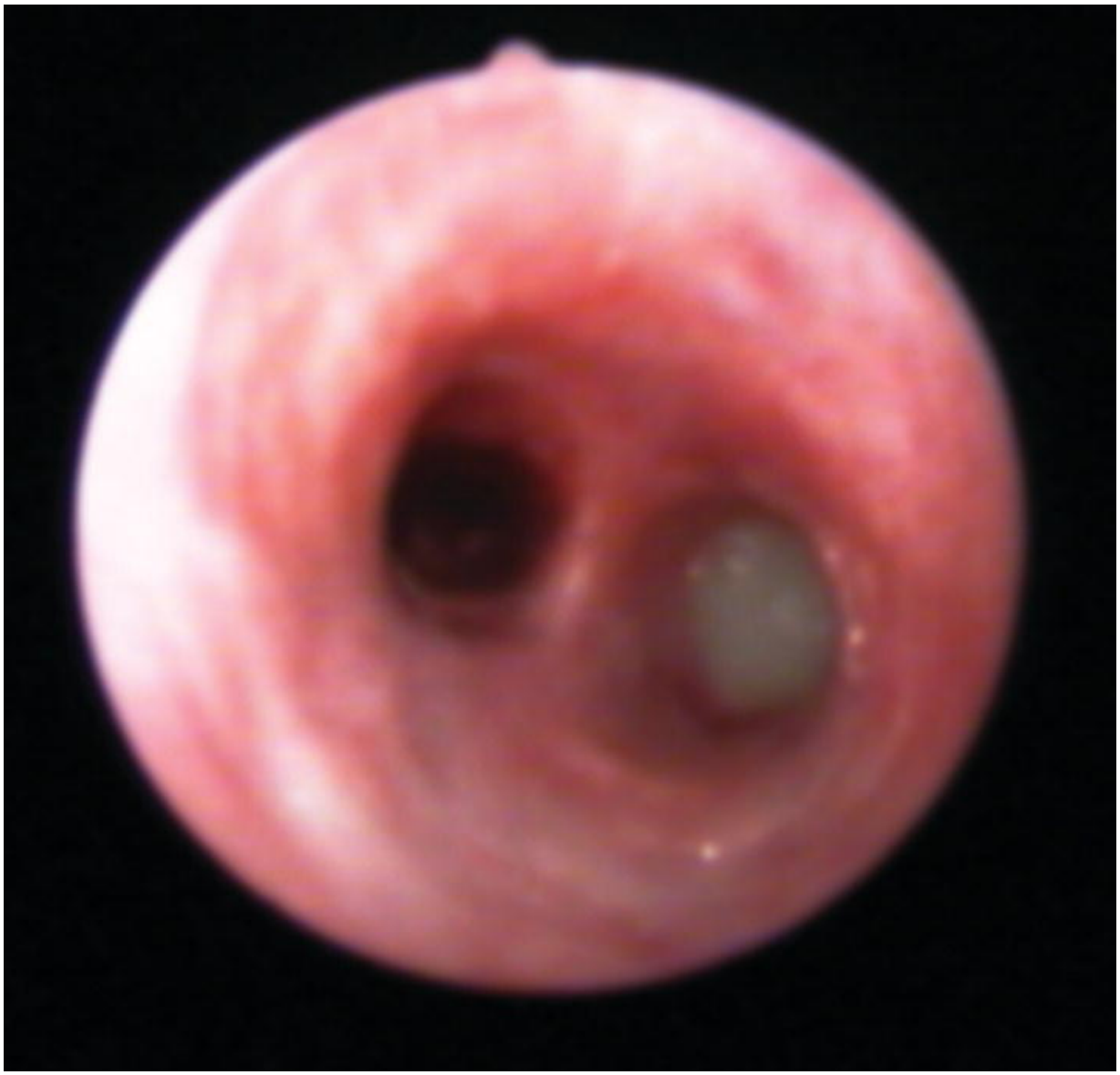


Figure 6.6 Bronchoscopy image from a dog with *Mycoplasma* pneumonia reveals airway hyperemia and marked mucus plugging of an isolated airway.

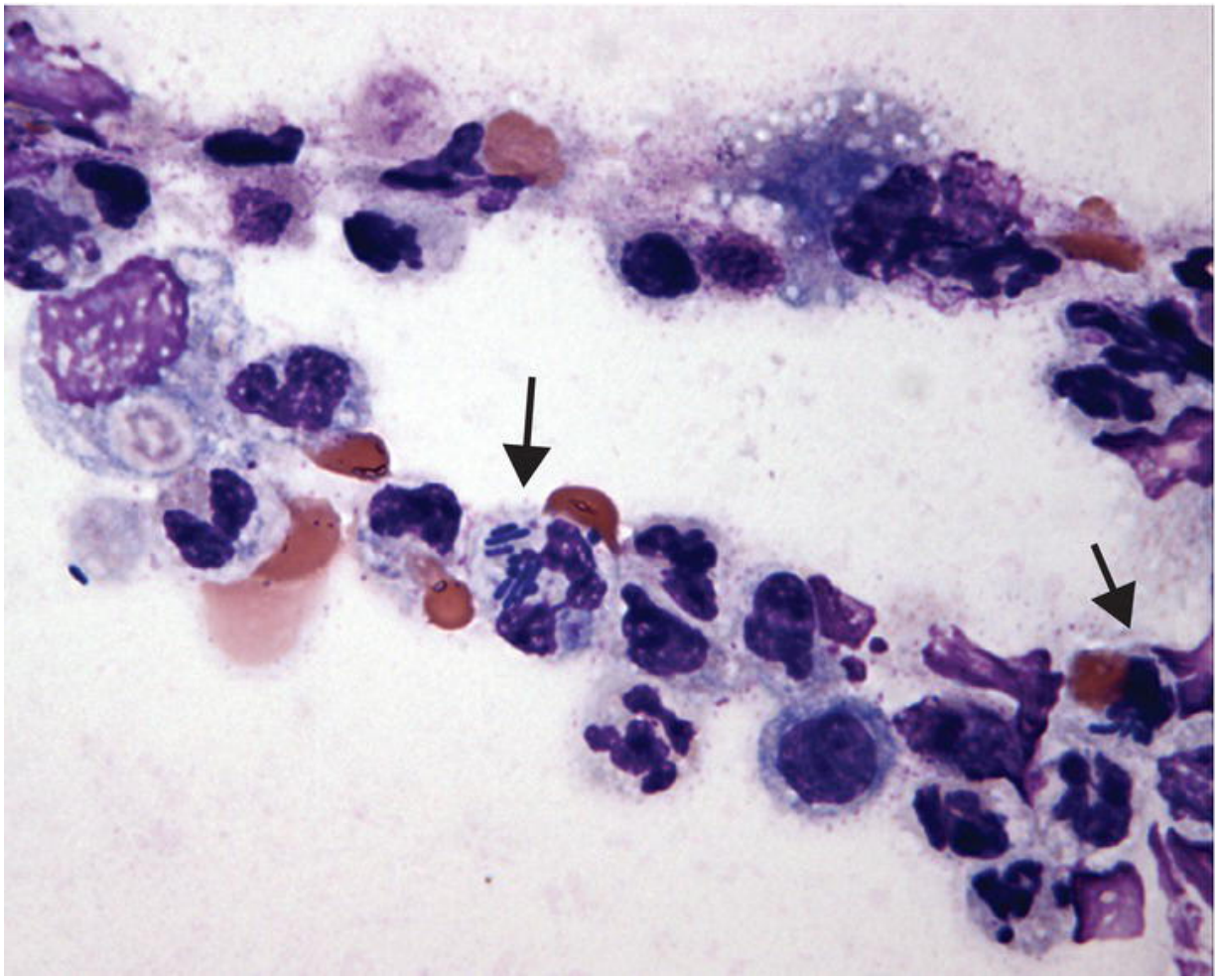


Figure 6.7 Airway cytology from bronchoalveolar lavage (BAL) fluid confirms bacterial pneumonia by the presence of dark blue rod-shaped bacteria within neutrophils (arrows). Note the swollen nuclei and degenerate changes in neutrophils throughout the slide. Bacterial culture identified *Escherichia coli*.

Various bacteria can be recovered from the airways of healthy cats and dogs; therefore documentation of pneumonia requires isolation of bacteria in conjunction with detection of septic suppurative inflammation on airway cytology in an animal with clinical suspicion of pneumonia (Figure 6.7). Importantly, some animals will have observable intracellular bacteria on cytology but lack growth on culture while others (up to 25%) will lack intracellular bacteria yet still have a clinical diagnosis of pneumonia with growth of pathogens in culture. Interpretation of diagnostic results in light of the clinical

picture is necessary, particularly when considering appropriate use of antibiotics.

In the past, pneumonia in the dog was typically caused by Gram-negative enteric bacteria; however, with widespread use of fluoroquinolone antimicrobials, alternate bacteria are encountered. In a study from a university teaching hospital of dogs diagnosed with pneumonia (likely complicated pneumonia cases), *Mycoplasma*, *Bordetella*, and *Pasteurella* were isolated most commonly (Table 6.1). Multiple species were isolated in almost 50% of all cases, and almost 20% of infections were complicated by the presence of anaerobic bacteria (Johnson et al. 2013). Bacterial pneumonia is clinically recognized much less commonly in the cat than in the dog, and less information is available about potential causes. When specific cultures are performed, *Mycoplasma, Pasteurella,* and anaerobic species were found most commonly (Dear et al. 2021), although *Streptococcus* species were also found in many cases. An earlier study implicated *Mycoplasma* spp. as the most common isolate in feline pneumonia (Foster et al. 2004), although the role of *Mycoplasma* in lower respiratory tract infection in adult dogs or in cats remains controversial.

Treatment

While waiting to obtain results of cultures, antimicrobial treatment should be initiated using antibiotics likely to be effective against the organisms involved. The combination of a fluoroquinolone and penicillin derivative is used most commonly for initial therapy. Antibiotics are usually required for 1–2 weeks in cases with uncomplicated pneumonia, although the appropriate length of antibiotic therapy remains unknown. Obviously, any agents used for long-term treatment should be based on results obtained from culture and susceptibility testing. Biomarkers such as C-reactive peptide (CRP) continue to be investigated for use in determining the length of treatment necessary, and one study suggested shorter duration of antimicrobial use when CRP was used as a biomarker of infection (Viitanen et al. 2017). However, clinically the respiratory rate and effort, presence of cough or abnormal lung sounds, and pulse oximetry or blood gas data are used to determine when therapy

can be discontinued. When bronchiectasis is the underlying condition, >6 weeks of therapy can be required (Table 6.2).

Table 6.1 Bacterial organisms commonly found in dogs with lower respiratory tract infection.

Source: Adapted from Johnson et al. (2013).

	% of isolates	% in pure culture	Gram stain characteristics
Escherichia coli	17	4	Gram-negative rods
Klebsiella pneumoniae	2	0	Gram-negative rods
Pasteurella	21	5	Gram-negative rods
Bordetella bronchiseptica	22	10	Gram-negative coccobacilli
Mycoplasma spp.	30	9	None (no cell wall)
Pseudomonas aeruginosa	6	5	Gram-negative rods
Actinomyces spp.	5	0	Gram-positive cocci
Staphylococcus	5	3	Gram-positive cocci
Streptococcus	12	2	Gram-positive cocci
Enterococcus	2	0	Gram-positive cocci
Anaerobes	17	4	Gram-positive or -negative

Table 6.2 Bacterial organisms commonly found in cats with lower respiratory tract infection.

Source: Adapted from Dear et al. (2021).

Isolate	Percentage of isolates	Gram stain characteristics
Bordetella bronchiseptica	4%	Gram-negative coccobacilli
Pasteurella species	31%	Gram-negative rods
Mycoplasma	42%	None (no cell wall)
Escherichia coli	4%	Gram-negative rods
Streptococcus	27%	Gram-positive cocci
Obligate anaerobes	42%	

Bronchodilators are sometimes considered for animals with pneumonia. Theoretically there is a concern that use of a bronchodilator could increase ventilation to a consolidated lung region and worsen gas exchange; however, this is unlikely to play a substantial clinical role, particularly if using extended-release theophylline, which is a very weak bronchodilator. Beta-agonists could be considered as adjunct therapy in a cat with pneumonia given the high incidence of reactive airway disease in this species. This class of drug might also be considered in a puppy in which *Bordetella* bronchopneumonia is suspected or documented, because this organism has been demonstrated to increase lung resistance during experimental infection. Finally, dogs with aspiration pneumonia might benefit from a short course of a beta-2-agonist to combat acid-induced bronchoconstriction. In general, bronchodilators can reduce the work of breathing and improve diaphragmatic strength; however, the potential for gastrointestinal toxicity associated with a methylxanthine drug must be considered. Also, use of enrofloxacin in combination with theophylline is not advised because of inhibition of theophylline metabolism, leading to higher plasma theophylline levels and potential toxicity.

Generalized supportive care and ancillary respiratory therapy will aid in resolution of pneumonia. Oxygen supplementation is beneficial in

decreasing respiratory effort and improving clinical status. Promoting systemic hydration through use of intravenous fluids is very important for maintaining hydration of respiratory secretions and facilitating their removal from the respiratory tree. Saline nebulization followed by coupage is also beneficial in treatment of pneumonia by providing direct hydration of the lower airways, although clinical studies are lacking. See Chapter 3 for more information.

Prognosis

Most dogs and cats can be treated successfully for pneumonia, but therapy must be closely monitored and employed for an adequate amount of time depending on clinical response. In an animal with non-resolving pneumonia, the possibility of a foreign body, pulmonary abscess, or underlying neoplastic process should be considered. In these cases, lung lobectomy is a viable option for the management of disease, although some dogs can have persistence of disease despite surgery. In one study, over half of the animals treated with lung lobectomy had resolution of disease (Murphy et al. 1997).

Fungal Pneumonia

Pathophysiology

Organisms most commonly involved in systemic mycotic infections are thermally dimorphic fungi, existing as molds in the environment with transformation into yeasts following inhalation into the respiratory tract. In some cases, infection is resolved by the immune response. In an unknown percentage of dogs and cats, infection persists or progresses throughout the lung and regional lymph nodes or disseminates to other parts of the body. While ethnicity and immune status are recognized factors in the dissemination of disease in humans, less is known in veterinary species. The fungal organisms involved are characterized by specific geographic distribution. *Histoplasma capsulatum* and *Blastomyces dermatitidis* are found primarily in the Ohio/Mississippi river valley. *Coccidioides immitis* is found in the southwestern United States and in Central and South America. Other fungal organisms that occasionally cause pneumonia include *Cryptococcus*, *Aspergillus*, and *Conidiobolus* and these have

world-wide distribution. *Pneumocystis* is a rare cause of fungal pneumonia and is discussed under protozoal and other pneumonias, because the clinical syndrome is different from that of the mycotic infections described here.

Fungal organisms differ not only in geographic distribution but also in tissue trophism. In addition to pulmonary infection, all organisms tend to affect peripheral and internal lymph nodes; ocular and central nervous system tissue can also be involved. *Histoplasma* organisms infect the gastrointestinal tract, liver, spleen, and bone marrow, while causing skin lesions in cats. *Blastomyces* has a predilection for bone, skin, and the reproductive tract. *C. immitis* infects bone and cardiac structures in dogs, but often results in skin lesions in cats, as well as respiratory, bone, and ocular or neurologic signs in both species. Multi-systemic involvement is one of the reasons these diseases are sometimes difficult to distinguish from neoplastic or septic processes. The widespread nature of disease also enhances the challenge of resolving infection, because therapeutic choices must be targeted to achieve specific tissue penetration depending on organ involvement.

History and Signalment

Dogs are infected with fungal pneumonia more frequently than cats and most animals are young, outdoor-hunting breeds. Interestingly, cats with fungal pneumonia are often described as indoor pets, suggesting exposure to infecting organisms through fomites or via air flow through homes. A variety of historical complaints can be reported depending on the organ(s) affected. With respiratory system involvement, the most common complaints include tachypnea, cough, and respiratory difficulty. The pre-patent period appears to be 2–4 weeks, and signs are often chronic (4 weeks or more), resulting in inappetence and weight loss. Depending on the organism involved, owners might report blindness with exophthalmos due to glaucoma or limited vision resulting from retinal lesions, lameness due to bone lesions, non-healing skin lesions, or neurologic signs. Histoplasmosis can result in a severe protein-losing enteropathy with diarrhea and weight loss, or

spontaneous bleeding associated with thrombocytopenia and bone marrow involvement.

Physical Examination

Dogs and cats with fungal infections often present with fever, peripheral lymphadenopathy, and obvious signs of systemic illness. Abnormalities detected in the respiratory tract include labored respirations, tachypnea, and harsh bronchovesicular sounds or crackles. Wheezing or loud bronchial noises can be present when hilar lymphadenopathy results in bronchial compression, most often on the right side of the thorax. Tracheal sensitivity is often present. Ocular lesions include glaucoma, anterior uveitis, and chorioretinitis. Both central and peripheral neurologic deficits can be noted depending on the site of fungal granuloma formation. Ulcerated, draining skin lesions, testicular or prostatic enlargement, and bone pain can also be found depending on the infecting organism. Histoplasmosis affecting the bone marrow can result in severe thrombocytopenia and petechiation. Hepatosplenomegaly or a thickened gastrointestinal tract can also be found in animals with histoplasmosis.

Diagnostic Findings

Fungal infection should be suspected in an animal with multi-systemic disease that has a history of travel to an area endemic for a fungal organism. However strict boundaries do not exist for the environmental niches, and given climate changes that are occurring world-wide, the geographic localization of some fungal organisms seems to be expanding or changing. Laboratory testing commonly reveals a mild non-regenerative anemia, neutrophilic and monocytic leukocytosis, hypoalbuminemia associated with chronic disease or gastrointestinal fungal infection, thrombocytopenia due to bone marrow involvement, and potentially hypercalcemia (primarily with blastomycosis).

Thoracic radiographs reveal a variety of pulmonary infiltrative patterns including a miliary or nodular infiltrates, generalized interstitial or bronchial pattern, lobar consolidation, or a mass effect. Hilar or sternal lymphadenopathy is relatively common in dogs

(Figure 6.8). Many of the radiographic findings in dogs affected with fungal disease can mimic those found in primary or metastatic neoplasia. In cats, a miliary or nodular interstitial pattern is relatively common (Figure 6.9), although sometimes radiographs can mimic those found in feline bronchial disease or pulmonary fibrosis.

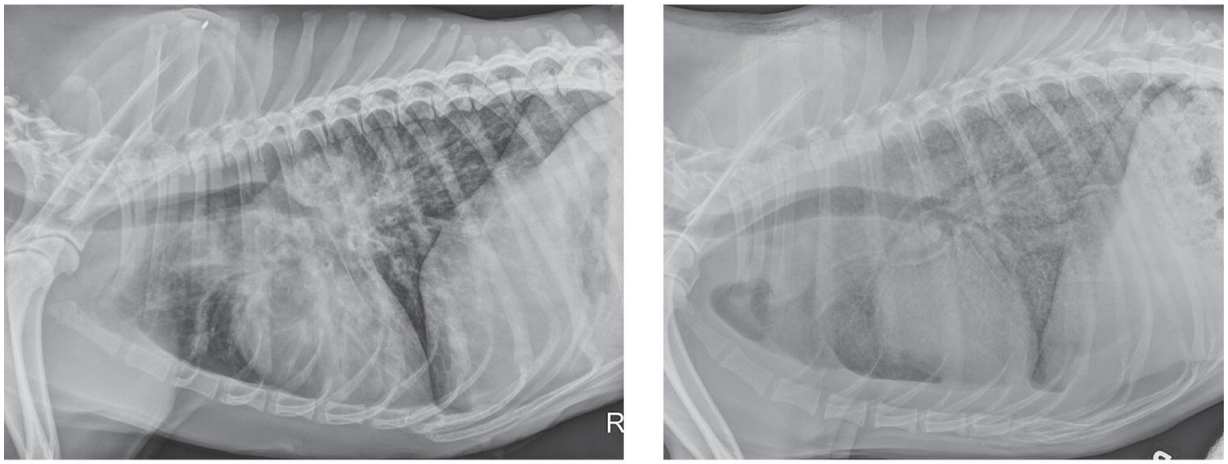


Figure 6.8 Right lateral thoracic radiographs from a dog with (a) coccidioidomycosis and (b) blastomycosis. Hilar lymphadenopathy is prominent along with a marked peribronchial pattern (a). A diffuse miliary interstitial pattern is seen characterized by similarly sized nodules throughout the lung lobes (b).

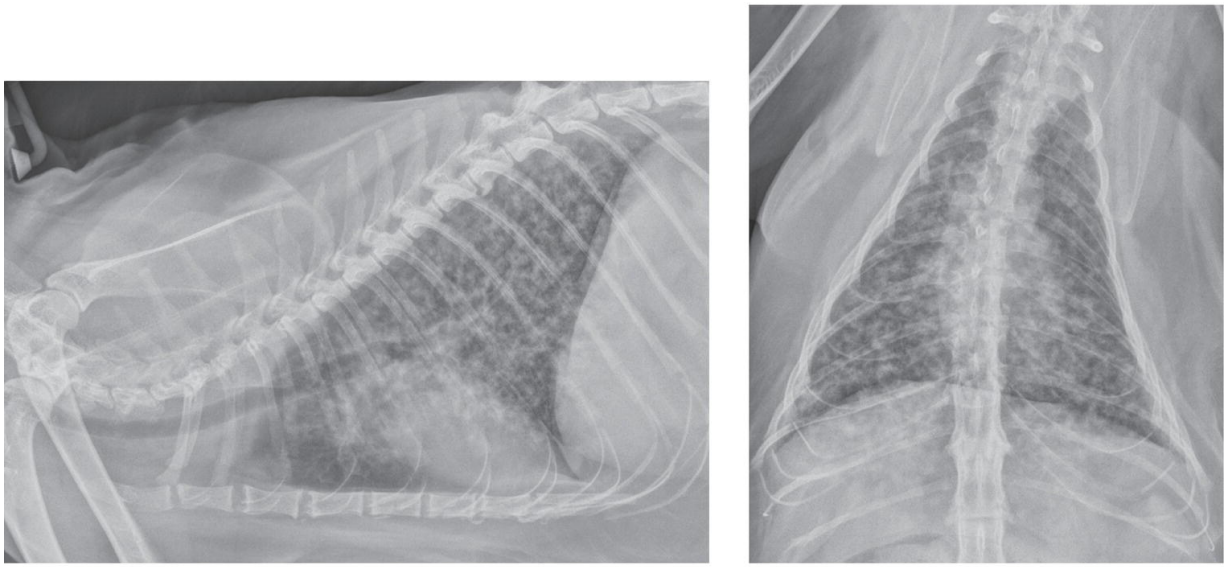


Figure 6.9 (a) Right lateral and (b) dorsoventral radiographs from a 2-year-old spayed female domestic short hair (FS DSH) with disseminated histoplasmosis.

Serologic assays for most fungal infections (histoplasmosis, blastomycosis, and coccidioidomycosis) are variably useful, because animals in endemic regions will usually develop a positive antibody

titer due to exposure to the organism. Also, a serologic response takes time to mount and dogs with fulminant infection due to blastomycosis are often negative in the early stages of disease. In contrast, serology for antibodies to coccidioidomycosis remains a useful screening tool. In a dog or cat with appropriate clinical findings and travel to an area endemic for *C. immitis*, a positive coccidioidomycosis titer can be considered relatively diagnostic, particularly if a quantitative agar gel immunodiffusion test for immunoglobulin (Ig) M and IgG is performed (University of California, Davis School of Medicine, www.ucdmc.ucdavis.edu/medmicro/cocci). *Coccidioides* antibody lateral flow assays are rapid tests that can provide early suspicion of the diagnosis of coccidioidomycosis, (Grill et al. 2024) although cross-reactivity is noted in cases of histoplasmosis with some tests. Follow-up quantitative immunodiffusion titers are recommended to provide more information on the likelihood of infection and to follow the course of disease.

Serum or urine antigen tests have better accuracy in the diagnosis of blastomycosis and histoplasmosis despite cross-reactivity for these fungal organisms. An enzyme immunoassay (MiraVista Diagnostics, Indianapolis, IN) directed against the galactomannan antigen on the cell wall of fungal organisms demonstrated slightly better sensitivity when performed on urine samples than when applied to serum (Spector et al. 2008). In addition, this test can be useful in monitoring response to therapy, because antigen levels decline with azole treatment and rebound with relapse (Foy et al. 2014).

Diagnosis of a fungal infection can be confirmed by cytologic or histologic assessment of lymph node or organ aspirates, airway samples obtained by tracheal wash or BAL, skin impression smears, rectal scrapes, aqueocentesis samples, or bone marrow evaluation. Fungi are of distinctive sizes and shapes and are usually surrounded by pyogranulomatous inflammation (Table 6.3). Culture is rarely needed to confirm the diagnosis and is not advised in cases suspected of coccidioidomycosis because of zoonotic concerns for laboratory personnel.

Treatment

Depending on the severity and extent of illness, fungistatic or fungicidal therapy might be preferred in an animal with fungal pneumonia (see Chapter 3). In animals with a severe fungal burden in the respiratory tract, die-off of organism can result in respiratory distress syndrome. In select cases, a non-steroidal anti-inflammatory agent or a glucocorticoid is employed to reduce the risk of severe pulmonary inflammation. Glucocorticoids are also sometimes used to reduce hilar lymphadenopathy when it is creating a substantial contribution to respiratory distress and cough because of bronchial obstruction. Despite concerns about immunosuppression impacting control of fungal disease, short-term use of glucocorticoids has not resulted in worsened outcome.

Long-term therapy with azoles (5–9 months) should be anticipated in all cases, and frequent monitoring is required to ensure effective treatment of fungal infection. Remission rates in dogs or cats with blastomycosis and histoplasmosis range from 60 to 90% and no difference has been found when using fluconazole versus itraconazole (Mazepa et al. 2011; Wilson et al. 2018). Higher urine or serum antigen titers at the time of diagnosis in dogs might mean that azole therapy will be required for a longer period of time.

Prognosis

Survival rates for animals with fungal pneumonia are not specifically known, although dogs that survive the first week of treatment are often cured of disease with long-term treatment. Dogs with lower urine antigen concentration and less severe radiographic scores for lung lesions tended to have better survival than those with higher scores (Motschenbacher et al. 2021). The need for oxygen supplementation is often reported as a negative prognostic indicator for animals with fungal pneumonia and this likely reflects the severity of pulmonary dysfunction. The final outcome depends not only on the severity of lung disease, but also on the presence of other organ involvement. Surgery is often required for a dog with a painful glaucomatous eye, in an intact male dog that might sequester organisms in the prostate, or in a dog with a consolidated lung lobe. Despite appropriate therapy, relapses still occur in 20–30% of dogs

with histoplasmosis or blastomycosis (Mazepa et al. 2011; Wilson et al. 2018). This rate of relapse is likely similar for infection with *C. immitis* as well as fungal infections in cats.

Table 6.3 Characteristics of common fungal organisms.

Fungus	Primary ecologic niche	Cytologic characteristics
Blastomyces dermatitidis	Mississippi/Missouri river valleys	Broad-based budding yeast, 5–20 μm, generally extracellular
Histoplasma capsulatum	Mississippi/Missouri river valleys	2–4 μm, usually found in clusters within macrophages
Coccidioides immitis	Arizona/New Mexico/California	10–80 μm, double-walled structure containing endospores

Protozoal and Similar Pneumonias

Pathophysiology

Although rare, pneumonia can result from infection with protozoan organisms such as *Neospora caninum* and *Toxoplasma gondii*. In addition, *Pneumocystis canis*, an organism that shares some characteristics of protozoans but has been classified as a fungal organism, can result in presentation for pneumonia. *Pneumocystis* organisms can be found in the lungs of normal, healthy individuals at a low level (considered colonization) and development of infection is typically associated with immunosuppression allowing expansion of the number of organisms present (Danesi et al. 2017). In dogs, a combined congenital immuno-deficiency is suspected in the Miniature Dachshund (Lobetti 2000) and an IgG deficiency has been proposed in Cavalier King Charles Spaniels (Watson et al. 2006) that results in *Pneumocystis* pneumonia in these breeds. Iatrogenic immunosuppression has the potential to reactivate or worsen infection by any of these organisms. All of these protozoal and similar organisms can cause neutrophilic inflammation and interstitial pneumonia.

History and Signalment

Pneumonia due to *Neospora* can be seen in congenitally infected puppies in conjunction with ascending paralysis of the limbs. Disease is associated with a high fatality rate. *Toxoplasma* pneumonia of cats or kittens is usually associated with severe systemic disease and rapidly progresses to death. In the dog, toxoplasmosis is less common, but infection can also result in pneumonia. Pneumocystosis has been reported most commonly in Miniature Dachshunds less than 1 year of age and in adult Cavalier King Charles Spaniels, as well as sporadically in other breeds. Typical presenting complaints with *Pneumocystis* pneumonia include progressively worsening exercise intolerance and tachypnea, chronic cough, and gradual weight loss.

Physical Examination

Tachypnea with labored respiration or increased respiratory effort is common. Fever is generally absent or body temperature only mildly elevated, and animals display a poor body condition score. Respiratory auscultation is generally unremarkable or harsh bronchovesicular sounds are noted, and a dry cough can be triggered by tracheal palpation. Systemic or neurologic signs can be seen in animals with toxoplasmosis or neosporosis. Chorioretinitis has been reported with *Pneumocystis* pneumonia (Johnson et al. 2023) and is also possible with infection by *Toxoplasma* organisms, where uveitis, iritis, iridocyclitis, or chorioretinitis can be seen.

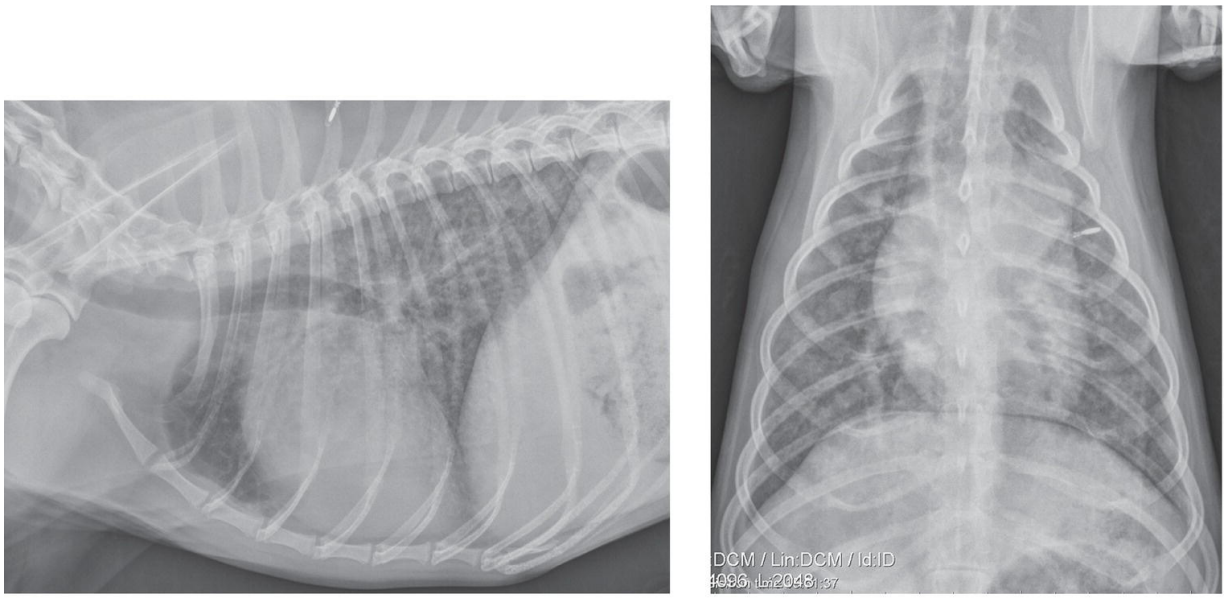
Diagnostic Findings

Standard laboratory tests reveal non-specific findings of neutrophilic leukocytosis. Positive serology for *Neospora* in conjunction with clinical signs provides a presumptive diagnosis. A diagnosis of *Toxoplasma* would be suspected in an animal with relevant clinical findings that has a positive IgM titer or a fourfold increase in IgG titer in conjunction with a positive response to treatment. It is rare to document *Toxoplasma* oocysts in the feces. In Cavalier King Charles Spaniels suspected of pneumocystosis, measurement of serum immunoglobulins should be considered.

Thoracic radiographs in protozoal or *Pneumocystis* pneumonia most commonly reveal diffuse interstitial or nodular infiltrates (Figure 6.10), although alveolar densities are occasionally seen. *Pneumocystis* can be identified in tracheal wash, BAL fluid, or fine-needle lung aspirate, although detection can be challenging. *Pneumocystis* organisms appear as trophic forms ranging in size from 2 to 8 μm, or as cysts which are 5–10 μm in size and contain two to eight small inclusions that are 1–3 μm in diameter (Figure 6.11). Fine-needle aspirate samples might have greater diagnostic yield, and Giemsa staining of airway fluid can sometimes enhance recognition (Weissenbacher-Lang et al. 2018). Quantitative PCR-based testing has recently been reported and likely will become the diagnostic standard (Danesi et al. 2017). *Toxoplasma* tachyzoites that can be found in BAL fluid are 2 × 6 μm and are found extracellularly or intracellularly within macrophages. Necropsy findings in protozoal-type pneumonias are typically diagnostic.

Treatment

Toxoplasma is most commonly treated with clindamycin (12.5 mg/kg orally [PO] twice a day [BID]) or trimethoprim-sulfa (15 mg/kg PO daily to BID) for >4 weeks. Clindamycin might also be effective for *Neospora*. Treatment of *Pneumocystis* pneumonia relies on the use of trimethoprim-sulfa at 15–30 mg/kg PO BID–TID for 4 weeks or longer as needed. Dogs treated with trimethoprim-sulfa should be monitored for development of keratoconjunctivitis sicca, anemia due to folate deficiency, and liver toxicity throughout treatment. Standard supportive care for pneumonia with oxygen supplementation should also be employed as needed.



(a) (b)

Figure 6.10 (a) Right lateral and (b) dorsoventral radiographs from a 3-year-old male castrated (MC) Cavalier King Charles Spaniel with *Pneumocystis* pneumonia reveal a marked interstitial pattern.

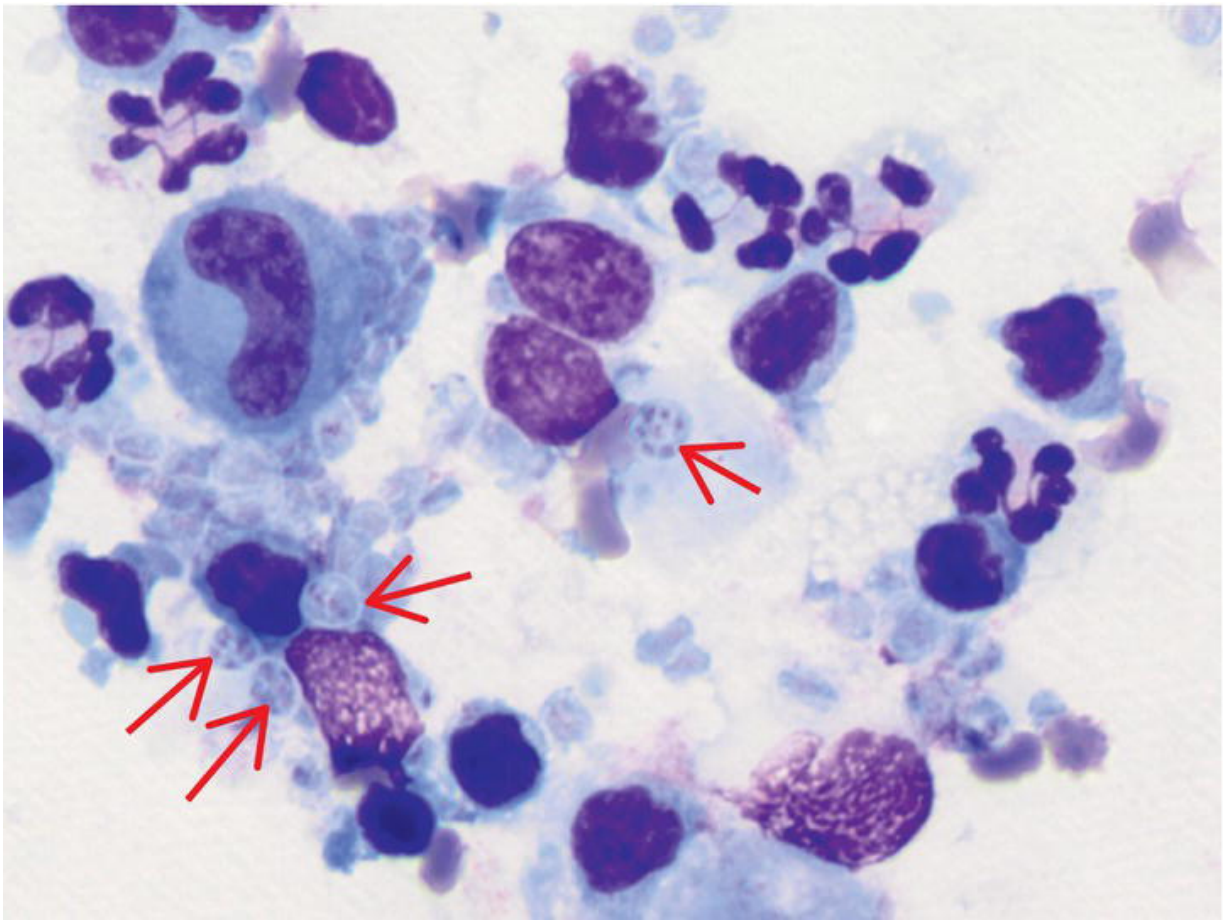


Figure 6.11 BAL cytology from a dog with *Pneumocystis* pneumonia reveals classic cystic forms (arrows).



Figure 6.12 Gross necropsy findings from a dog with pyogranulomatous pneumonia due to *Pneumocystis* reveals consolidation with hemorrhage throughout the lungs. Small pinpoint to miliary, firm, nodular white foci of infection are evenly distributed throughout all lung lobes.

Prognosis

Pulmonary toxoplasmosis or neosporosis is often fatal in young animals. Young adult Cavaliers with pneumocystosis might have a relatively good prognosis (Watson et al. 2006), although other scattered reports suggest <50% survival in animals with *Pneumocystis* pneumonia. It is likely that the degree of lung involvement determines response to therapy (Figure 6.12).

Inflammatory Disorders

Eosinophilic Lung disease

Pathophysiology

Eosinophilic lung disease in the dog is a poorly understood disorder. Heartworm disease, lung parasitism, and larval migration of parasites are recognized causes of pulmonary eosinophilia; however, primary eosinophilic infiltration of the lung can occur in the absence of an identifiable inciting cause. The finding of increased CD^{4+} T-cells in BAL fluid suggested that a type II hyper-sensitivity response might be responsible for eosinophilic bronchopneumopathy (EBP) (Clercx et al. 2002), although cytokine profiles in airway tissues from affected dogs did not support a Th2 or allergic response (Peeters et al. 2006). Eosinophilic lung disease can result in a spectrum of clinical syndromes including a condition described as similar to chronic bronchitis (EB), a more severe pneumonic form (EBP), and eosinophilic granuloma (EG), characterized by nodules or masses within airways (Johnson et al. 2019). This might be an artificial categorization of eosinophilic lung diseases in dogs, and it is unclear whether these disorders share the same etiopathogenesis or have differing stimuli for induction of disease.

History and Signalment

Dogs with eosinophilic lung disease are usually young adults, ranging from ~1 year to 8 years of age, and can be of any breed or size. Owner complaints can be present for months to years prior to presentation and generally include a harsh, unrelenting cough and progressive respiratory difficulty with exercise intolerance. Some dogs have concurrent nasal discharge or are systemically ill with lethargy and anorexia. Lack of response to antibiotics is common in the history.

Physical Examination

Increased or harsh bronchovesicular lung sounds are frequently present and harsh crackles can be detected, particularly in animals with concurrent airway collapse. In some cases, expiratory wheezes might also be heard. Tracheal palpation often results in a moist, productive cough with expectoration of white foam, although some dogs have a more honking nature to the cough. Some dogs display yellow-green nasal discharge but nasal airflow is preserved, regional lymph nodes are normal, and no other abnormalities in physical

examination findings are anticipated. Body temperature is sometimes elevated in dogs with pneumonic signs.

Diagnostic Findings

Leukocytosis is found in approximately 50% of cases, and peripheral neutrophilia or eosinophilia can be observed. Importantly, while peripheral eosinophilia can be profound in dogs with EBP and EG, some will show normal eosinophil counts. When eosinophilic lung disease is suspected based on clinical presentation and blood work, parasitism should be ruled out by performing heart-worm tests and fecal analyses (see parasitic bronchitis, Chapter 5). Pulse oximetry and arterial blood gas analysis (where available) are recommended, because hypoxemia can be marked in affected dogs and can persist after clinical and radiographic resolution of disease, suggesting that eosinophilic disorders can be associated with permanent lung damage. This is not terribly surprising given the toxic nature of eosinophils.

Radiographs in dogs with eosinophilic lung disease are generally abnormal, with a bronchial pattern reported most commonly (Figure 6.13). Alveolar infiltrates and bronchiectasis are also encountered frequently, and mass-like lesions can be seen on both radiographs and CT in dogs with EG (Figure 6.14). Airway examination is remarkable for yellow-green tinged mucus in some affected dogs, indicating the presence of eosinophils. Mucosal irregularities and airway collapse have also been reported, although cases with EB might show only pronounced airway hyperemia (Figure 6.15). Normal dogs have ~5% eosinophils on a differential count of BAL fluid, while dogs with eosinophilic lung disease can have up to 90% eosinophils (Figure 6.16). Bacterial culture of airway fluid is negative or reveals a light growth of normal flora, although occasionally affected dogs can have infection coincident with eosinophilic lung disease. Quantitative PCR testing has failed to show a specific role for respiratory pathogens such as *Bordetella* and *Mycoplasma* (Canonne et al. 2018), although dogs with severe clinical signs were more likely to have higher numbers of *Bordetella* organisms detected. Testing for fungal organisms in mass-like lesions has failed to confirm a role for infection in dogs tested.

Rhinoscopy has been performed in some dogs with concurrent nasal discharge and has demonstrated hyperemia and eosinophilic nasal cytology (Clercx et al. 2000). Intradermal skin testing has occasionally been employed in an attempt to identify a potential allergic stimulus for EBP, but results have been equivocal.

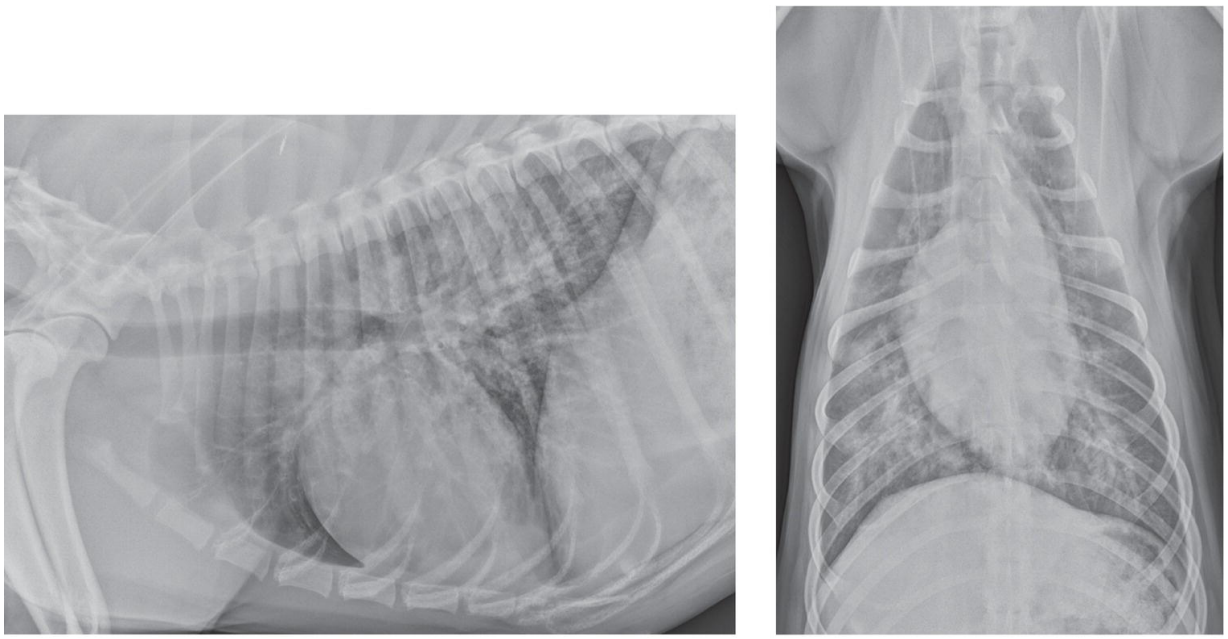
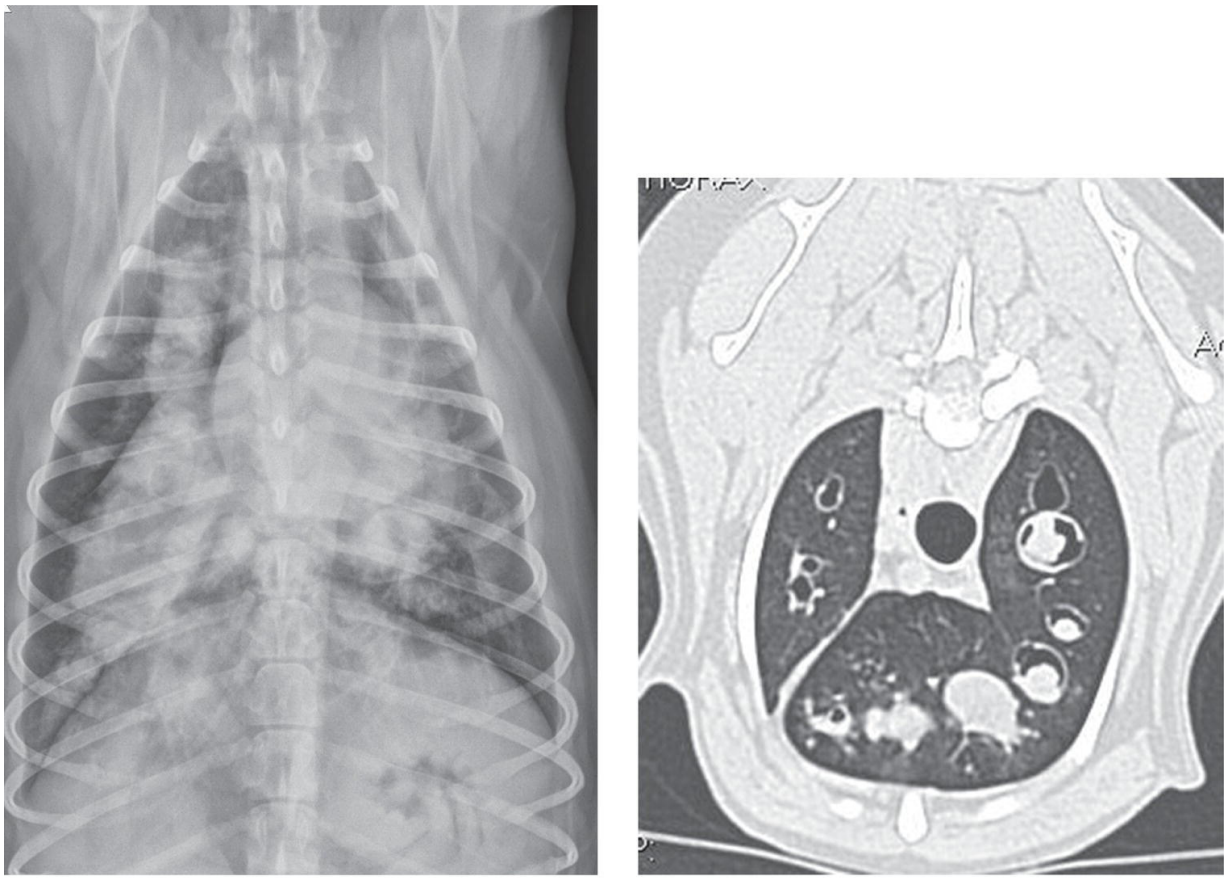
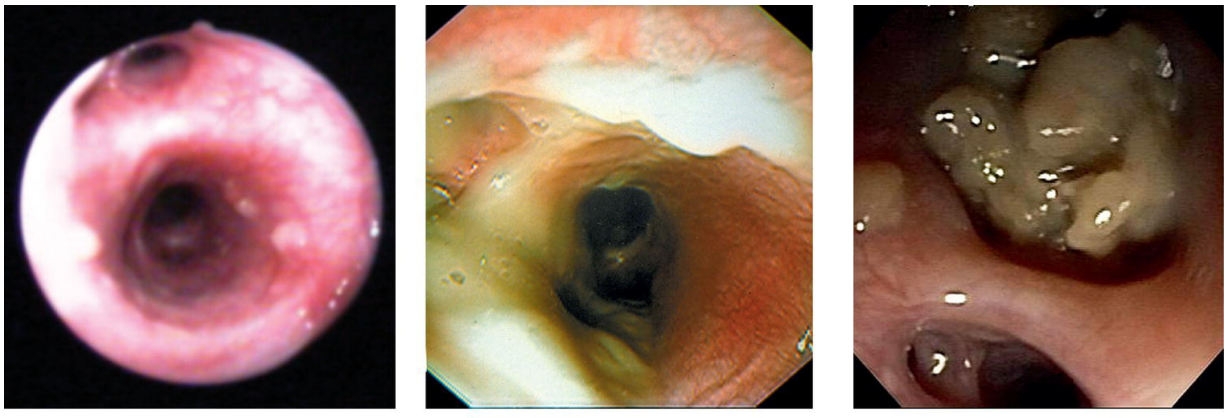


Figure 6.13 (a) Right lateral and (b) dorsoventral radiographs from a 1-year-old FS Labrador Retriever with eosinophilic lung disease reveal a severe diffuse bronchial pattern.



(a) (b)

Figure 6.14 (a) Dorsoventral radiograph and (b) cross-sectional computed tomography (CT) slice in a dog with severe eosinophilic granulomatous disease and bronchiectasis. In the radiographs, large mass effects in the right cranial and caudal lung lobes are bronchi filled with eosinophilic material. In the CT, multiple dilated airways are partially or completely filled with amorphous material.



(a) (b) (c)

Figure 6.15 Bronchoscopic images from dogs with eosinophilic lung disease can reveal dramatic airway hyperemia with mild mucus accumulation–EB (a), yellow-green mucus–EBP (b) or eosinophilic masses within the lung–EG (c).

Treatment

Dogs with eosinophilic lung diseases are often treated prophylactically for parasites or larval migration with fenbendazole (50 mg/kg/day for 14 days), either before diagnostic testing has been performed or while bacterial cultures are pending. Specific therapy requires the use of immunosuppressive doses of prednisone or prednisolone (1 mg/kg PO BID). If clinical signs diminish in the first 10–14 days, a gradual decrease in corticosteroid dose and lengthening of the dosing interval are recommended; however, long-term therapy (4–6 months) should be anticipated. Peripheral eosinophilia should resolve relatively quickly, and pulse oximetry or arterial blood gas analysis demonstrates improvements in oxygenation prior to resolution of radiographic infiltrates. If clinical signs do not respond to systemic steroids or side effects are dose limiting, use of inhaled steroids could be implemented (see Chapter 3), although one study failed to show control of clinical signs in dogs treated with inhaled fluticasone propionate (Canonne et al. 2016). This could be related to failure of the drug to gain access to epithelial receptors because of airway mucus, and adjunct therapy, including nebulization and coupage, can be of value in dogs with thick airway secretions (Figure 6.15b). Dogs with large airway granulomas (Figure 6.15c) can require surgical resection if only one or two lung lobes are affected. Debulking of airway granulomas with cryotherapy, laser treatment, or endoscopic curettage can be attempted, but often the disease is too widespread for this to be effective.

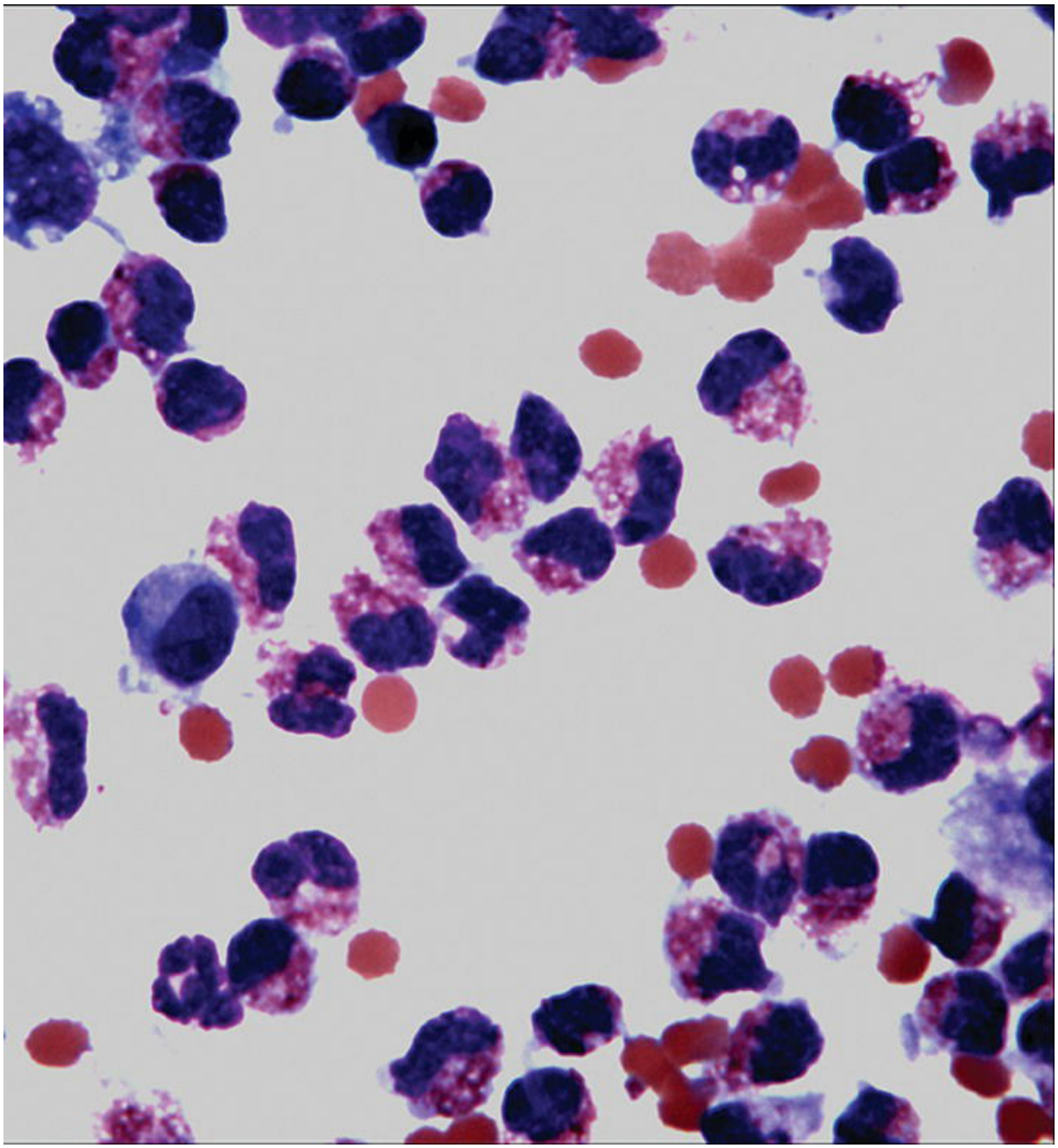


Figure 6.16 Airway cytology from a dog with eosinophilic lung disease confirms the diagnosis.

Inhaled steroids might be implemented as oral drugs are tapered and addition of other immunosuppressive agents such as cyclosporine or azathioprine is occasionally employed. Resolution of luminal filling with eosinophilic material has been reported in one dog with EG (Katajavuori et al. 2013) and reasonable response to therapy sometimes can be achieved in these severely affected dogs (Johnson

et al. 2019). The utility of allergy testing (serum IgE or intradermal testing) has not been fully assessed, therefore currently there is not a role for hyposensitization therapy in EBP. Limiting exposure to irritants in the environment would likely be wise.

Prognosis

Degranulation of eosinophils during bronchoscopy or tracheal wash can lead to bronchoconstriction or non-cardiogenic pulmonary edema. This is manifest by decompensation and dramatic respiratory distress requiring emergency intervention after airway sampling. Rapid confirmation of airway eosinophilia and administration of steroids can be life-saving. Reversal of bronchoconstriction with terbutaline can also be effective, therefore pre-treatment with terbutaline before tracheal wash or bronchoscopy should be considered in dogs suspected of eosinophilic lung disease. Dogs with eosinophilic lung disease generally respond to therapy; however, long-term treatment is often required to avoid relapses, and side effects of steroids can be significant. Secondary bacterial or fungal infections can occur due to the altered environment within the lung or as a result of immunosuppression, and follow-up examinations and diagnostic testing are essential.

Aspiration Pneumonia

Pathophysiology

Aspiration pneumonia is a serious and potentially life-threatening inflammatory and/or infectious lung process that occurs secondary to inhalation of gastric or oropharyngeal contents. Pulmonary injury results from chemical pneumonitis and the effect of particulate matter in the lung, inflammatory pulmonary responses, and development of bacterial pneumonia. Initially, aspiration of gastric acid alters surfactant function, resulting in loss of surface tension and atelectasis. Injury to epithelial cells allows bacterial invasion and also exposes nerve endings between epithelial cells, resulting in bronchoconstriction. Resultant inflammation and infection increase mucus production, causing airway obstruction and difficulty breathing. Ventilation/perfusion mismatching results in hypoxemia.

Severe aspiration injury is associated with increased alveolocapillary permeability and development of acute respiratory distress syndrome due to non-cardiogenic pulmonary edema (see Chapter 8).

Aspiration pneumonia can often be ascribed to one underlying disease, but multiple predisposing factors can also be found. Esophageal dysfunction or megaesophagus, vomiting or chronic enteropathies, neurologic disorders associated with recumbency or loss of consciousness, laryngeal dysfunction or surgery, and anesthetic-related aspiration events are identified most commonly (Kogan et al. 2008b; Ovbey et al. 2014; Levy et al. 2019). In the latter, regurgitation while under anesthesia and use of hydromorphone at induction were most relevant in the development of aspiration pneumonia (Ovbey et al. 2014). The type of procedure also played a role in the occurrence of aspiration, with animals requiring upper airway surgery at the highest risk, followed by endoscopic procedures, thoracotomy, laparotomy, and neurosurgery. Brachycephalic syndrome can also result in aspiration pneumonia or pneumonitis, because many dogs have concurrent respiratory and gastrointestinal dysfunction associated with conformational issues and require surgical correction of upper airway obstruction.

History and Signalment

Aspiration pneumonia appears to be much more common clinically in dogs than in cats, and any age or breed can be affected because of the multitude of predisposing diseases that result in aspiration pneumonia. Large breed dogs predominate in some studies because of the commonality of esophageal and laryngeal dysfunction, although brachycephalic breeds have been found to have approximately a fourfold increase in the incidence of aspiration pneumonia (Darcy et al. 2018). Interestingly, large breed dogs and Pugs tend to be older at the time of diagnosis, while Bulldogs and French Bulldogs are younger (Kogan et al. 2008a; Darcy et al. 2018). Cough and increased respiratory rate or effort are noted in more than half of the canine cases. Generally the history will provide clues to the underlying disease process leading to aspiration, such as a recent vomiting episode, seizure, or anesthetic event; however, it is uncommon for the aspiration episode to be witnessed. Also, occult

and micro-aspiration likely account for more lower respiratory disease than is currently recognized.

Cats with aspiration pneumonia tend to have a shorter duration of illness (<2 weeks) compared to cats with bacterial bronchopneumonia (up to 9 months), and cough is less common in cats with aspiration compared to bronchopneumonia (Dear et al. 2021). Increased respiratory effort can be obvious to owners (Levy et al. 2019).

Physical Examination

Abnormal lung sounds are found in over half of dogs and cats with aspiration pneumonia, although many will be described as harsh or loud lung sounds, while a lesser percentage will have detectable crackles or wheezes. Normal lung sounds have been reported in 30% of dogs and approximately 10% had dampened lung sounds (Kogan et al. 2008a). Fever (temperature >39.2°C [>102.5°F]) or tachypnea (respiratory rate >30 breaths/minute) is expected in dogs with pneumonia, but these are found in less than half of affected dogs. In contrast, cats with aspiration pneumonia tend to be hypothermic and tachypnea is relatively common with any lower respiratory disease (Dear et al. 2021).

The remainder of the physical examination is important for determining the underlying etiology of aspiration. Stridor over the larynx is suspicious for laryngeal disease, and some dogs with laryngeal paralysis display a reduced gag reflex associated with generalized neuromuscular disease, along with decreased proprioceptive placing, more prominent in the rear limbs and sometimes only unilateral. In such animals, complete neurologic assessment is warranted. Careful observation of the animal prehending and eating food or drinking water is beneficial in detecting subtle abnormalities in pharyngeal or esophageal function. Abdominal pain might support ongoing pancreatitis as a cause for vomiting, with secondary aspiration injury, or thickened bowel loops caused by an enteropathy can occasionally be found (although this would be much more commonly identified in a cat than in a dog).

Diagnostic Findings

Neutrophilia with a left shift is present in the majority of affected dogs and cats, indicating a response to inflammation, and albumin is often mildly decreased, perhaps due to lung inflammation and vascular leakage. Pulse oximetry or arterial blood gas analysis can be helpful in assessing the degree of lung dysfunction because some dogs are markedly hypoxemic.

The classic radiographic description of aspiration pneumonia is an alveolar infiltrate in the cranioventral or middle lung lobe region; however, approximately 25% of dogs can have an interstitial infiltrate at the time of diagnosis. Aspiration into the right lung occurs in over 50% of canine cases, while both sides of the lung are involved in 12% (Kogan et al. 2008a). The most commonly involved lung lobe is the right middle lobe (Figure 6.17), followed by the right cranial and the caudal segment of the left cranial lobe, and the cranial segment of the left cranial lung lobe, although any lung lobe can be involved, depending on the position of the animal at the time of aspiration. Cats with aspiration tend to have alveolar infiltrates and a more multifocal distribution in comparison to cats with bacterial bronchopneumonia. Right middle lobar consolidation also occurs in cats with aspiration (Levy et al. 2019; Dear et al. 2021) and must be differentiated from right middle lobar collapse, which is common in cats with inflammatory airway disease. The left cranial lung lobe is also commonly involved in aspiration events in cats (Levy et al. 2019).

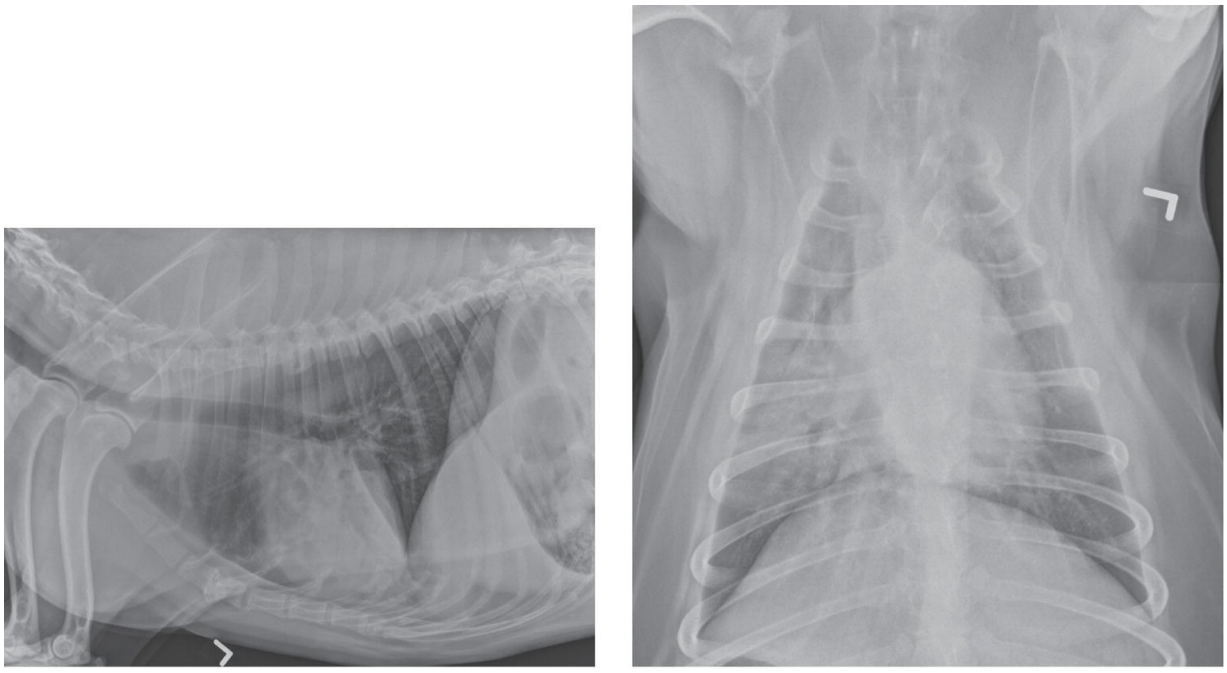


Figure 6.17 (a) Left lateral and (b) dorsoventral radiographs from a 12-year-old spayed female (FS) Labrador Retriever with aspiration pneumonia, following unilateral arytenoid lateralization for treatment of laryngeal paralysis. Air bronchograms are visible in both views, primarily in the right middle lung lobe.

Airway samples are not always obtained in animals suspected of aspiration injury because of concerns about further aspiration following sedation or because anesthesia is required for collection of airway fluid. When infection is present, airway wash samples would be expected to reveal septic suppurative inflammation and various bacterial species, particularly *Pasteurella*, enteric organisms, and *Mycoplasma* (Darcy et al. 2018), although *Mycoplasma* and anaerobes appear to predominate in cats (Dear et al. 2021). If only chemical injury is present, neutrophilic inflammation in the absence of intracellular bacteria would likely predominate.

Treatment

Antibiotic administration in the patient with presumed aspiration pneumonia is controversial because not all aspiration events are associated with infection, and some dogs can recover without the use of antimicrobials (Cook et al. 2021). When infection is confirmed,

clinical disease is severe, or systemic manifestations are suggestive of infection, broad-spectrum agents are usually given for 1–2 weeks. Depending on the severity of disease, a potentiated penicillin derivative is typically chosen, or the combination of a penicillin and fluoroquinolone is used. A bronchodilator trial using terbutaline might be considered in the acute stage of disease, particularly if expiratory effort or wheezing suggests bronchoconstriction. Maintenance of airway hydration with intravenous fluids is important. Saline nebulization can be helpful but coupage is not usually recommended in animals with aspiration pneumonia because of the potential to increase intraabdominal pressure and augment vomiting. Also, coupage is challenging to perform in recumbent patients. Glucocorticoids are not recommended despite the fact that an inflammatory response contributes to pulmonary injury, and non-steroidal agents are typically not administered due to concerns about gastrointestinal side effects.

Animals that are not markedly hypoxemic or exhibiting dramatic respiratory effort can be maintained without supplemental oxygen, because experimental evidence suggests that oxygen can enhance acid-induced injury in models of aspiration injury. However, aspiration pneumonia can lead to acute respiratory distress syndrome (see Chapter 8), and in these patients, mechanical ventilation can be required to support oxygenation while pulmonary injury resolves.

Perhaps the most important consideration in the animal with aspiration pneumonia is to provide appropriate management of the primary disease responsible for aspiration. This will assist in avoidance of further aspiration and perpetuation of airway injury. Suppression of gastric acid can be helpful in some cases, although there is a theoretical concern that allowing gastric pH to rise will increase bacterial load in the aspirated material and possibly worsen the infectious component of aspiration injury. Some acid suppressants can promote vomiting, thus increasing the potential for aspiration events. Continual monitoring is advised. Providing food and water in an upright position is important for animals with esophageal or laryngeal disease. Modification of the consistency of the diet should be instituted in dogs, because some animals are

better able to prehend and swallow kibble while others do well with meatball feeding.

Prognosis

Aspiration pneumonia carries a relatively good prognosis, with survival rates of 75–80% despite the presence of more than one predisposing disorder for aspiration (Kogan et al. 2008b; Levy et al. 2019). Radiographic severity of disease does not necessarily correlate with survival and further classification of disease severity is likely necessary to establish factors important in prognosis.

Interstitial Lung Disease and Idiopathic Pulmonary Fibrosis

Pathophysiology

In human medicine, interstitial lung diseases (ILD) have been reported to develop secondary to infectious organisms (bacteria, viruses, or fungi), immune-mediated disease, exposure to drugs (e.g. antimicrobial or anti-arrhythmic agents) or inhaled toxins (e.g. paraquat, hydrocarbon-containing sprays, industrial flavorings), and in association with neoplasia. It is suspected that similar disorders or exposures that damage the alveolar-capillary membrane can lead to ILD in dogs and cats. Epithelial cell activation, induction of inflammation, and dysregulated mesenchymal repair lead to structural changes in the alveolar unit with enhanced interstitial collagen deposition. This results in reduced lung compliance and dysfunctional gas exchange.

Various pathologic forms of ILD have been described in dogs and cats, including idiopathic pulmonary fibrosis (IPF), cryptogenic fibrosing alveolitis, and bronchiolitis obliterans with organizing pneumonia. Some of these diseases are characterized by inflammation, while in others, the interstitium is infiltrated by fibroblasts and there is collagen deposition, smooth muscle and alveolar epithelial metaplasia, with very little inflammation. This is of obvious importance when considering the value of treatment with anti-inflammatory agents.

An IPF-like condition has been described in the cat (Cohn et al. 2004) and is the most common form of ILD in the West Highland White Terrier. In the Westie, transforming growth factor beta, endothelin-1, and micro-aspiration injury likely play key roles in the pathogenesis, although a genetic predisposition is also suspected (Heikkilä et al. 2011; Syrjä et al. 2013; Krafft et al. 2014; Määttä et al. 2018). Failure of collagenolysis has also been implicated as part of the pathology in the West Highland White Terrier. Some dogs can be affected by concurrent bronchitis, which results in chronic cough and can obscure dysfunction associated with the underlying lung disease. In the cat, coincident pulmonary neoplasia has been noted in 25% of pulmonary fibrosis cases (Cohn et al. 2004).

History and Signalment

IPF afflicts West Highland White Terriers more commonly than other Terrier breeds and can also be found in various types of cats. Animals are usually middle-aged to older at the time of presentation, and there is generally a long history of chronic deterioration in respiratory function. Tachypnea develops over time and exercise intolerance becomes more pronounced. These changes are often ascribed to aging and pulmonary dysfunction goes unrecognized until late in the course of disease. A dry, non-productive cough predominates in some animals, or owners may report loud respirations or rapid breathing. Systemic signs of lethargy, anorexia, and weight loss are relatively common, especially in cats. Severely affected animals can develop syncope due to hypoxemia or pulmonary hypertension.

Occasionally, younger (2–5-year-old) large breed dogs develop ILD of unknown etiology, and acute onset of severe tachypnea can be the only sign of disease in these dogs. Potential etiologies include an autoimmune or hypersensitivity disorder, inhalational exposure to a toxin or particulate matter, paraquat ingestion, or an unrecognized viral infection. Sporadic cases have been poorly characterized.

Physical Examination

Tachypnea can be dramatic in affected animals, with respiratory rates of 100–150 breaths/minute in the absence of panting. The

classic auscultatory finding in Westies with IPF is inspiratory crackles, which can be soft or loud and often present diffusely throughout all lung fields. In cats, lung sounds can be harsh or loud or adventitious sounds (crackles and wheezes) might be ausculted. Animals with secondary pulmonary hypertension can develop a right-sided systolic murmur of tricuspid regurgitation or a split-second heart sound. The remainder of the physical examination is usually unremarkable unless cor pulmonale results, which could be associated with ascites, pleural effusion, or distended jugular veins.

Diagnostic Findings

The minimum database is used to rule out concurrent systemic diseases. Laboratory findings of a neutrophilic leukocytosis and mild hyperproteinemia reflect chronic inflammation. Pulse oximetry (or arterial blood gas) is recommended to assess the degree of dysfunction, because dramatic hypoxemia – partial pressure of oxygen (P_aO_2) <50 mmHg – can be seen in some dogs. The search for serum and BAL biomarkers that would provide a less invasive means of confirming a diagnosis of IPF is ongoing.

Thoracic radiographs in dogs typically show a generalized or diffuse mild, moderate, or severe interstitial pattern that obscures visualization of the vasculature, and CT can highlight the severity of the infiltrate (Figure 6.18). Moderate cardiomegaly is relatively common in affected dogs and is primarily right-sided. Variable diffuse or patchy interstitial, bronchial, and/or coalescing alveolar infiltrates are observed in cats, and radiographic changes are generally described as severe, with caudal lobes more prominently involved (Cohn et al. 2004). Additional findings include bronchiectasis (Figure 6.19) or cavitated lesions, which could indicate concurrent neoplasia. Right-sided heart enlargement or pulmonary artery dilation could be a sign of pulmonary hypertension in cats also. Whether present or not, echocardiography should be considered in the diagnostic work-up of suspected cases of ILD to document pulmonary hypertension (see Chapter 8).

CT identification of ground-glass opacities and the pattern of honeycombing are considered the gold standard in the diagnosis of IPF in humans. Ground glass opacities are described as a hazy

attenuation of the lung parenchyma that preserves visualization of bronchovascular structures. Honeycombing is the descriptive term used for the clusters of uniformly sized cystic airspaces that represent collapse of fibrotic alveoli and dilation of the alveolar duct. This finding is considered indicative of end-stage lung disease. While thoracic CT is being used more commonly in veterinary medicine than previously, the need for anesthesia to obtain breath-hold images in dogs along with the cost of the procedure can prohibit use of this imaging modality. Sedated high-resolution CT was capable of identifying ground-glass opacifications and mosaic patterns more commonly in affected West Highland White Terriers than in controls (Roels et al. 2017), although it is unclear whether these lesions should be considered pathognomic in the absence of histologic confirmation of disease.

Definitive diagnosis of ILD requires histopathologic evaluation of a lung sample obtained through thoracotomy, thoracoscopy, or key-hole lung biopsy. Preoperative CT is recommended to identify the extent of parenchymal changes and, importantly, to identify a site for lung biopsy or lobectomy, because the disease is often patchy in distribution. Histopathologic findings of alveolar septal fibrosis, type II pneumocyte hyperplasia, smooth muscle cell hyperplasia, and epithelial metaplasia can be locally extensive or diffuse. Airway sampling by tracheal wash or bronchoscopy can be performed as a less invasive alternative to lung biopsy, although a non-specific increase in non-degenerate neutrophils and/or lymphocytes is typically seen.

Treatment

Unfortunately, treatment options for IPF are limited and fibrotic changes do not respond to anti-inflammatory therapy, although signs of concurrent bronchitis can be alleviated by oral or inhaled glucocorticoids. Anti-fibrotic drugs used in humans (pirfenidone, nintedanib) or anti-mediator drugs have not been fully evaluated in dogs and can be toxic, as well as expensive. Exposure to toxins and inhalational injury should be avoided, microaspiration should be managed, weight control is important, and a trial on extended-release theophylline could be considered to lessen respiratory effort.

In some animals, oxygen therapy at night can improve daytime activities, and treatment of pulmonary hypertension with sildenafil or tadalafil can improve overall health and well-being (see Chapter 8). Alternate therapy remains under investigation pending further information regarding the etiology of disease.

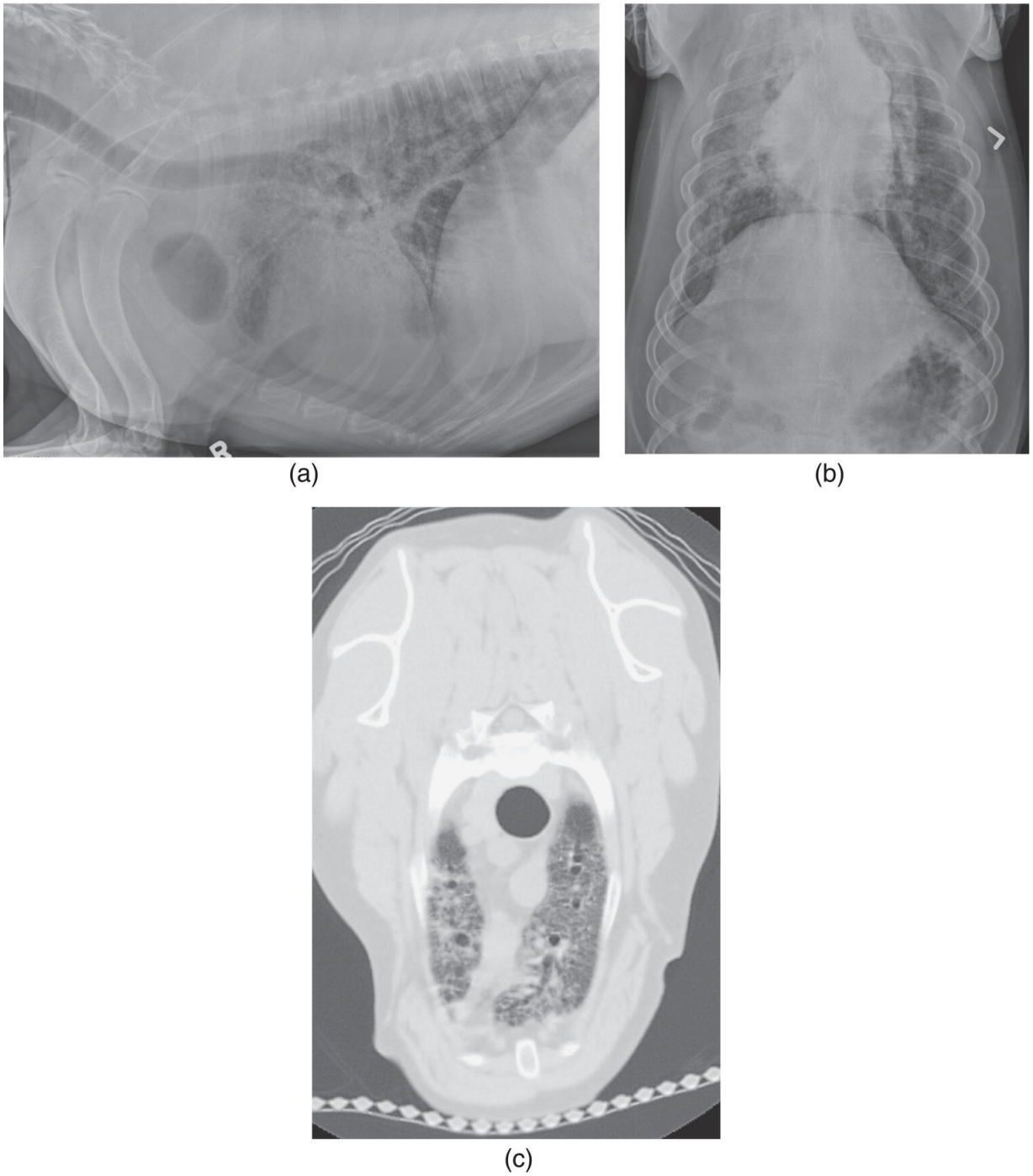


Figure 6.18 (a) Right lateral and (b) dorsoventral radiographs of a 2-year-old castrated male (MC) Chesapeake Bay Retriever reveal severe, diffuse miliary interstitial infiltrates throughout all lung lobes and mild perihilar lymphadenopathy. The right heart and pulmonary arteries are moderately enlarged. (c) CT demonstrates concurrent bronchial and alveolar infiltrates throughout all lung lobes.

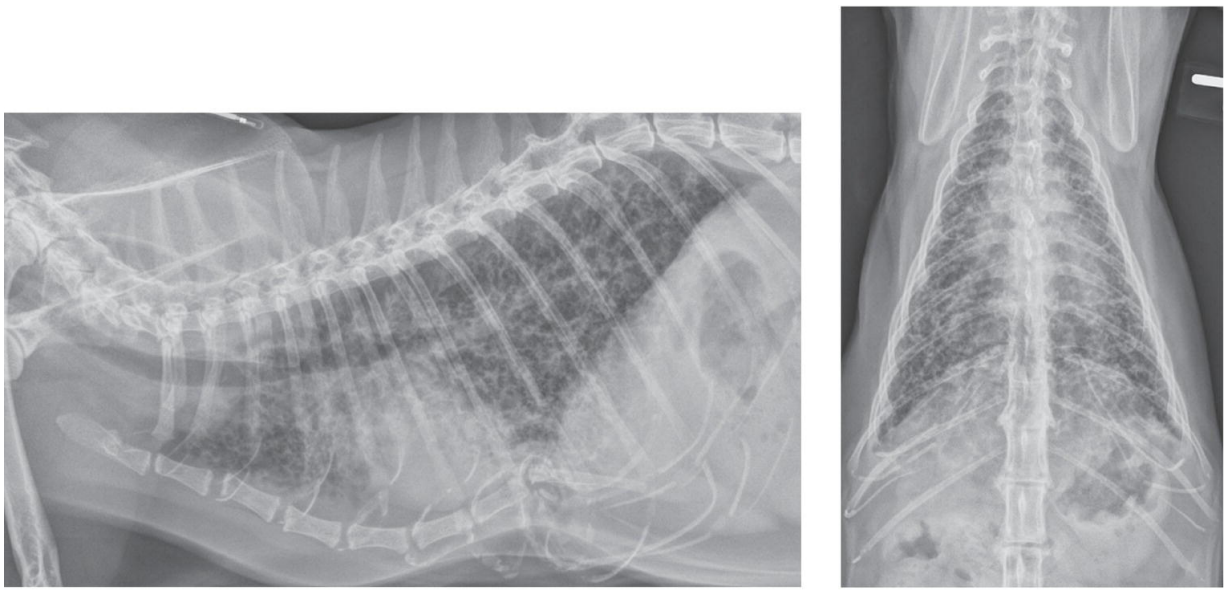


Figure 6.19 (a) Right lateral and (b) dorsoventral radiographs from a 12-year-old castrated male domestic short hair (MC DSH) reveal a severe and diffuse bronchial pattern with bronchiectasis throughout all lung lobes.

Prognosis

Prognosis is guarded, because animals are often older at the time of diagnosis or suspected diagnosis, and no effective treatment for IPF has been detailed to date. Most dogs succumb to disease within 1–2 years. The presence of concurrent pulmonary neoplasia in cats results in survival times from weeks to months.

Neoplastic Lung Disease

Pathophysiology

Primary pulmonary neoplasia is almost always malignant and is characterized by the histology of the cell origin. The most common lung tumor in dogs and cats is pulmonary carcinoma but pulmonary adenocarcinoma, bronchoalveolar carcinoma, histiocytic sarcoma (which can be primary or disseminated with pulmonary metastasis), and neuroendocrine tumors can be encountered, among other less common tumors (Fowler et al. 2020; McPhetridge et al. 2022). Pulmonary lymphosarcoma is relatively uncommon. Primary

neoplasms are staged based on the TNM (Tumor–Node–Metastasis) classification, with T1 indicating a solitary mass, T2 multiple masses, and T3 a tumor invading local tissues or with distal metastasis. N0 and M0 indicate no nodal involvement or metastasis.

Pulmonary neoplasia in humans is caused predominantly by smoking, which results in the generation of endobronchial lesions. Studies to date have not confirmed a definitive association between smoke, pollutants, or environmental particulate matter such as anthrocosis, silicosis, and pneumoconiosis in the development of pulmonary neoplasia in dogs and cats, although exposure to household radon appears to increase the risk of pulmonary neoplasia by two-fold (Fowler et al. 2020).

The lung is a very common site for metastasis from carcinomas or sarcomas because of its rich capillary bed, and metastatic disease is much more common than primary. Tumors that commonly metastasize to the lung include hemangiosarcoma, osteosarcoma, thyroid carcinoma, and mammary carcinoma. Also, primary pulmonary neoplasia in dogs and cats often results in intrapulmonary metastasis, which can make it hard to differentiate primary from metastatic disease, particularly in cats. Cats can also demonstrate metastasis to the digits (Gottfried et al. 2000) or to the tail.

History and Signalment

Primary and metastatic pulmonary neoplasia affects older animals most commonly. It has been suggested that brachycephalic breeds might be affected more commonly because the foreshortened nasal cavity fails to filter out environmental carcinogens, although this has not been clearly established. Pulmonary histiocytic sarcoma commonly affects Bernese Mountain dogs and Labrador Retrievers (Marlowe et al. 2018). Clinical complaints can be indicative of respiratory disease and include cough, labored breathing, tachypnea, or hemoptysis, but in many cases (particularly in cats) non-respiratory signs of anorexia and weight loss are reported. It is not uncommon for pulmonary neoplasia to be found as an incidental lesion on radiographs performed as screening tests for other diseases. Cats can also be presented for lameness associated with

digital metastasis from a primary pulmonary neoplasia (Gottfried et al. 2000).

Physical Examination

Affected animals often display tachypnea associated with either neoplastic parenchymal infiltration or pleural effusion associated with neoplasia. Lung sounds can be harsh or abnormal with parenchymal disease, or they may be muffled when lobar consolidation or pleural effusion is present. Some animals develop acute clinical signs if a neoplasm ruptures and results in pneumothorax. In those cases, lung sounds are absent dorsally and hyper-resonance might be detected.

Diagnostic Findings

Primary pulmonary neoplasia in the dog is usually focal on radiographs and appears as a well-defined, solitary mass lesion (Figure 6.20) or as lobar consolidation. Occasionally, a diffuse nodular interstitial pattern can be observed. Histiocytic sarcoma typically affects an entire lung lobe or only a peripheral segment and involves the right middle, left cranial lung lobe, or right caudal lung lobe (Barrett et al. 2014; Marlowe et al. 2018), while adenocarcinoma is more commonly found in a caudal lobe (Barrett et al. 2014). Primary pulmonary neoplasia in the cat most often occurs as a mass lesion in the caudal lung lobes, with other foci of infiltrates suspicious for metastasis at the time of diagnosis (Aarsvold et al. 2015). Bronchogenic carcinoma in the cat can have a cystic appearance on radiographs or CT associated with tumor necrosis (Figure 6.21). A diffuse pulmonary infiltrative pattern can also be found, particularly when a primary lung tumor has undergone intrapulmonary metastasis. Special attention is paid to the assessment of hilar and sternal lymph nodes due to the worsened prognosis in the case of metastatic disease. Unfortunately, intrapulmonary lymphadenopathy is difficult to assess on radiographs and contrast CT is preferred for assessment.

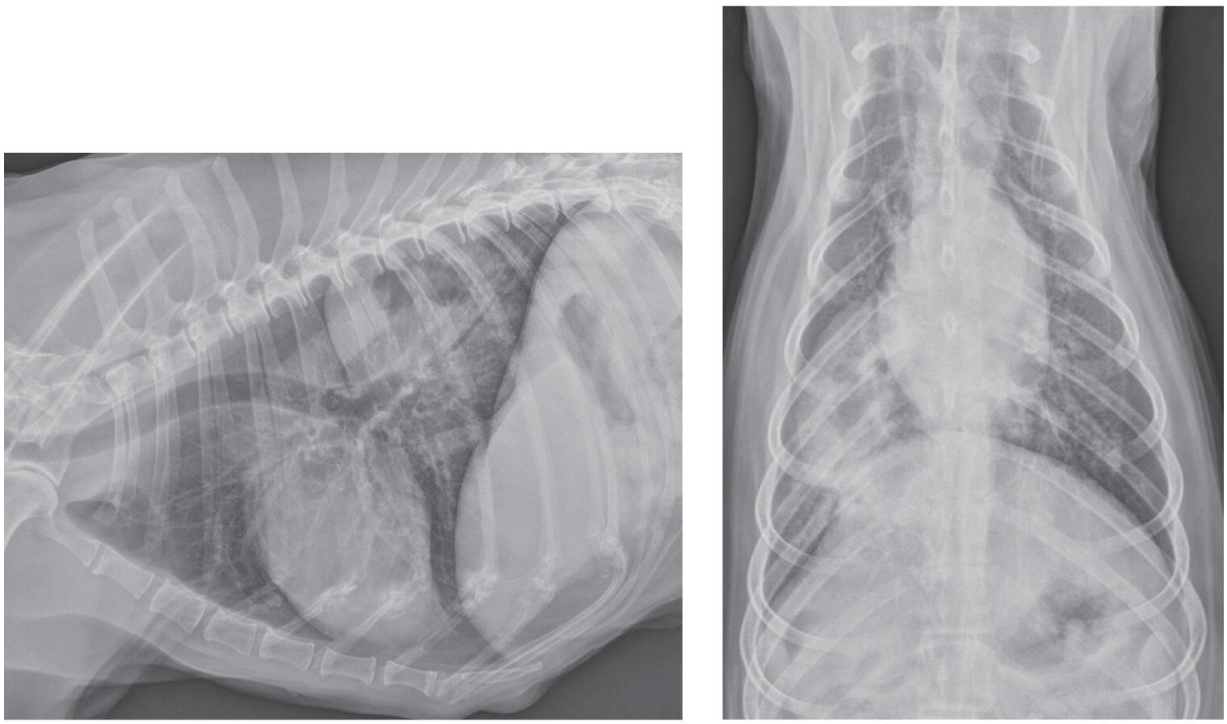


Figure 6.20 (a) Right lateral and (b) dorsoventral radiographs from a 17-year-old spayed female (FS) Husky mix with a primary lung tumor in the right caudal lung lobe. CT revealed hilar lymphadenopathy, suggesting the presence of metastatic disease.

Metastatic disease in the dog is often characterized radiographically by multiple, discrete, interstitial nodules of variable sizes (Figure 6.22), or a diffuse interstitial pattern can be seen (Figure 6.23). In the cat, ill-defined nodules or diffuse, patchy, mixed alveolar patterns are found most commonly (Forrest and Graybush 1998). In either species, pleural effusion can obscure visualization of a mass lesion.

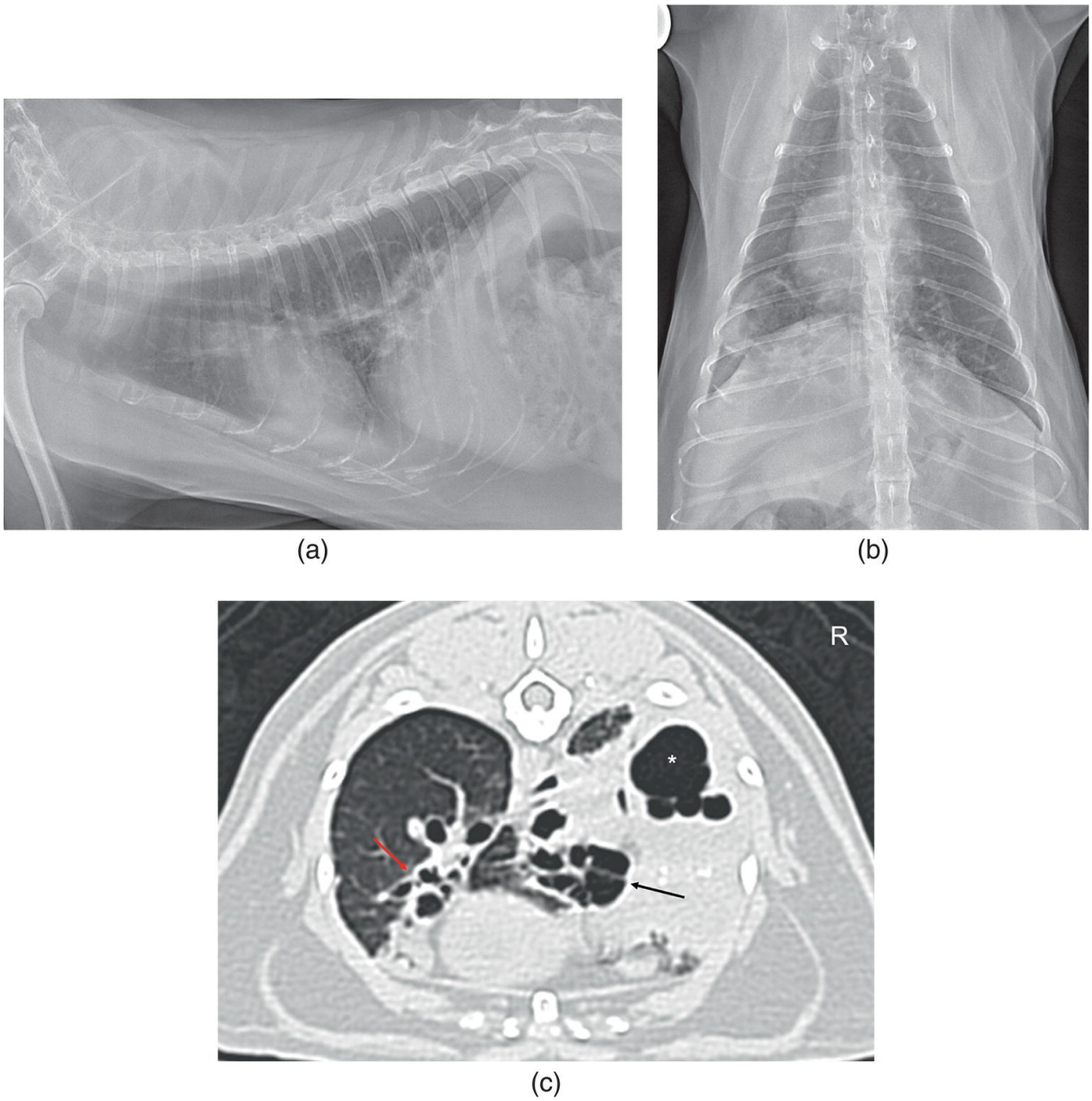
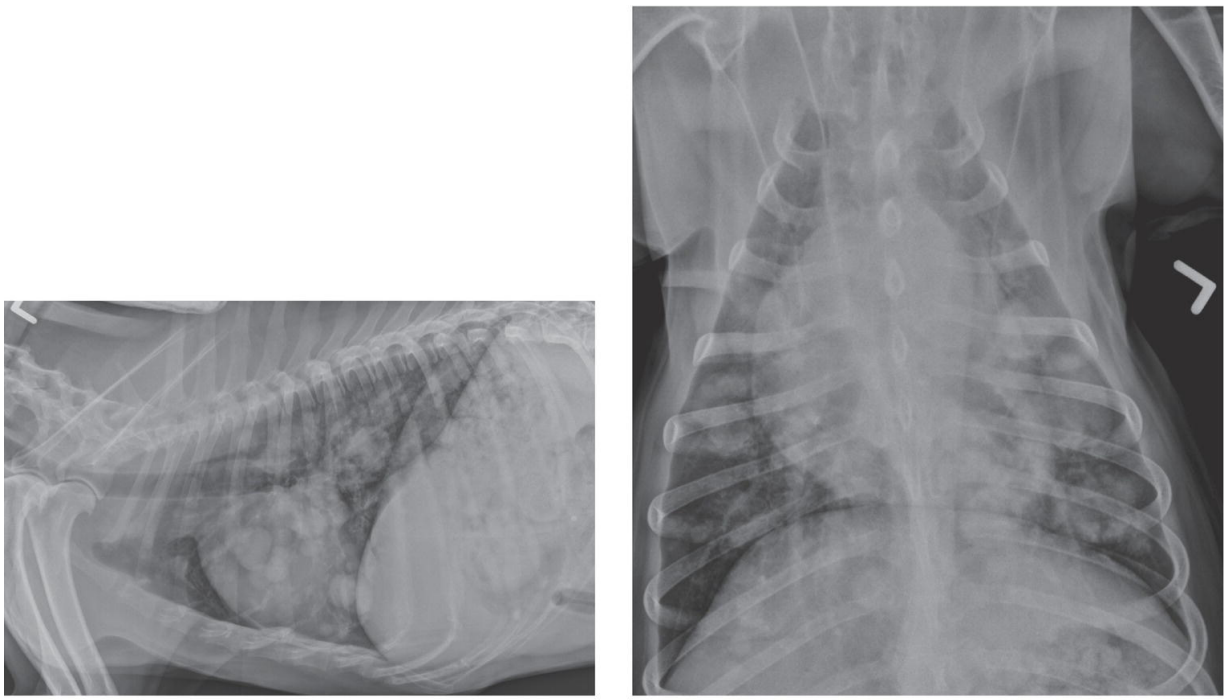


Figure 6.21 (a) Right lateral and (b) dorsoventral radiographs from a 10-year-old spayed female domestic long hair (FS DLH) with a primary lung in the right caudal lung field with metastasis throughout the lung. Note the cavitated appearance of the primary lung mass. (c) A CT section through the mass highlights the cavitated mass in the right caudal lobe (asterisk) as well as cavitation in the accessory (black arrow) and left cranial (red arrow) lung lobes suspicious for intrapulmonary metastatic disease.

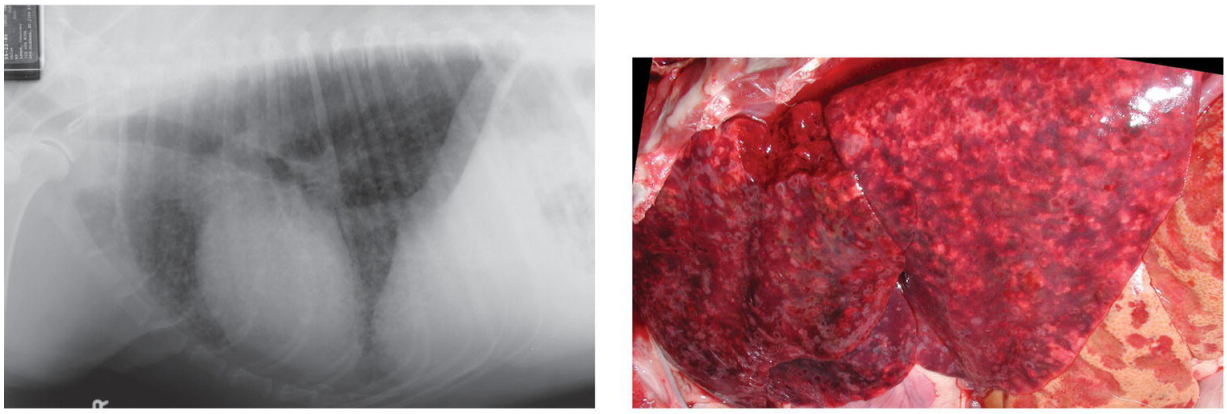
Diagnosis can be obtained ~75% of the time by performing an aspirate of the lung mass (McPhetridge et al. 2022). Samples that

appear to be of low cellularity on initial scrutiny should still be submitted for official evaluation because a diagnosis might still be achieved. Ultrasound, CT, or fluoroscopic guidance is helpful when performing the fine needle aspirate (see Chapter 2). Rarely, intraluminal masses are visualized bronchoscopically (Figure 6.24) and a BAL or biopsy sample can be obtained to confirm the diagnosis by cytology or histopathology (Figure 6.25).



(a) (b)

Figure 6.22 Pulmonary metastasis of a thyroid carcinoma in a 13-year-old spayed female (FS) English Shorthair Pointer. Variably sized nodules of soft tissue density are scattered throughout the lung parenchyma on the left lateral (a) and dorsoventral (b) views.



(a) (b)

Figure 6.23 (a) Right lateral radiograph and (b) gross necropsy findings in a 10-year-old spayed female (FS) Standard Poodle with miliary pulmonary metastasis from a primary hemangiosarcoma.

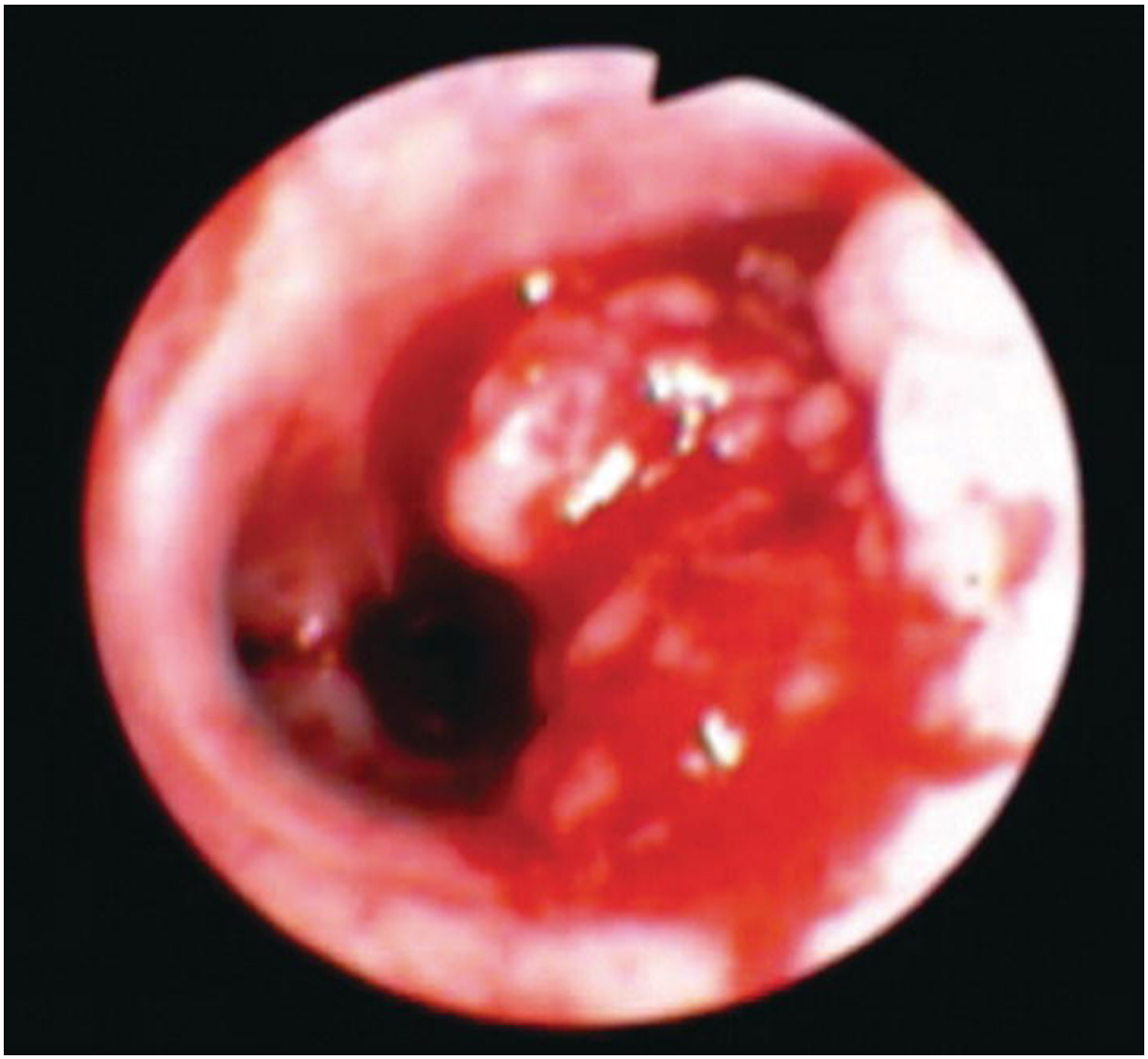


Figure 6.24 Bronchoscopic image from a 10-year-old male castrated domestic short hair (MC DSH) presented with a 2-month history of a dry cough and weight loss. A polypoid irregular bleeding mass can be seen partially obstructing a bronchus. Histopathology revealed a carcinoma combining properties of malignant epithelial and mesenchymal cells.

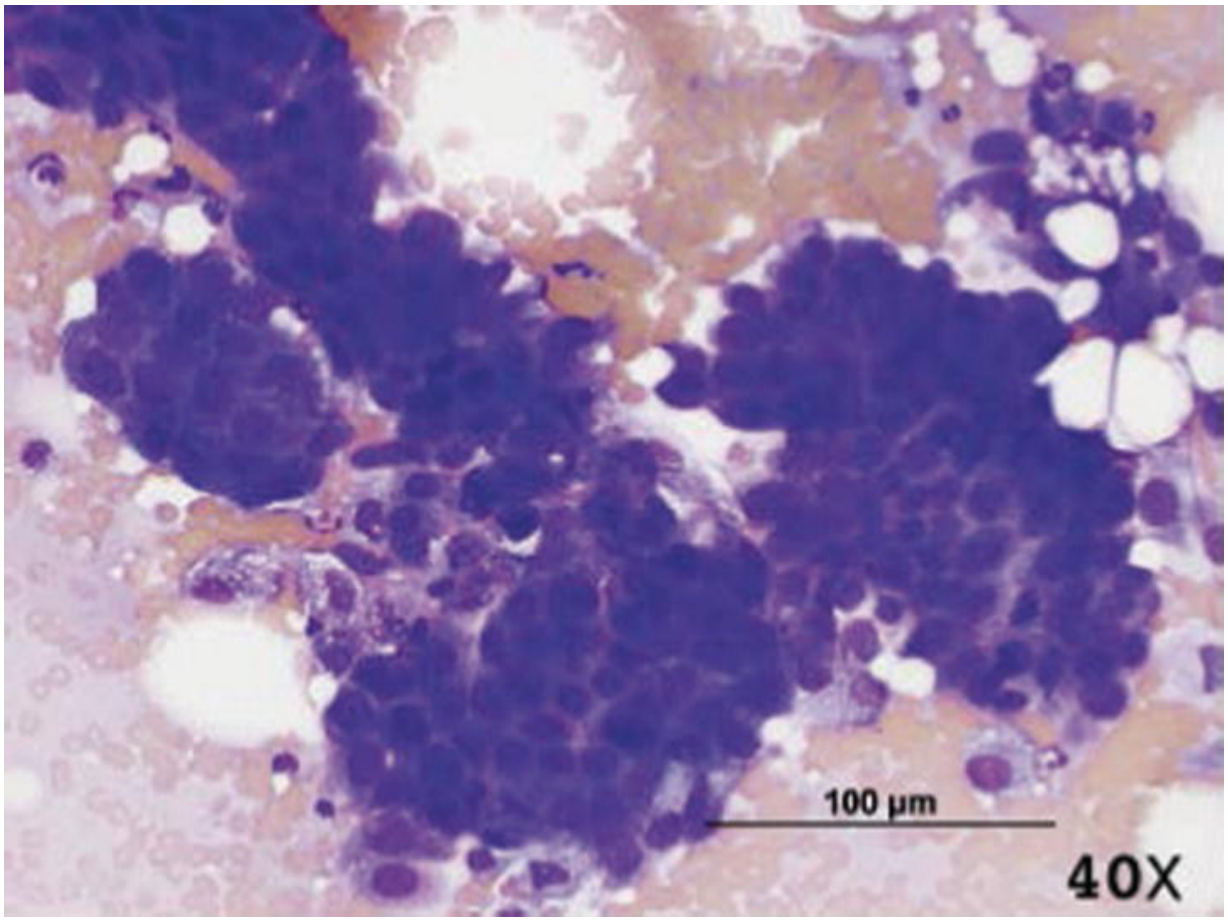


Figure 6.25 Cytology from a BAL sample in a 13-year-old castrated male (MC) Bassett Hound presented for chronic cough and hemoptysis. Characteristics of malignancy include a high nuclear/cytoplasmic ratio with some cells displaying marked anisocytosis and anisokaryosis with multiple large prominent nucleoli.

Treatment

Surgical resection can be performed through video-assisted thoracoscopy or an open thoracotomy when primary or metastatic neoplasia affects a single lung lobe, or when multiple nodules are detected in one or two lung lobes. Attempts should be made to obtain lymph node samples due to the importance of establishing tumor stage in providing owners with a prognosis. Unfortunately, limited information is available on postoperative chemotherapy for primary lung tumors in dogs or cats. Vinorelbine is used most commonly, although carboplatin, CCNU, Palladia, and adriamycin are

sometimes used, depending on tumor type and concurrent diseases. Currently, no improvement in outcome has been reported when surgery is followed by chemotherapy (Lee et al. 2020).

Prognosis

The presence of respiratory signs at the time of diagnosis appears to be associated with a worsened prognosis in dogs and cats. Prognosis also depends on tumor histology, state of differentiation, and mitotic index. Abnormal appearance of local lymph nodes on thoracic CT or intrapulmonary metastasis are negative prognostic indicators, as is tumor size >7 cm (Lee et al. 2020). In some situations, the presence of pleural effusion worsens prognosis.

In dogs treated with lobectomy for a solitary pulmonary mass, median survival for various forms of primary pulmonary carcinoma ranges from 2 to 30 months. Localized pulmonary histiocytic sarcoma has a better prognosis than disseminated disease, with a survival time of approximately 13 months following surgery and chemotherapy (Marlowe et al. 2018). In cats with histologically well-differentiated pulmonary tumors, median survival is 2 years, while those with poorly differentiated neoplasms have <3 months median survival (Hahn and McEntee 1998). Unfortunately, many animals with primary pulmonary neoplasia have metastasis to bronchial lymph nodes, other lung lobes, pleura, skeletal muscle, skin, liver, spleen, or brain at the time of diagnosis. In addition, recurrence of neoplasia or metastasis can be encountered later in life.

In dogs that were not surgical candidates, improved quality of life and acceptable survival (median ~6 months) was reported with use of metronomic chemotherapy that included piroxicam, cyclophosphamide, and thalidomide (Polton et al. 2018). Metronomic chemotherapy is long-term, low-dose treatment designed to control neoplastic growth through anti-angiogenic and anti-inflammatory mechanisms, rather than to kill neoplastic cells. Piroxicam alone can be palliative in some dogs with pulmonary neoplasia that are not surgical candidates and is associated with few side effects when administered at 0.3 mg/kg/day. In cats with metastatic pulmonary carcinoma, palliative treatment with chemotherapy may result in a mildly better response than those

treated only with a glucocorticoid or non-steroidal agent, although the median survival time in either group was <2 months in one study (Treggieri et al. 2021). Clinical signs appeared to improve in both groups of cats.

Clinical Case

An 8-year-old female spayed domestic short hair (FS DMH) was presented for evaluation of coughing and nasal discharge that had been managed for years with intermittent oral and transdermal prednisolone, antibiotics (amoxicillin, amoxicillin-clavulanate, doxycycline), and inhaled fluticasone propionate (125–250 mcg/puff). The owner had noted wheezing and increased respiratory effort.

On physical examination, the cat was quiet with a temperature of 100°F (37.8°C), heart rate of 150 beats/minute, and respiratory rate of 28 breaths/minute. Body weight was 5.7 kg with a body condition score of 6/9. There was moderate yellow nasal discharge bilaterally with preservation of nasal airflow. Increased, harsh bronchovesicular lung sounds were ausculted in all four quadrants but no crackles or wheezes were present. Cardiovascular auscultation was normal.

Given the history and signalment, inflammatory airway disease was on the differential list for cough; however bronchopneumonia (aspiration or infectious) was also considered. Baseline bloodwork was recommended along with thoracic radiographs. CBC revealed a hematocrit of 38.1% and a white blood cell count of 6.030/µl with a normal differential cytology. Thoracic radiographs were remarkable for diffuse opacification of the right middle lung lobe with reduction in volume (Case Figure 1). A diffuse mild bronchial pattern was present in the remaining lung fields.

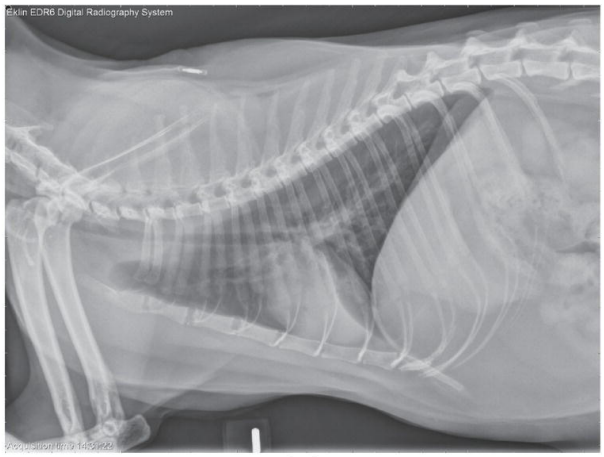
Bronchoscopy revealed hyperemia and injection of the vasculature in the trachea with purulent, patchy secretions throughout its length. Severe thick, mucopurulent secretions obstructed the opening of the right middle lung lobe (Case Figure 2) and filled many other airways. The opening to the left caudal lung lobe was stenotic. BAL fluid was hypercellular (1340, RI 300–400) with 79% neutrophils (RI 5–8%) containing rare intracytoplasmic fine, long, beaded rod-shaped bacteria (Case

Figure 3). Culture was positive for a resistant *Stenotrophomonas maltophilia*.

The cat was discharged on marbofloxacin, intermittent subcutaneous terbutaline for intermittent respiratory difficulty, oral *N*-acetylcysteine, and saline nebulization. A favorable response was noted initially, with progressive resolution of cough and nasal discharge after 6 weeks of treatment. Two days after discontinuing antimicrobials, the wet cough returned and marbofloxacin was re-started but response was not adequate and owners elected for euthanasia. A nasal biopsy specimen was submitted for evaluation of ciliary dyskinesia but qualitative and quantitative abnormalities of the microtubular structure in the respiratory epithelium were not consistent with primary structural ciliary dyskinesia. Ultrastructurally, nasal histology revealed squamous metaplasia, hypociliosis and compound cilia, suggestive of a secondary ciliary dysfunction.



(a)

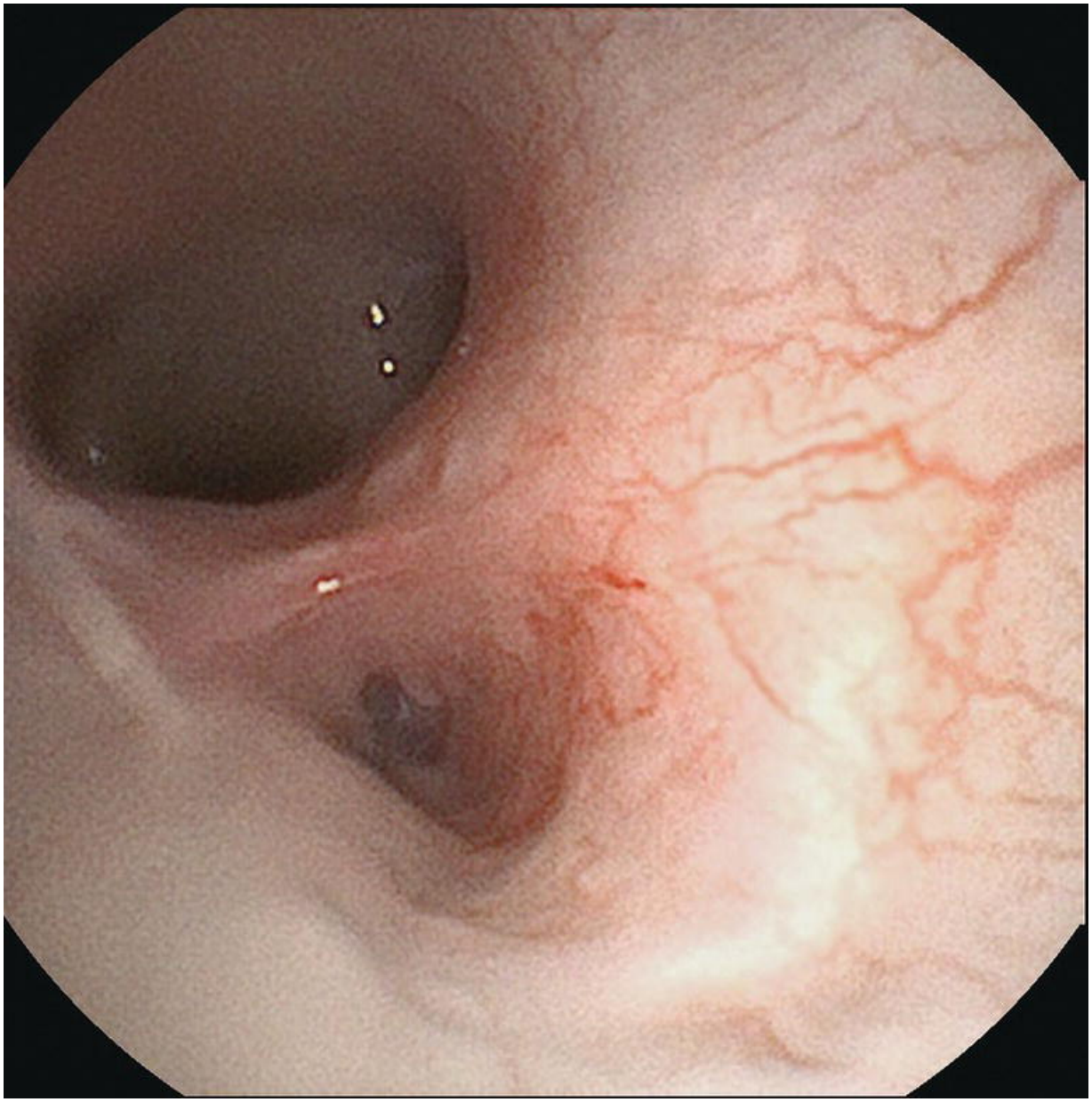


(b)

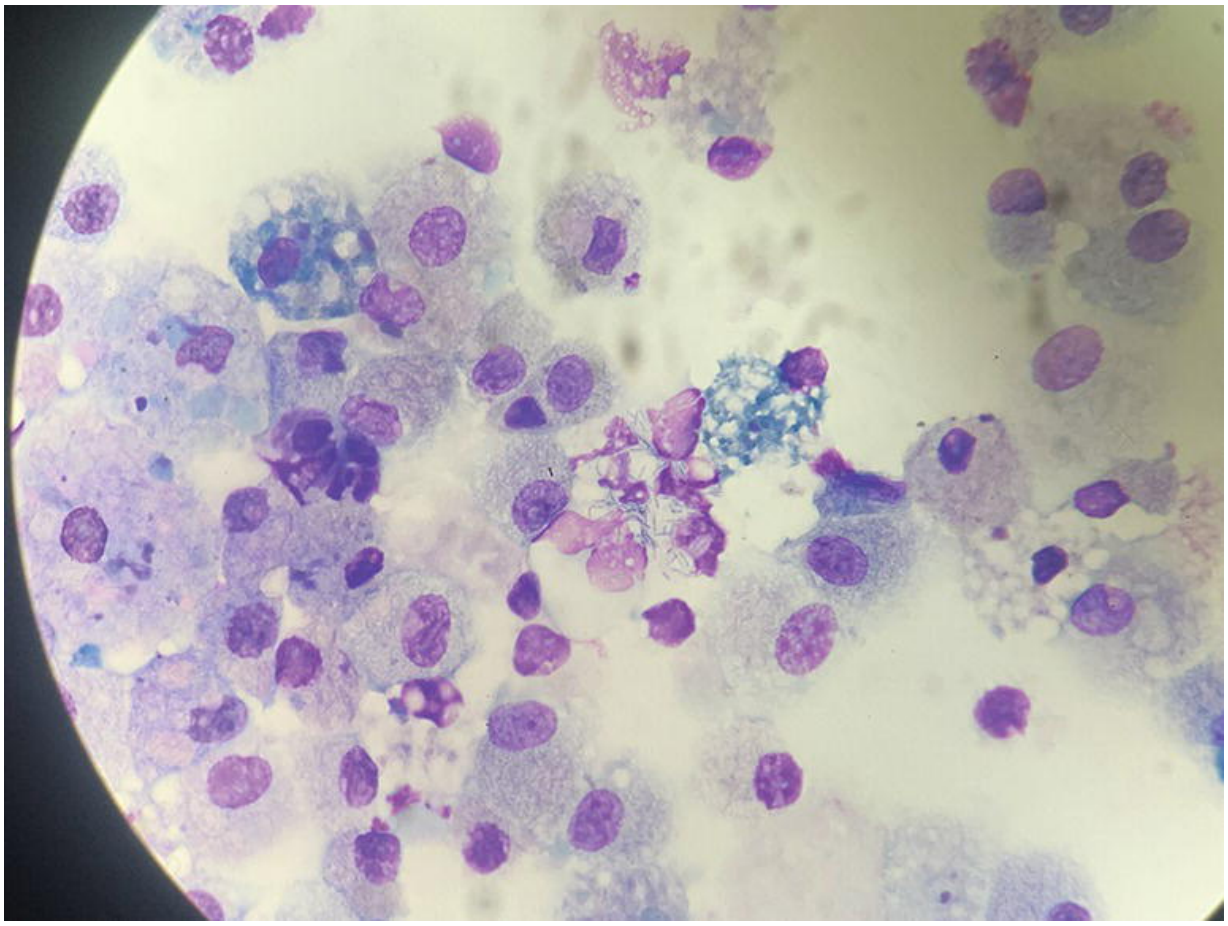


(c)

Case Figure 1 Lateral (a and b) and dorsoventral (c) thoracic radiographs.



Case Figure 2 Bronchoscopy.



Case Figure 3 BAL fluid was hypercellular.

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7
Pleural and Mediastinal Disease

Structural Disorders

Pneumothorax

Pathophysiology

Entrance of air into the pleural space causes intrapleural pressure to become positive, which results in collapse of the lungs with a subsequent drop in venous return and cardiac output. Pneumothorax can be closed or open depending on whether or not there is communication between the pleural space and outside the thorax. The most common causes of pneumothorax in dogs are likely blunt force trauma from car collisions or penetrating trauma from an inhaled foreign body. Exposure to porcupine quills has also resulted in pneumothorax in the northern United States and Canada (Sevy et al. 2023). In the cat, blunt trauma occurs from a car accident or fall from a height, although inflammatory lower airway disease is also a common cause of pneumothorax (Mooney et al. 2012). In dogs or cats, esophageal perforation can lead to pneumothorax, and it can also result from rupture of an emphysematous bulla, pleural bleb, neoplasm, *Paragonimus* cyst, or abscessed lung lobe. Lung necrosis due to embolization associated with heartworm disease or pulmonary thromboembolic disease has also been implicated in pneumothorax. Barotrauma during anesthesia or mechanical ventilation is recognized as an iatrogenic cause of pneumothorax and it can also occur post-thoracocentesis or fine-needle lung aspiration. Multiple lung lobes can be involved depending on the underlying disease process, and cranial lobes are affected most commonly in spontaneous pneumothorax.

A specific form of pneumothorax is a tension pneumothorax, where a piece of pulmonary tissue or pleura acts as a ball valve, allowing passage of air into the pleural space during inspiration, with

obstruction of escape of air via the same pathway. In this situation, air continues to accumulate in the pleural space, leading to a continual rise in intrapleural pressure and circulatory collapse. Tension pneumothorax is sometimes encountered in animals with pleural fibrosis secondary to a long-standing exudative effusion that develop a rent in the pleura allowing air to escape into the pleural cavity. Immediate thoracocentesis is required to allow lung expansion and to restore cardiac output.

History and Signalment

Any age or breed of dog or cat can develop pneumothorax depending on the underlying etiology. An animal kept out of doors is at increased risk for traumatic injury or foreign body inhalation, while a hospitalized patient would be more likely to develop iatrogenic injury. Spontaneous pneumothorax associated with underlying lung disease appears to be more common in young to middle-aged deep-chested dogs.

The primary clinical complaint associated with pneumothorax is difficulty breathing or tachypnea that develops immediately after an injury or rupture of a pulmonary lesion. Signs can be acute in onset, however with foreign body inhalation or quill exposure, they can occur 2–6 months after the episode (Gibson et al. 2019; Sevy et al. 2023) Some cases with spontaneous pneumothorax lack a history of signs referable to the respiratory tract and will display chronic, non-specific signs of lethargy and anorexia, prior to the development of acute, worsening respiratory difficulty associated with accumulation of air in the pleural space.

Physical Examination

Accumulation of air in the pleural space untethers chest expansion to lung expansion, leading to rapid and shallow breathing and dampening of lung sounds. Air in the pleural space will rise, leading to an absence of breath sounds dorsally and hyperresonance on percussion. Lung sounds might be heard in the ventral lung fields only. Animals involved in traumatic encounters should be closely evaluated for additional injuries, including broken ribs, lung damage, and cardiac bruising. Pulmonary contusions coincident with

pneumothorax can lead to harsh lung sounds focally and myocardial contusions can result in tachycardia or an arrhythmia. In some cases of foreign body inhalation, a grass awn can form a palpable abscess on the body wall or can be seen migrating out of the subcutaneous space.

Diagnostic Findings

Pneumothorax is usually bilateral because the mediastinum is incomplete. It is recognized radiographically by an absence of lung parenchyma and pulmonary vasculature in the periphery of the lung. The heart is typically lifted off the sternum on the lateral view (Figure 7.1). Pneumothorax can also be detected on thoracic ultrasound by an absence of the "glide sign," which is the movement of normal lung along the pleura. While pneumothorax is readily apparent on thoracic radiographs, the underlying lesion is often not visible, particularly when bullous lung disease or pleural blebs are the cause of the pneumothorax. Cross-sectional imaging with computed tomography (CT) improves definition of lung regions (Figure 7.2); however, it has low sensitivity for detection of bullae associated with spontaneous pneumothorax (Reetz et al. 2013).

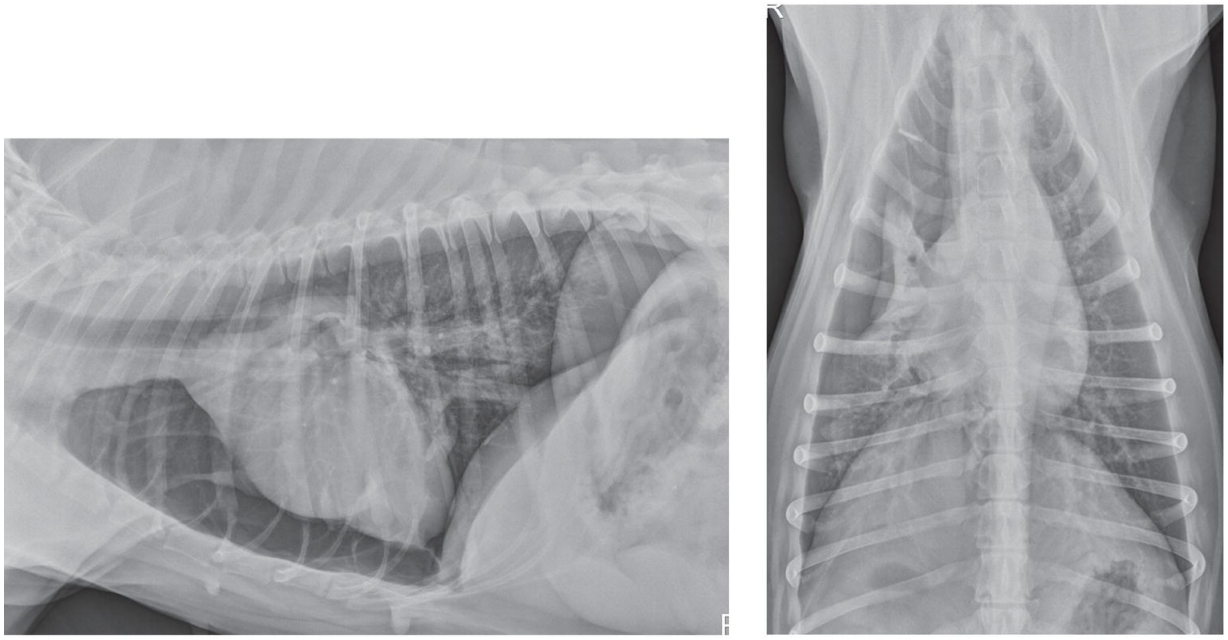


Figure 7.1 (a) Right lateral and (b) dorsoventral radiographs from a 7-year-old spayed female (FS) Australian Shepherd with recurrent episodes of spontaneous pneumothorax demonstrate collapse of the right cranial lung lobe.

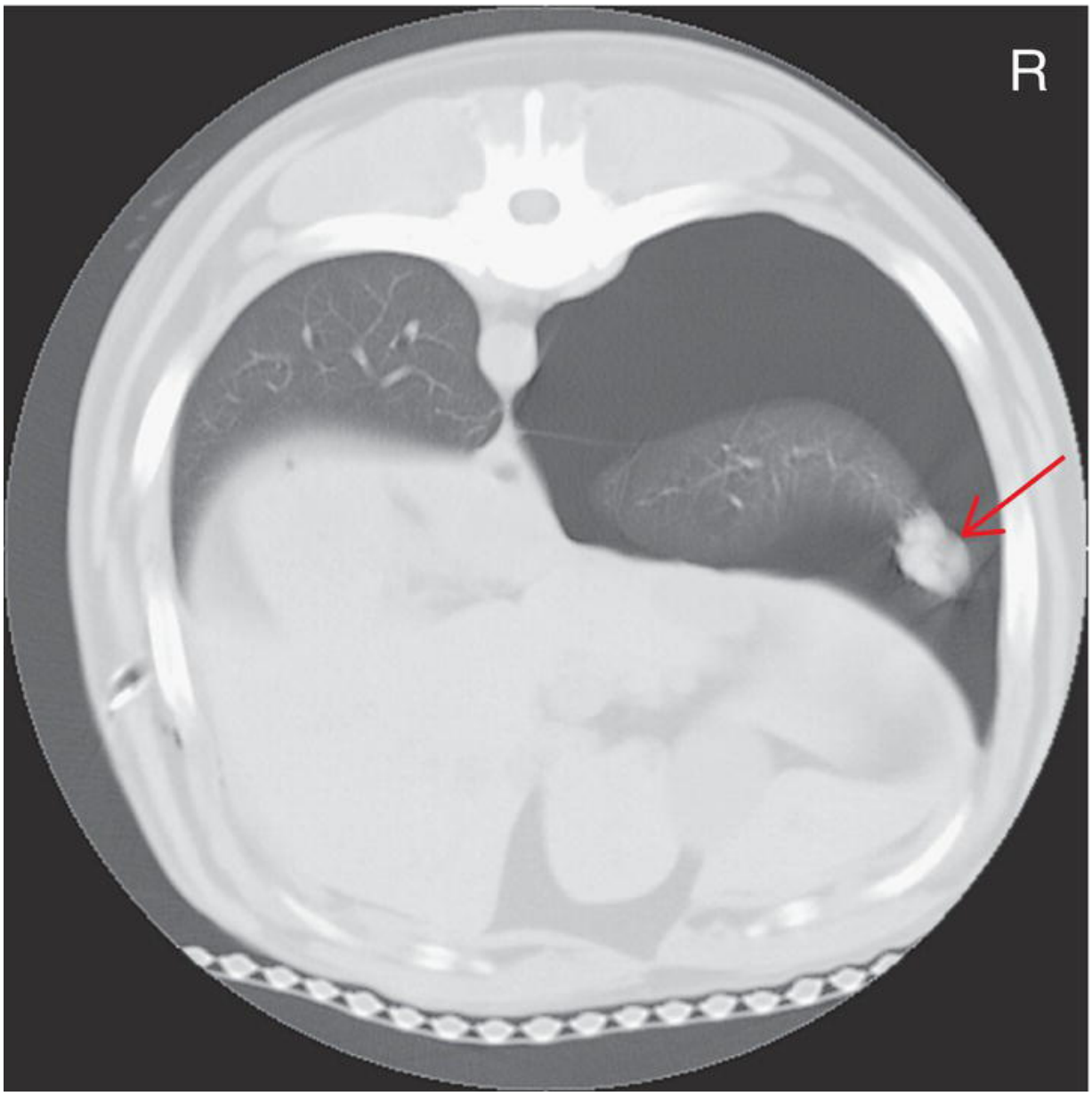


Figure 7.2 Computed tomographic slice through the caudal thorax of a 6-year-old male intact (MI) Labrador Retriever with spontaneous pneumothorax. A soft tissue structure is present in the distal portion of the right caudal lung lobe. Histopathology revealed a pulmonary adenocarcinoma.

For animals with suspected exposure to *Paragonimus*, a trematode that employs snails and crustaceans as intermediate hosts, a fecal sedimentation or zinc sulfate centrifugation–flotation should be performed. *Paragonimus kellicotti* is endemic in Canada and in the USA (typically the Midwest or Gulf states), while in Japan, boar-

hunting dogs are at risk for infection by *Paragonimus westermani* (Kirino et al. 2008). Paragonimiasis is recognized as a shared zoonosis (affecting both animals and humans) and is caused by ingestion of the crayfish intermediate host, which migrates from the peritoneal cavity through the diaphragm to enter the lungs. The trematode has not yet been reported in Europe. In infected dogs, thoracic radiographs or CT can show multiple thin-walled cavitated cysts, while in cats, thick-walled granulomatous lesions and pleural involvement are more typical.

Treatment

Thoracocentesis should be performed when pneumothorax is suspected and it might be required as a life-saving procedure prior to radiographic or ultrasonographic confirmation of air accumulation. With traumatic pneumothorax, a single chest tap with alleviation of respiratory difficulty through sedation and administration of oxygen will often restore pleural integrity and result in cure. If *Paragonimus* is diagnosed, praziquantel (25 mg/kg orally [PO] three times a day [TID] for 3 days) or fenbendazole (50 mg/kg/day for 2 weeks) can be employed to treat infection (Bowman et al. 1991), although surgical resection of the diseased lung regions can be required.

If air continues to accumulate within the pleural space after several chest taps, placement of a chest tube should be considered (see Chapter 3). Generally, spontaneous pneumothorax and tension pneumothorax will require placement of a chest tube and constant thoracic drainage to resolve air leakage. Because underlying lung disease is often present with spontaneous pneumothorax, surgical intervention is usually required to avoid recurrence. Therefore, when pneumothorax does not resolve within 3–5 days or if parenchymal lesions causing pneumothorax are visualized on radiographs, an exploratory thoracotomy should be performed. Pre-operative CT is usually performed to investigate possible pulmonary lesions. Video-assisted thoracoscopy is a minimally invasive procedure that can be used to investigate and manage causes of pneumothorax; however, it has a high rate of transition to an open approach in cases with bullous disease (Case et al. 2015). In that event, median sternotomy is usually preferred to allow full exploration of the lungs.

When thoracotomy is not possible, use of autologous blood as a pleural patch can be considered. To perform this, the dog or cat is sedated or anesthetized, a sterile preparation of the thoracic wall is performed, and the chest is evacuated of air. Fresh whole blood (5–10 ml/kg) is collected aseptically from the jugular vein and injected immediately into the pleural space through a chest tube or catheter to achieve pleurodesis. Isotonic fluids are administered intravenously to replace the blood withdrawn. In one study, pneumothorax resolved after one treatment in four out of eight dogs (Oppenheimer et al. 2014).

Prognosis

Traumatic pneumothorax generally has a good prognosis if myocarditis and pulmonary contusions do not complicate the presentation. The prognosis for spontaneous pneumothorax depends on the underlying disease responsible for air leakage. Surgical resection of the affected area is associated with an excellent outcome in most dogs with emphysematous lung disease, foreign body pleuropneumonia, or *Paragonimus* infection; however, the presence of neoplasia can warrant a guarded prognosis, depending on the extent and type of the neoplasm.

Pneumomediastinum

Pathophysiology

The mediastinum is a potential space running through the middle of the thorax from the thoracic inlet to the diaphragm and the sternum to the vertebral column (Figure 7.3). It is continuous with the fascial planes in the neck and retroperitoneal space and contains the carotid arteries, vagosympathetic trunks, trachea, esophagus, and cranial vena cava cranially, the heart and great vessels in the mid-section, and the esophagus caudally. It is lined by pleura and excludes the left and right lung. Pneumomediastinum is an accumulation of air around the structures in the cranial mediastinum. It occurs most commonly from endotracheal tube injury or over-inflation of the cuff, traumatic jugular venipuncture, or a transtracheal wash. It can also result from trauma associated with a dog fight, from over-ventilation during anesthesia, or due to bronchial injury from a foreign body or

neoplastic infiltration. Emesis is a cause of pneumomediastinum in the cat. A leaky tracheostomy tube can result in pneumomediastinum. Finally, pneumomediastinum can occur with bronchial, tracheal, or alveolar rupture when air tracks along fascial planes to reach the mediastinum. Spontaneous or idiopathic pneumomediastinum has been reported in approximately one-third of cases in cats (Thomas and Syring 2017) and an unknown number of dogs. Pneumothorax can be found in conjunction with pneumomediastinum, particularly when the cause is traumatic.

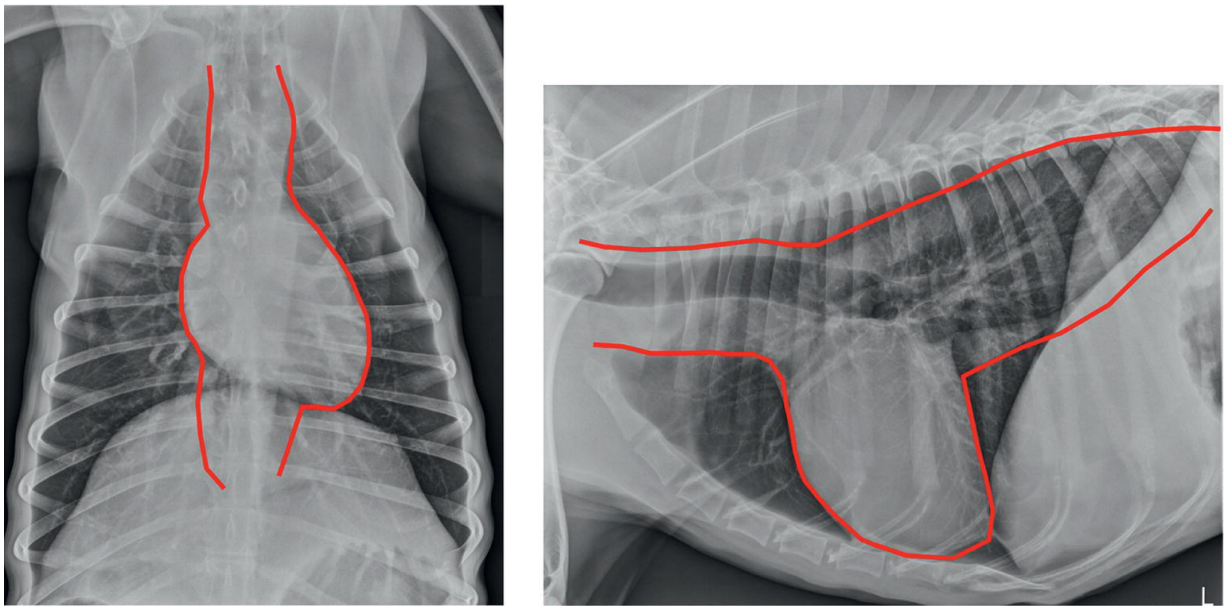


Figure 7.3 Thoracic radiographs with red markings outlining the boundaries of the mediastinum.

History and Signalment

Any age of dog or cat can be affected. Usually a history of trauma or iatrogenic injury is present immediately prior to the onset of signs or within a week of presentation. In cats, a recent dental procedure is often found in the history, with tracheal rupture resulting from damage to the dorsal tracheal membrane at the thoracic inlet. Respiratory difficulty can be noted or owners might detect subcutaneous emphysema concentrated over the neck, thorax, and head. Frequently clinical signs are absent, and pneumomediastinum is an incidental finding on radiographs following a venipuncture or tracheal wash.

Physical Examination

Pneumomediastinum often does not result in any respiratory abnormalities but coincident subcutaneous (SQ) emphysema can be detected as a crackling under the skin during palpation. In some cases, this SQ emphysema can restrict ventilation. In more severely affected animals, tachypnea and respiratory distress can occur, or collapse can result from pneumomediastinum accompanied by pneumothorax. When pneumothorax is present, lung sounds are absent dorsally.

Diagnostic Testing

Diagnosis is based on radiography. Pneumomediastinum is evident when outer borders of the trachea, esophagus, carotid arteries, aorta, and azygous veins are visible because of contrast with mediastinal air. Subcutaneous emphysema is often detected over the trunk (Figure 7.4). If tracheal rupture is suspected, tracheoscopy can occasionally be helpful in locating the lesion. Surgical exploration is usually required when conservative measures fail.

Treatment

Generally no specific treatment is required for pneumomediastinum and air will resorb within 10–20 days. Air resorption is hastened by placing the patient in an oxygen-enriched environment. This will decrease the work of breathing to facilitate sealing of any rents in the tissue and hasten oxygen resorption by creating a more favorable oxygen gradient for diffusion. Judicious use of sedatives to reduce stress is important. In rare instances when subcutaneous emphysema is severe and causes restriction of ventilation, needle aspiration of air trapped under the skin can sometimes be helpful. Concurrent pneumothorax requires thoracocentesis. If tachypnea or respiratory effort increases, surgical repair of the lesion is necessary.



Figure 7.4 Right lateral radiograph from an 18-month-old spayed female domestic short hair (FS DSH) that had been anesthetized 2 weeks previously and developed pneumomediastinum and subcutaneous emphysema.

Prognosis

Prognosis is usually excellent for resolution of disease. When pneumomediastinum is detected, restraint methods and diagnostic techniques should be reviewed for predisposing features that might have led to airway injury. In cats undergoing anesthesia, <3 ml of air is required for sufficient inflation of the endotracheal tube cuff.

Diaphragmatic Hernia

Pathophysiology

Blunt trauma to the abdomen from a car accident or fall from a height increases intracavitary pressure, leading to rupture of the muscular portion of the diaphragm and herniation of abdominal organs into the thoracic cavity. The liver is involved most frequently, followed by the small intestine and stomach. The lungs collapse because of loss of contact between visceral and parietal pleura that would normally coordinate thoracic excursions to lung expansion. Compression by abdominal organs also contributes to lung collapse. Fluid accumulation in the thorax due to hemorrhage or transudation from the organ surface further restricts lung expansion and worsens oxygenation and ventilation. Animals with herniation of the stomach into the chest cavity can suffer rapid decompensation if aerophagia results in continual expansion of the stomach. The space-occupying effect of gastric dilation augments lung compression, with a decrease in venous return and subsequently cardiac output.

Congenital diaphragmatic hernias that can affect dogs or cats include pleuroperitoneal or peritoneopericardial diaphragmatic hernias (PPDH). Of these, PPDH is more common. It is likely related to trauma or a failure of development during the embryonic stage of growth. In some cases, other congenital lesions such as umbilical hernia, pectus excavatum, or congenital heart defects can be recognized concurrently (Burns et al. 2013).

History and Signalment

Affected animals can have an acute history of trauma within the past several hours or may have experienced injury weeks to years in the past. Most dogs and cats are young (3–4 years) because these are the individuals that are more often exposed to traumatic events, and those with congenital hernias can be very young at the time of diagnosis. PPDH is more common in cats than in dogs (Burns et al. 2013). Clinical signs are usually respiratory in origin and include tachypnea and difficulty breathing, but some animals are presented for acute or chronic vomiting or regurgitation associated with gastrointestinal (GI) obstruction or strangulation. Still others can

develop progressive exercise intolerance or respiratory difficulty associated with gradual accumulation of pleural fluid from organ transudation.

With PPDH, extrusion of abdominal organs into the pericardial sac can result in GI signs or signs of cardiac tamponade, including ascites or collapse. In some animals, PPDH is an incidental finding.

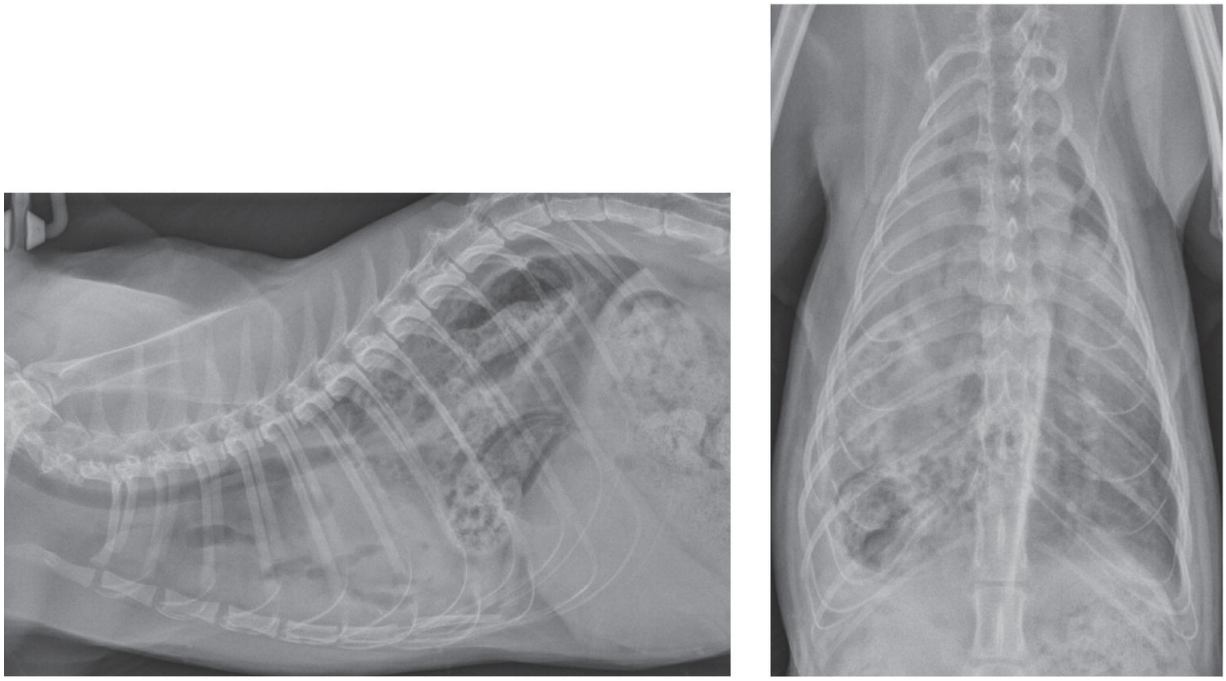
Physical Examination

Animals with organ herniation or pleural effusion often have muffled heart and lung sounds ventrally or on one side of the chest. When intestinal herniation has been present for >24–48 hours, borborygmi can sometimes be auscultated over the thorax (Figure 7.5). Occasionally, abdominal palpation will reveal an absence of contents. Traumatic injury to other structures in the thorax, abdomen, or skeleton can be found in 25–40% of cases, and a complete physical examination should be performed to detect findings consistent with traumatic myocarditis, urinary system rupture, rib fractures, or orthopedic injuries (Gibson et al. 2005).

Diagnostic Findings

Thoracic and abdominal radiographs can usually confirm the diagnosis of a diaphragmatic hernia; however, if pleural effusion is present, thoracocentesis and repeat radiographs might be required to provide definition of the diaphragmatic silhouette and thoracic structures. Chronic cases are often more difficult to diagnose radiographically. A barium series can confirm the presence of intestines in the thoracic cavity or better define the position of the liver or small intestines, and ultrasound can occasionally be helpful. However, CT and/or exploratory surgery can be required for confirmation of the diagnosis.

With PPDH, the most remarkable finding on thoracic radiographs is massive cardiomegaly and loss of distinction of the border of the diaphragm. Echocardiography is useful for confirming the presence of organs in the pericardial space as well as investigating possible concurrent congenital cardiac disease. However, echocardiography can be challenging to perform because of constriction of structures by the pericardial sac.



(a) (b)

Figure 7.5 (a) Right lateral and (b) dorsoventral radiographs of a 2-year-old cat presented for chronic increased respiratory effort and periodic wheezing. Heart and lung sounds were muffled bilaterally. Herniation of the small intestine and proximal colon into the pleural space is noted.

Treatment

Surgical repair of the diaphragm is indicated for traumatic diaphragmatic hernia and is usually performed in animals with clinical signs associated with PPDH. Animals with chronic diaphragmatic hernias and those that are subclinical for PPDH do not necessarily require surgery. Standard stabilization methods with intravenous fluid support and withdrawal of pleural fluid prior to anesthesia are important, although cases with stomach herniation generally represent a surgical emergency because respiratory difficulty causes aerophagia, progressive stomach distention, and further cardiorespiratory compromise. When surgery is pursued, artificial ventilation must be provided to create lung expansion once the abdominal cavity has been opened. Oxygenation, ventilation, and cardiac rhythm must be monitored carefully throughout the procedure.

Prognosis

Improvements in anesthetic drugs, monitoring, and assisted ventilation have vastly improved response to surgery. Diaphragmatic hernia repair is associated with an 80–90% survival rate (Gibson et al. 2005; Burns et al. 2013), regardless of whether the hernia is acute or chronic in nature and regardless of the time between admission and surgery. Owners should be aware that additional surgery might be required to repair soft tissue or orthopedic injuries that are not as life-threatening as the diaphragmatic hernia. In cats with chronic diaphragmatic hernia, there is concern about development of re-expansion pulmonary edema when abdominal contents are removed from the thoracic cavity. Controlled expansion of the lungs during the procedure might diminish occurrence of this, but typically re-expansion injury carries a grave prognosis because it is not responsive to supportive therapy.

Older animals with PPDH diagnosed as an incidental finding can have extended survival and excellent quality of life without surgical intervention.

Infectious Disorders

Pyothorax

Pathophysiology

The etiology of pyothorax cannot always be determined. Bacteria can enter the pleural space through a bite wound, penetrating injury, foreign body inhalation, direct puncture of the chest wall, or esophageal rupture. Less commonly, bacteria can spread to the pleura from a pulmonary infection or hematogenously. In dogs, foreign body inhalation is often believed to be the most common etiology, while in cats, bite wounds are suspected, despite the fact that external evidence of wounds is often lacking (Johnson et al. 2023). Iatrogenic pyothorax results when aseptic technique is breached during thoracocentesis. Infection can be involve a single species of bacterium (Eiras-Diaz et al. 2021; Kramer et al. 2021) but is often multi-microbial (Walker et al. 2000; Johnson et al. 2023),

and the anaerobic environment within the pleural space promotes growth of various types of bacteria.

A rare cause of pyothorax in cats in some areas of the world is infection with the organism *Rhodococcus equi* (previously *Corynebacterium equi* or *Mycobacterium equi*). This organism is well known to cause pulmonary infection in foals and has rarely been documented to cause infection in cats in the US, Italy, and Australia, with more cases reported in Malaysia (Aslam et al. 2020). Disease is caused by inhalation or ingestion of a Gram-positive coccobacillus found in manure, and interestingly, exposure to horses was not common for cases encountered in Malaysia. Outdoor cats <1 year of age were most commonly affected and exhibited a neutrophilic leukocytosis with monocytosis and thrombocytopenia. Some cats had skin lesions rather than pleural infection, and mortality was high (58%) despite some positive responses to marbofloxacin or azithromycin combined with rifampin (Aslam et al. 2020).

History and Signalment

Pyothorax most commonly occurs in young, outdoor animals. Large breed or hunting dogs and cats from multi-cat households are affected most often. In some animals, clinical signs are primarily respiratory in origin, with tachypnea or labored breathing; however, however, more animals have prominent systemic signs, including weight loss, anorexia, inactivity, and exercise intolerance. Clinical signs can be present for days to months before presentation.

Physical Examination

Pyothorax is anticipated to result in a rapid, shallow breathing pattern; however, both the rate and amount of fluid accumulation influence the severity of respiratory difficulty, and respiratory rate can be only mildly elevated in some cases. Fever may or may not be present at the time of presentation, despite the presence of severe infection. Muffled heart and lung sounds are expected ventrally, although pyothorax can affect a single side of the thorax when the proteinaceous fluid occludes fenestrae in the mediastinum to create non-communicating halves to the thorax. This could result in unilateral absence of lung sounds and could potentially displace

cardiac sounds. Careful physical inspection of the thoracic wall will occasionally reveal recent or healed bite wounds or areas where foreign material has migrated out of the thoracic cavity.

Diagnostic Findings

In chronically affected animals, hematology usually shows a mild normocytic, normochromic, non-regenerative anemia in conjunction with leukocytosis characterized by neutrophilia and monocytosis. Increased serum globulin is a non-specific indicator of chronicity and a marked inflammatory response, and this can result in a compensatory drop in serum albumin. Thoracic radiographs reveal unilateral or bilateral pleural effusion with obscuring of the cardiac silhouette and diaphragm, scalloping of ventral lung margins, and blunting of costophrenic angles (Figure 7.6). Evidence of a foreign body or a consolidated lung lobe is occasionally present. Thoracic ultrasound can be helpful in revealing flocculent or viscous pleural fluid and can sometimes detect lobar consolidation or the linear appearance of a foreign body.

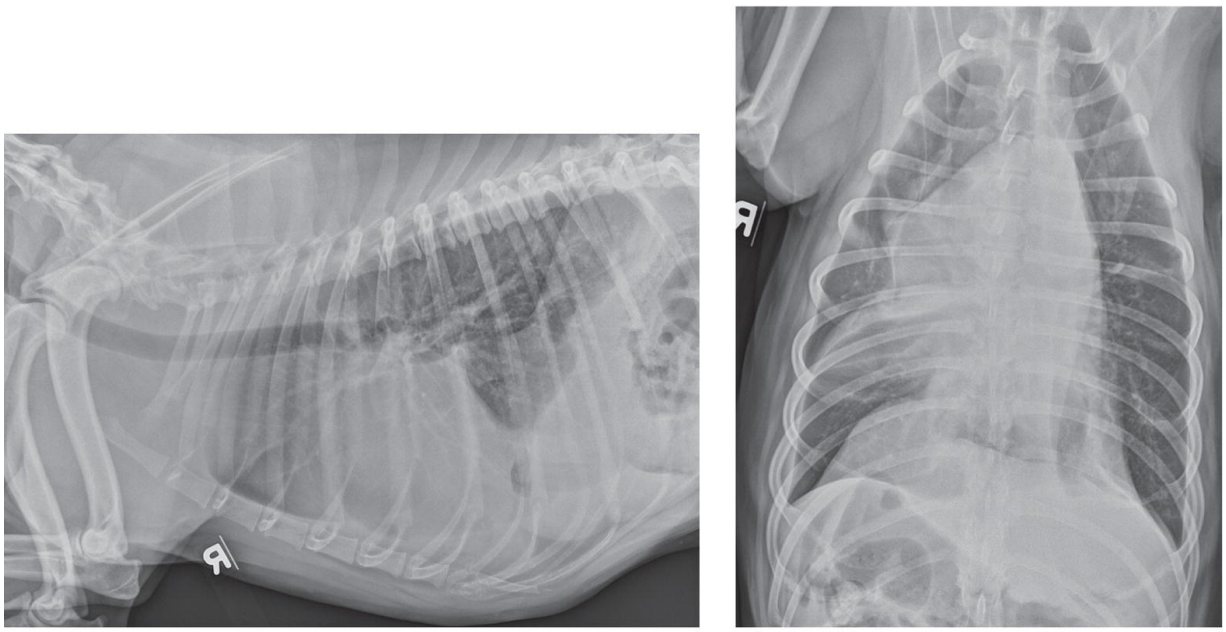


Figure 7.6 (a) Right lateral and (b) ventrodorsal radiographs from a 6-year-old castrated male (MC) Labrador Retriever presented for a 2 week history of anorexia and weight loss. Physical examination revealed absent lung sounds ventrally, and radiographs confirmed the presence of pleural fluid obscuring the cardiac silhouette and blunting of the costophrenic angle, particularly on the right side.

The initial step in confirming a diagnosis of pyothorax is to perform thoracocentesis (see Chapter 2). Cytologic analysis reveals an exudative fluid (high protein and high cell count) comprised primarily of degenerate neutrophils. Intracellular bacteria (Figure 7.7) are observed in 62–93% of cats and 68–73% of dogs (Walker et al. 2000; Kramer et al. 2021; Johnson et al. 2023) despite previous antibiotic therapy. Both aerobic and anaerobic cultures should be requested on a pleural exudate because mixed bacteria are usually found (Table 7.1). Note that special transport medium is sometimes required to obtain an accurate result for anaerobic bacteria.

A point of care test that assesses luminescence released by bacterial ATP (Test&Treat Ltd., Kentford, Newmarket, UK) shows promise in assisting in the diagnosis of a septic effusion (Vezzi et al. 2024). Similar to cytology, previous antimicrobial therapy does not appear to impact the result, although large-scale studies are lacking. Hemorrhagic effusions cannot be accurately assessed and a 30

minute incubation period is required; however when cytologic assessment is not immediately available, a positive test could aid in the early diagnosis of pyothorax.

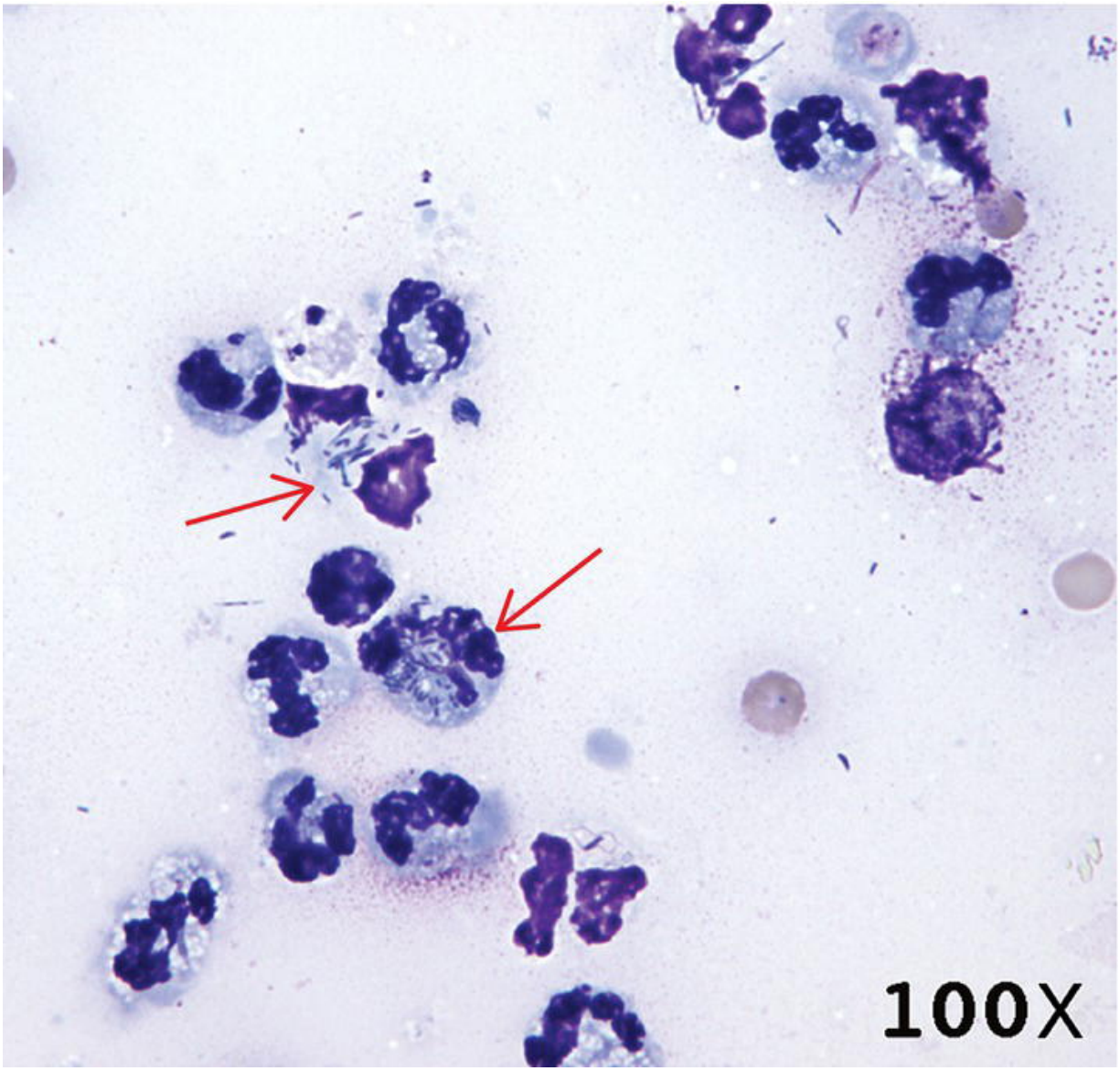


Figure 7.7 Pleural fluid cytology from a cat with pleural effusion reveals degenerate neutrophils and intracellular bacteria (arrows) consistent with pyothorax.

Table 7.1 Organisms commonly identified in animals with pyothorax.

Source: Walker et al. (2000) and Johnson et al. (2023).

	Dog	Cat
Aerobes		

	Dog	Cat
• Enteric organisms – *Escherichia coli, Klebsiella, Enterobacter*	17–22%	4–7%
• Non-enteric organisms – *Pasteurella, Acinetobacter, Pseudomonas, Staphylococcus, Streptococcus*	37–57%	48–70%
• *Actinomyces*	19–22%	15–24%
Anaerobes		
• *Peptostreptococcus*	18–27%	20–34%
• Bacteroides	25%	24–48%
• Fusobacterium	21–27%	17–45%
• Porphyromonas	7–9%	10–12%

Treatment

Successful treatment of pyothorax usually requires placement of uni- or bilateral chest tubes (see Chapter 3). The use of thoracic lavage with warm saline (10–20 ml/kg 2–4 times a day [BID–QID]) is controversial, but it can be helpful in reducing the amount of inflammation present in the pleural space. Addition of heparin to the lavage fluid (1500 units/100 ml) is also controversial, although some clinicians believe it can reduce adhesions and promote drainage. When lavage is used, the fluid is left in the chest cavity for <1 hour

and then aspirated. The patient resorbs 10–25% of the fluid and it is not possible to retrieve all fluid, therefore some will be left in the pleural cavity. There is no advantage to adding antibiotics to the lavage fluid because the primary route of exposure of the pleura to antibiotics is through the systemic circulation.

Intravenous fluids are typically used for supportive care as needed, and this also allows systemic administration of broad-spectrum antibiotics that are active against both aerobes and anaerobes. Anaerobic coverage should be provided even if cultures are negative due to the difficulty in isolating anaerobic bacteria in some instances. Penicillins, cephalosporins, and clindamycin can be used in combination with a fluoroquinolone. Trimethoprim-sulfa is often employed if infection with *Nocardia* spp. is suspected, although long-term therapy contains the risk of side effects, including keratoconjunctivitis sicca, thrombocytopenia, hypothyroidism, anemia, and fatal liver toxicity.

Each day before instituting thoracic lavage, fluid is extracted from the pleural cavity to evaluate the number and type of cells present and to check for the presence or absence of bacteria. Successful therapy is indicated by a reduction in cell numbers and decline in intracellular bacteria over several days of treatment. Medical therapy can take 3–7 days to be effective. Thoracic radiographs, ultrasound, or CT are used as indicated to detect a mass lesion or foreign body. Prior to removal of the chest tube, a fluid sample should be submitted for aerobic and anaerobic culture to ensure successful resolution of infection.

Thoracotomy or video-assisted thoracoscopy is required to remove a foreign body or to debride necrotic lung or mediastinal tissue. Surgical exploration is indicated when new radiographic findings are detected or if cell numbers or bacteria rise despite lavage and drainage therapy. Preoperative CT can help localize disease. In areas where foxtails are prevalent, bronchoscopy is often performed prior to surgery to remove foreign material and potentially salvage a lung lobe affected by foreign body pneumonia.

For owners lacking sufficient funds for intensive hospitalization and treatment, consideration can be given to conservative medical management. One study reported successful management of 15 dogs

with pyothorax by use of a single pleural drainage and antibiotics (ampicillin TID with metronidazole BID most commonly) for >6 weeks (Johnson and Martin 2007). The risk of persistent or recurrent infection must be communicated to the client if this mode of therapy is chosen.

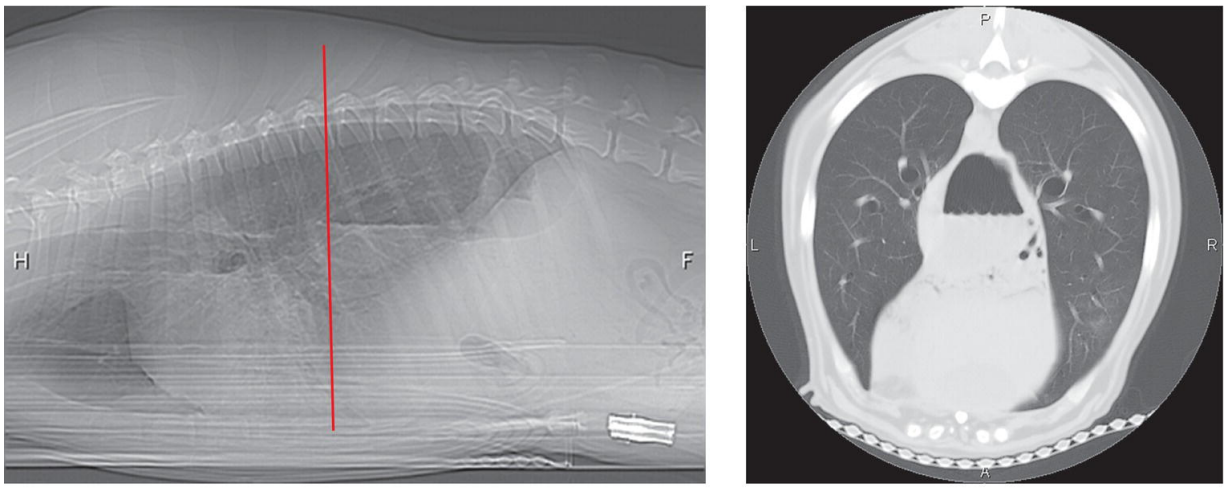
Prognosis

Short-term survival in animals with pyothorax ranges from 72% in cats (Kramer et al. 2021) to 85% in dogs (Eiras-Diaz et al. 2021), however the debate regarding the benefits of medical versus surgical treatment of pyothorax is difficult to resolve because surgery is often delayed until medical therapy has failed or is undertaken because an obvious need for surgical intervention is noted, such as a foreign body or mass lesion. Dogs might be taken to surgery earlier in the course of disease because of the increased likelihood of a foreign body as the cause of pyothorax. Overall survival rates beyond 70% can be anticipated when aggressive medical and surgical treatment is pursued. Lack of surgical debridement or early discontinuation of antibiotics can allow recurrent infection, and chronic pyothorax can be associated with fibrosing pleuritis (see section on chylothorax).

Mediastinitis/Mass Effect/Hemorrhage

Pathophysiology

Mediastinitis is an infectious or inflammatory process involving the cranial or caudal mediastinum. It can be caused by bacteria directly inoculated into the mediastinum through the thoracic wall or entering via an esophageal or tracheal route. Because the accessory lung lobe is commonly involved in foreign body inhalation, migration through the airway into the caudal mediastinum can result in a contained abscess (Figure 7.8). A cranial mediastinal mass effect can result from fungal infection causing enlargement of mediastinal lymph nodes (see Chapter 6) or by neoplasia (thymoma or lymphoma most commonly). Finally, mediastinal hemorrhage from rodenticide intoxication can result in a similar clinical picture to an infectious or inflammatory etiology. It is important to consider ingestion not only of the rodenticide, but also of the animal killed by the poison.



(a) (b)

Figure 7.8 (a) Lateral scout image from computed tomography and (b) a cross-sectional image demonstrate a fluid meniscus through a caudal mediastinal abscess in the region of the accessory lung lobe. The red line in (a) approximates the level of the cross-sectional image.

Spirocerca lupi, a worm that lives in the esophagus or stomach of the dog and causes neoplastic transformation of tissue, can cause caudal mediastinitis. *Spirocerca* has a world-wide distribution, but is found more often in warm climates, and disease appears to occur most commonly in Israel. A dog becomes infected with *Spirocerca* by eating a coprophagous beetle intermediate host or an animal that has eaten the beetle. The larvae gain access to the circulation and travel to the aorta, where they enter the esophagus. Adult worms (5–7 cm in length) live inside nodules in the esophagus, and rupture of the nodule can result in mediastinitis. Usually infection either is subclinical or results in neoplastic transformation of tissue.

History and Signalment

Young, outdoor dogs are more likely to develop fungal infection as well as gain exposure to foreign bodies, rodenticides, or dead animals through foraging behavior. Outdoor dogs and dogs that hunt are also more likely to be exposed to injury or foreign bodies and also to the carriers of a disease such as *Spirocerca*. Animals with mediastinitis can present with non-specific complaints of anorexia, weight loss, and lethargy, more localizing signs related to respiratory

compromise caused by obstructed breathing, or signs due to esophageal impingement can be noted. Esophageal disease related to injury or spirocercosis generally results in signs of difficulty swallowing or regurgitation. Esophageal rupture is associated with acute onset of pain, labored respirations, and tachypnea.

Physical Examination

The respiratory pattern is altered depending on the type and location of infection and any subsequent mass effect. Large mass lesions compress the trachea and result in inspiratory obstruction and stridor. In some cases, expiration can also be compromised and loud wheezing noises are heard. If pleural effusion develops secondary to a mass effect, tachypnea would be expected. Due to the proximity of neurovascular bundles to the mediastinum, a cranial mediastinal mass effect can disrupt venous return, resulting in edema of the front limbs, neck, and face (cranial vena caval syndrome), and interruption of nerve transmission. Neurological signs are primarily manifest as Horner's syndrome (ptosis, enophthalmos, protrusion of the third eyelid, and miosis; Figure 7.9) and laryngeal paresis or paralysis might be recognized by inspiratory effort with stridor.



Figure 7.9 This 9-year-old spayed female (FS) Mix breed dog demonstrates ptosis, enophthalmos, protrusion of the third eyelid, and miosis of the left eye consistent with Horner's syndrome on the left.

Fever is expected with systemic fungal infections and with bacterial infection in the mediastinum. Depending on the level of lung or pleural involvement, abnormal lung sounds can be auscultated, with muffling of lung sounds ventrally detected most commonly. A mass lesion or hemorrhage that affects primarily one side of the mediastinum can cause a shift in heart sounds away from the lesion and loss of lung sounds in the affected area. In cats and small dogs with mediastinitis, it can sometimes be difficult to compress the cranial thorax.

Diagnostic Testing

The mediastinum is not usually visualized on thoracic imaging in normal animals except in brachycephalic dogs, which typically have a widened cranial mediastinum (Figure 7.10). If history, physical examination, or routine blood work suggest that a coagulopathy could be playing a role in the clinical presentation, prothrombin time (PT)/partial thromboplastin time (PTT) should be performed prior to invasive testing that could worsen bleeding (see Chapter 2). In diseased animals, radiographs can reveal a mass effect within the cranial or caudal mediastinum. Delineation of a lesion can require contrast esophagoscopy or angiography, although CT is often employed instead to outline the lesion more precisely. Ultrasound of cranial mediastinal masses is useful to determine whether the mass lesion is cystic or solid and to determine vascularity. Cytology of an aspirate can confirm neoplasia, as well as fungal or bacterial infection, which will help determine the need for medical versus surgical therapy. Aerobic and anaerobic culture of aspirated material is recommended when bacterial infection is suspected, because Bacteroides spp. are often involved in the disease process.

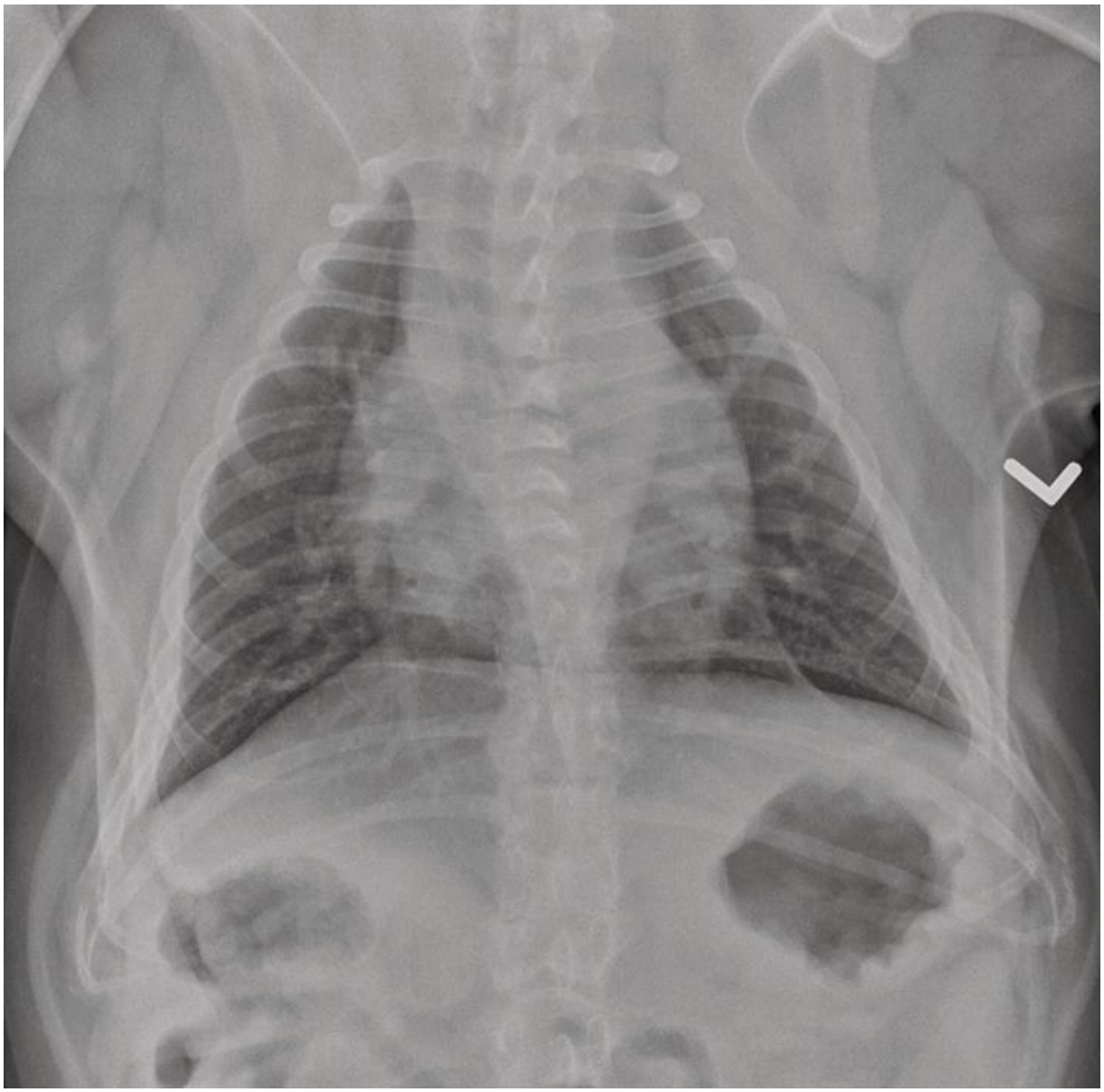


Figure 7.10 Dorsoventral radiograph from a Bulldog demonstrates widening of the cranial mediastinum.

Spirocercosis most typically results in a caudal mediastinal mass; aortic mineralization or spondylitis in the caudal thorax can also be detected (Dvir et al. 2001). Diagnosis is confirmed by finding small, elongated nematode eggs in a fecal flotation, or by documenting nodular lesions within the esophagus using radiography or endoscopy.

Treatment

Bacterial mediastinitis represents an encapsulated abscess. Surgical drainage in combination with the use of antibiotics with a good spectrum against oral and GI flora are indicated. Antifungal medication will generally resolve lymphadenopathy associated with fungal infection. Coagulopathic conditions resulting in mediastinal hemorrhage are treated with vitamin K1 (see hemothorax).

Spirocerca can be eliminated with various anthelminthics, including fenbendazole and albendazole, although long-term therapy with ivermectin or milbemycin oxime may be needed. Ivermectin should not be used in Collie-type dogs.

Prognosis

If surgery is required to repair the esophagus or to remove a large helminth granuloma, prognosis is guarded for recovery. Development of neoplasia secondary to spirocercosis is a recognized complication that can result in death due to primary or metastatic disease.

Neoplastic Disorders

Pathophysiology

The most common mass lesions in the cranioventral mediastinum are thymoma and lymphosarcoma. Thymoma is a unique neoplasm that can trigger auto-immune paraneoplastic syndromes, with myasthenia gravis being one of the more common events (Robat et al. 2013; Hague et al. 2015). Mediastinal lymphoma has been associated with feline leukemia virus positivity to a variable extent depending on geographic location and overall FeLV positivity. Heart base tumors (chemodectomas), ectopic thyroid neoplasia, or metastatic lymphadenopathy can be found craniodorsally or in the perihilar region (Figure 7.11). Neoplastic mass lesions must always be distinguished from a granuloma or an abscess.

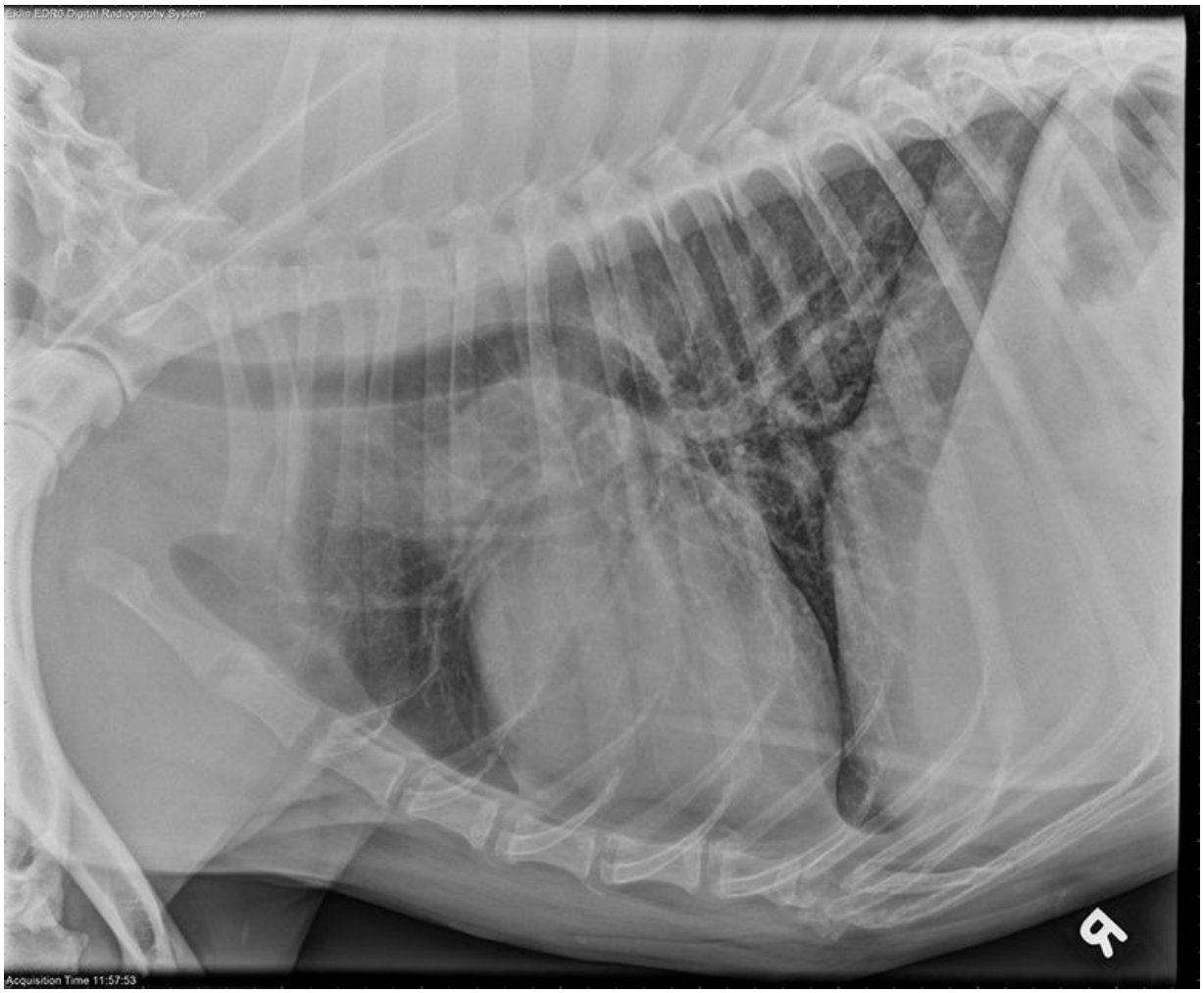


Figure 7.11 Right lateral radiograph from an 11-year-old Labrador reveals a mass lesion at the heart base consistent with a chemodectoma.

The pleura is more commonly affected by metastatic lesions, leading to thoracic effusion associated with lymphatic or vascular obstruction or due to altered vascular permeability. The most common primary tumor affecting the pleural surface is mesothelioma, which is relatively rare in veterinary patients.

History and Signalment

Mediastinal lymphoma in the cat appears to have a predilection for young (<2 years of age) cats, while thymoma tends to occur in older cats and dogs. Clinical complaints associated with mediastinal masses are often related to compression of adjacent structures by a

mass lesion. Impingement on the trachea leads to labored respiration (on inspiration and/or expiration). Thymoma can cause difficult or abnormal swallowing due to compression of the esophagus, and if secondary myasthenia gravis is present, progressive weakness, esophageal dysfunction, or collapse can be noted. A mediastinal mass can also cause inspiratory difficulty or changes in bark or meow associated with damage to the recurrent laryngeal nerve. As discussed previously, cranial vena caval syndrome and Horner's syndrome can be present.

Neoplastic processes that affect the pleural space, both primary and metastatic, usually affect middle-aged to older animals. Clinical complaints associated with malignant pleural effusion are usually respiratory difficulty and signs of poor health, including weight loss and lack of appetite.

Physical Examination

A mediastinal mass that puts pressure on the intrathoracic trachea can lead to stridor due to airway obstruction or from damage to the recurrent laryngeal nerve impacting laryngeal abduction. Obstruction of venous return by a mediastinal mass can lead to cranial vena cava syndrome, with edema of the head, neck, and front limbs. Impingement on the sympathetic trunk can lead to Horner's syndrome (see Figure 7.9).

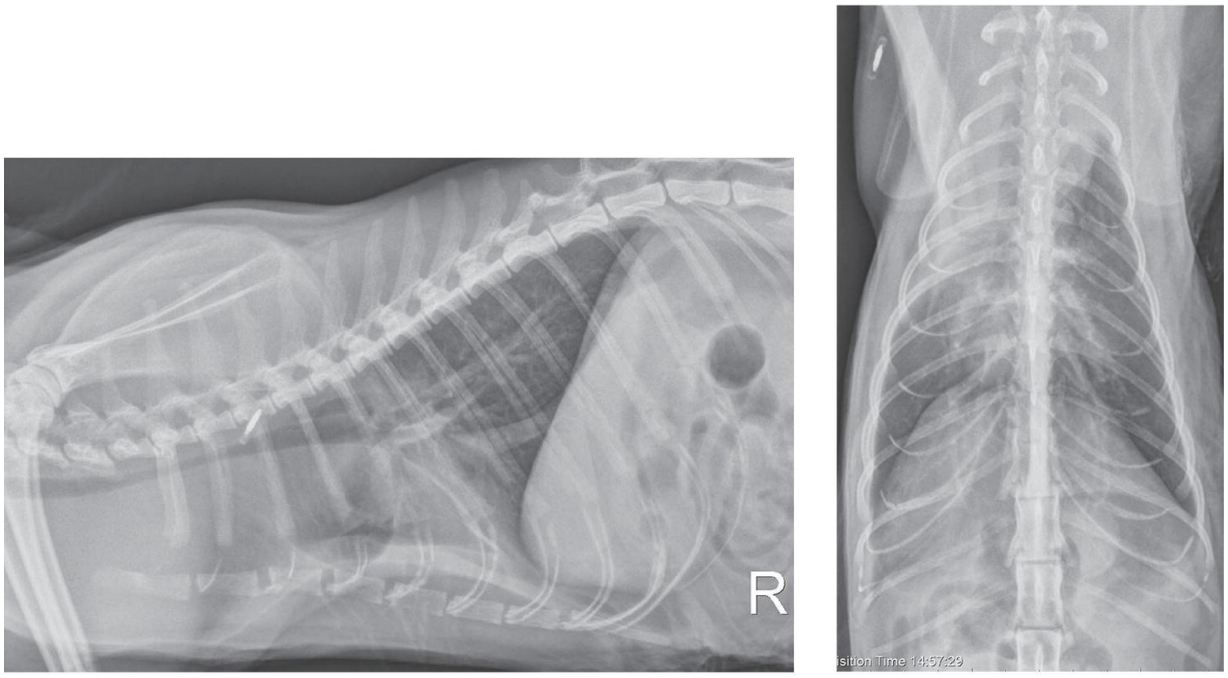
Pleural effusion leads to a restrictive pattern of respiration with increased respiratory rate and dampening of heart and lung sounds. Pleural effusion or a cranial mediastinal mass can lead to decreased thoracic compressibility.

Diagnostic Findings

Thoracic radiographic features of a mediastinal mass include dorsal deviation of the trachea (Figure 7.12) and widening of the mediastinum. Pleural effusion may or may not be present. Thoracic ultrasound is useful for identifying characteristics of mediastinal mass lesions and can guide aspiration for cytology. Pleural fluid cytology is often diagnostic for neoplasia, and polymerase chain reaction for antigen receptor rearrangement can be helpful in distinguishing thymoma from lymphoma (Lana et al. 2006).

Mesothelioma is anticipated to result in pleural effusion and mass lesions are generally not visible on radiographs. Pleural effusion cytology is often difficult to interpret in such cases, because reactive mesothelial cells are encountered with a number of pleural disease processes and are easily mistaken for neoplastic cells. CT can sometimes identify pleural lesions and will help direct surgical biopsies.

Animals with metastatic neoplasia can show evidence of nodular infiltrates or lymphadenopathy on radiographs after an effusion has been removed. Ultrasound or CT has improved the ability to detect lesions and also allows aspiration for diagnostic cytology.



(a) (b)

Figure 7.12 (a) Right lateral and (b) dorsoventral radiographs from a 7-year-old spayed female domestic short hair (FS DSH). There is a mild amount of pleural effusion and a soft tissue opacity in the cranial thorax, causing elevation and narrowing of the trachea. Ultrasound-guided aspiration confirmed thymoma.

Treatment

Protocols using various combinations of drugs, including cyclophosphamide, vincristine, cytosine arabinoside, l-asparaginase,

mitoxantrone, and prednisolone, are recommended rather than single-agent therapy for treating mediastinal lymphoma. Radiation therapy can also be pursued. Surgical resection is required for thymoma. No specific treatment is available for mesothelioma or metastatic neoplasia, although intracavitary cisplatin could be considered.

Prognosis

One study of lymphoma in the cat reported a median survival time of 9 months with a 49% survival rate at 1 year using cyclophosphamide, vincristine, and prednisolone (Teske et al. 2002) while a protocol with lomustine, doxorubicin, vincristine, and prednisolone reported over 80% survival in FeLV+ cats with mediastinal or multicentric lymphoma (Horta et al. 2021). Median survival time for cats with mediastinal lymphoma was ~8 months. Surgical removal of a thymoma by thoracotomy or thoracoscopy can be associated with prolonged survival, although when myasthenia gravis and mega-esophagus are present concurrently, a guarded prognosis must be offered. Pleural effusion associated with primary pulmonary neoplasia, mesothelioma, or metastatic neoplasia carries a grave prognosis.

Other Pleural Disorders

Pleural effusive diseases are categorized by the amount of protein in the fluid and cell count (see Chapter 2). After this initial characterization specific diagnostic tests are indicated to determine the most likely etiology of the effusion.

Hydrothorax

Pathophysiology

Hydrothorax refers to a low-protein, low-cellularity fluid that accumulates within the thorax due to a disturbance in Starling forces, the hydrostatic and oncotic pressures of the interstitial and vascular spaces (Eq. 7.1):

$$J_v = K_f\left[\left(P_c - P_i\right) - \sigma\left(\pi_c - \pi_i\right)\right] \quad (7.1)$$

where J_v is the net fluid movement, K_f is the filtration coefficient, P_c is the hydrostatic pressure in the capillary, P_i is the hydrostatic pressure in the interstitium, π_c is the oncotic pressure in the capillary, π_i is the oncotic pressure in the interstitium, and σ is the reflection coefficient. Both coefficients are related to permeability.

Hydrostatic pressure elevation associated with congestive heart failure generally results in production of a modified transudate with slightly higher protein and cell counts than a transudate. This is associated with right-sided or biventricular heart failure in the dog, although left ventricular failure alone can result in pleural effusion in cats.

Conditions that lead to loss of plasma oncotic pressure from low albumin result in transudative hydrothorax (very low protein and very low cell counts). This most commonly results from GI loss of albumin due to lymphangiectasia, inflammatory bowel disease, or intestinal lymphoma, from protein losing nephropathy due to amyloidosis or glomerulonephritis, or from hypoalbuminemia associated with liver dysfunction.

History and Signalment

The primary clinical complaints associated with hydrothorax are related to restriction of lung expansion due to fluid accumulation between the lung and chest wall, although in some cases, clinical signs associated with the primary disease process responsible for hypoalbuminemia can predominate over those associated with fluid accumulation. GI disease typically causes obvious signs of vomiting and diarrhea or weight loss, although dogs with lymphangiectasia sometimes have more subtle GI findings and more prominent signs associated with fluid accumulation. Liver failure can also result in subtle GI signs and can be accompanied by neurologic signs associated with hepatic encephalopathy or bleeding due to loss of clotting factors. Amyloidosis and glomerulonephritis are frequently clinically silent until renal insufficiency develops causing polyuria and polydipsia, and these disorders tend to lead to ascites more commonly than pleural effusion.

Physical Examination

Animals with hydrothorax usually display a rapid, shallow breathing pattern, and pleural effusion should result in dampening of lung and heart sounds ventrally. Concurrent ascites is found in some patients; accumulation of fluid in the subcutaneous space is rare. Careful attention to the remainder of the physical examination is indicated to determine the underlying cause of hydrothorax. Dogs with congestive heart failure virtually always have a systolic heart murmur, although the same is not true in cats. Dogs might also have enlarged jugular veins or an enlarged liver. In the cat, a gallop sound or arrhythmia would be more suggestive of cardiac disease. Infiltrative GI disease should be suspected if diffusely thickened bowel loops are palpated, although lymphangiectasia does not often result in palpable abnormalities. A palpably small liver could suggest liver failure, and enlarged kidneys are suspicious for amyloidosis, as well as pyelonephritis and renal neoplasia.

Diagnostic Testing

When hydrothorax is discovered, a systemic work-up including a complete blood count (CBC), chemistry panel, and urinalysis is required to determine the underlying cause. A CBC can show lymphopenia suggestive of lymphangiectasia. Hypoalbuminemia with concurrent hypoglobulinemia is suggestive of GI loss. Decreased levels of serum vitamin B12 levels can be used a crude marker of GI dysfunction, because B12 is absorbed in the ileum in normal individuals. In addition, abdominal ultrasound should be performed to look for thickened bowel loops suggestive of inflammatory bowel disease or lymphoma and tiger-striping of the bowel, which has been associated with lymphangiectasia. GI biopsies should be considered in some affected animals. If only low albumin is noted, a urinalysis should be evaluated for proteinuria. If a urine protein–creatinine ratio greater than 1 is detected in an animal with a negative urine culture, primary glomerular disease should be investigated in the presence or absence of azotemia. A tick panel, heartworm test, abdominal ultrasound, and kidney biopsy can assist in making the diagnosis in a dog with proteinuria. If low albumin is noted in conjunction with low blood urea nitrogen, low cholesterol, and low glucose, primary liver disease should be considered. Bile acids and

abdominal ultrasound should then be pursued to rule out a portosystemic shunt.

In the animal with hydrothorax, a colloid osmotic/oncotic pressure (COP) can be measured to assess the magnitude of disruption in Starling forces. Normal values are 21–25 mmHg in the dog and 23–25 mmHg in the cat.

Cardiac ultrasound is needed to rule out heart disease in cats, although an elevated NT-proBNP in serum from a cat with pleural effusion is highly suspicious for congestive heart failure, even when performed using a point-of-care test (Hezzell et al. 2016). In the emergency setting, NT-proBNP could be measured on pleural fluid using the point-of-care test if blood cannot be obtained. A positive test is not helpful, but a negative test can effectively rule out congestive failure (Hezzell et al. 2016).

Treatment

Animals in respiratory distress due to accumulation of pleural fluid should have sufficient volume removed to improve respirations; however, excessively rapid removal of fluid can theoretically lead to re-expansion pulmonary edema when effusion has been chronic. Treatment of the underlying disease and resolution of hypoalbuminemia should result in a rise in COP and reduction in fluid accumulation. In some cases, administration of plasma (6–10 ml/kg), hetastarch (1–2 ml/kg/hour of 6 g/100 ml solution), or potentially concentrated human albumin can raise oncotic pressure sufficiently to alleviate fluid accumulation temporarily. Side effects include fever, fluid overload, or hypersensitivity reaction with plasma, coagulopathy with dextrans, and coagulopathy, hypersensitivity, or anaphylactic-like reactions with human albumin. In addition, delayed immune-type reactions to human albumin are suspected to occur.

Prognosis

Prognosis depends on the underlying cause of disease. Unfortunately, the primary etiology of hydrothorax is not always

determined, and idiopathic pleural effusion is frustrating and challenging to treat.

Hemothorax

Pathophysiology

Accumulation of blood in the pleural space occurs because of trauma, a systemic coagulopathy, lung lobe torsion, or neoplasia. A secondary coagulation defect associated with clotting factor deficiency or inhibition due to rodenticide intoxication is more likely to result in hemorrhage into a body cavity than is a defect in platelet numbers or function. Some clinicians diagnose hemothorax when the hematocrit is 25–50% of that found in the peripheral circulation. When the packed cell volume of pleural fluid is only 5–10%, it might be called a hemorrhagic effusion.

History and Signalment

Young animals are more likely to suffer trauma or develop a coagulopathy secondary to rodenticide intoxication, while older animals are more likely to develop a hemorrhagic effusion due to neoplasia. Lung lobe torsion is reported in any age of animal (see Chapter 6). In animals with hemothorax or hemorrhagic effusion, systemic signs of weakness and blood loss can predominate over respiratory abnormalities. Rodenticide intoxication generally results in clinical signs 2–5 days after ingestion and signs of weakness and respiratory difficulty are often acute in onset. Dogs with neoplasia or lung lobe torsion have a gradual onset of lethargy or weakness followed by difficult or rapid breathing, but they can also present acutely in some instances.

Physical Examination

Animals with a coagulopathy can demonstrate pale mucous membranes, tachycardia, or evidence of hemorrhage elsewhere in the body, such as the abdominal cavity, skin (ecchymotic hemorrhages), joints, or eyes (hyphema or retinal bleeding). Tachypnea is often evident in animals with hemothorax, and heart and lung sounds will be muffled ventrally. Increased or harsh lung

sounds may be auscultated focally when parenchymal neoplasia is present.

Diagnostic Findings

Radiographs reveal pleural effusion and in animals with a coagulopathy, parenchymal and mediastinal infiltrates are usually found that are more severe than the pleural effusion (Berry et al. 1993). Bony structures of the thorax should be scrutinized for rib fractures in suspected trauma patients. Radiographs or ultrasound can be useful in detecting pulmonary lesions such as neoplasia or lung lobe torsion that might lead to hemothorax.

In an animal with hemothorax due to pure hemorrhage or a coagulopathy, additional evidence of hemorrhage can be found in laboratory test results including anemia, mild to moderate thrombocytopenia, and hypoalbuminemia. Prolongation of tests assessing secondary hemostasis (OSPT, APTT) confirms a coagulopathy (see Chapter 2).

Treatment

If a coagulopathy is documented, it is usually not necessary or wise to drain the chest, because respiratory distress in these patients is often due to parenchymal bleeding rather than pleural accumulation of blood. Therefore, when bloody fluid is obtained from a thoracocentesis, a PCV should be evaluated immediately and clotting tests performed as indicated. For rapid re-establishment of clotting ability, fresh frozen plasma should be administered at 6–10 ml/kg initially. Transfusion with fresh whole blood is indicated if the animal is anemic. Vitamin K_1 is initiated concurrently at a loading dose of 5 mg/kg subcutaneously, using a small gauge needle, followed by 1.5–2.5 mg/kg PO twice daily for 21–30 days. Clotting times are assessed during the initial 1–3 days of the stabilization period and again 2–3 days after halting therapy.

Conservative management of hemothorax due to trauma is warranted initially, with oxygen supplementation and judicious use of pain relief and sedation. Surgical intervention could be required if an artery is severed or if a broken rib causes persistent bleeding.

Prognosis

Animals that are documented to have a coagulopathy usually respond well to vitamin K therapy, although it is important to obtain follow-up testing to ensure normalization of clotting tests after the drug is discontinued and to confirm that re-exposure to anticoagulants has not occurred.

Feline Infectious Peritonitis (Coronavirus)

Pathophysiology

The disease syndrome associated with feline infectious peritonitis (FIP) is initiated when an enteric coronavirus undergoes spontaneous mutation into a virulent form that triggers immune-mediated disease. This occurs primarily in young kittens when there is rapid replication of the coronavirus. The virus develops a tropism for macrophages that initiates a cell-mediated immune response primarily, and then antibody production leads to a vasculitis. It appears that a strong cell-mediated response protects against the virus, while the humoral response may promote immunologically driven disease. Thus the clinical syndrome associated with FIP is characterized by two forms of disease. The effusive or wet form is thought to be associated with a strong humoral response that leads to an immune complex vasculitis, with increased vascular permeability and neutrophil-mediated vessel necrosis. Peritoneal effusion predominates, although pleural and pericardial effusions also can develop. The non-effusive disease or dry form of disease occurs in cats that develop a partial cell-mediated immunity and is associated with pyogranulomatous inflammation in any organ, including liver, kidney, lung, or brain. Some evidence suggests that there can be a transition between effusive and non-effusive disease.

History and Signalment

Mutation of the coronavirus and subsequent FIP-related disease are more common in young animals from multi-cat households, suggesting that environmental stresses play a role in the etiopathogenesis of disease. FIP most commonly affects purebred

kittens and young cats 4–16 months of age, but it can occur in any age of cat. Owner complaints include a failure to thrive, anorexia, and weight loss. A persistent or recurrent fever that does not respond to antibiotics is often present in the history. In the effusive form, progressive abdominal enlargement can be noted over weeks to months and may be accompanied by tachypnea and respiratory difficulty due to pleural effusion. Tachypnea and respiratory distress can also be found with granulomatous pneumonia.

Physical Examination

Cats with FIP usually have a fever and, in the effusive form, will display signs of abdominal and/or thoracic effusion. Abdominal distention, a ballotable fluid wave, muffled heart and lung sounds, and tachypnea are common features in affected cats.

Organ involvement by the dry form of FIP can result in chorioretinitis, neurologic deficits, irregular contour to the kidneys, or diffuse or focal thickening of intestines. Granulomatous pneumonia results in tachypnea and harsh lung sounds.

Diagnostic Findings

Clinical diagnosis of FIP is often suspected based on the presence of fever and thoracic and/or abdominal effusion in a young cat. Laboratory findings consistent with a diagnosis include anemia, lymphopenia, neutrophilia, hyperglobulinemia with a polyclonal gammopathy, hyperbilirubinemia, and decreased serum albumin/globulin ratio (<0.6). A very high coronavirus titer (>1:1600) is supportive of disease and a negative titer makes FIP less likely; however, antibody titers are not specific for the mutated virus. Abdominal or thoracic fluid is generally yellow, viscous, and highly proteinaceous (proteins 4–10 g/dl), with variable but often low cellularity (500–5000 cells/µl). Detection of increased levels of acute-phase proteins including α1-acid glycoprotein (AGP), haptoglobin, and serum amyloid A in serum and effusions is somewhat useful in supporting a diagnosis of FIP, with AGP levels in effusion being most sensitive and specific (Hazuchova et al. 2017). However, immunocytochemistry for detection of viral antigen in effusion remains the most useful non-invasive diagnostic test for FIP

(Hartmann et al. 2003; Tasker et al. 2023). Real-time reverse transcriptase polymerase chain reaction (RT-PCR) on pleural or peritoneal fluid that yields a strongly positive result for feline coronavirus nucleic acid is also highly suggestive of FIP-related disease, because the virus should not be detected outside the GI tract, although low levels of coronavirus DNA can be detected in cats with non-FIP disease. Definitive diagnosis can be made by identifying characteristic histopathologic lesions of pyogranulomatous inflammation and necrotizing vasculitis. Immunohistochemistry for viral antigens confirms the diagnosis, although variability in the reagents used can impact the reliability of this test and owners are not always willing to pursue a biopsy diagnosis.

Treatment

Initial promising results were reported in clinical trials involving protease inhibitors (Pedersen et al. 2018), and subsequent use of this medication (GS-441524, at 12.5–15 mg/kg PO once daily for 12 weeks) as well as a parent compound (remdesivir, at 25–30 mg/kg PO once daily for 12 weeks) has rapidly reversed the fatal prognosis of this disease (Pedersen et al. 2019; Cosaro et al. 2023). Approximately 80% survival was reported for cats that survived the first 2 days of treatment. Remdesivir has the advantage of being licensed by the FDA in the USA and is commercially available (albeit expensive), with well controlled pharmaceutical standards. Recently, the FDA reversed the requirement for GS-441524 to undergo specific testing as is usually needed for approval of new animal drugs, providing increased availability of this medication for a specific patient from compounding pharmacies. Supportive care with intravenous fluid therapy, nutritional support, and repeated fluid drainage can be used to keep the cat comfortable as needed.

Prognosis

FIP is fatal within days to months to years in the absence of specific antiviral therapy. Control of the disease in populations relies on management strategies that limit crowding, stress, and other illnesses in the environment. Genetic resistance or susceptibility in

breeding lines should be evaluated to help control disease within populations.

Chylothorax

Pathophysiology

Chylothorax is caused by leakage of lymphatic fluid from the thoracic duct into the pleural cavity. It is seen in both dogs and cats. The etiology is often idiopathic; however, diseases associated with increased right heart pressures that inhibit transport of chyle from the thoracic duct into the jugular vein or cranial vena cava in the mediastinum, such as cardiomyopathy, pericardial disease, congenital heart disease, and heartworm disease, have been reported as potential causes. Mediastinal masses (lymphosarcoma, thymoma) have been diagnosed in association with chylothorax, and chylothorax is seen in some dogs with lung lobe torsion, although it is unclear whether torsion is a cause or effect of chylous effusion. Traumatic rupture of the thoracic duct is a possible but relatively rare cause of chylothorax.

History and Signalment

Afghan hounds are thought to be predisposed to development of chylothorax and are a breed that is susceptible to lung lobe torsion, although the relationship between these two disorders remains unclear.

Clinical signs of pleural disease, specifically tachypnea or respiratory difficulty, can be acute or chronic with chylothorax. Cats with chylothorax will sometimes have a history of cough as well as labored breathing. This is likely due to airway compression from restricted lung expansion but could also reflect underlying inflammatory airway disease. Some animals with chylothorax suffer weight loss associated with loss of protein, fat, and vitamins into lymph fluid in the chest.

Physical Examination

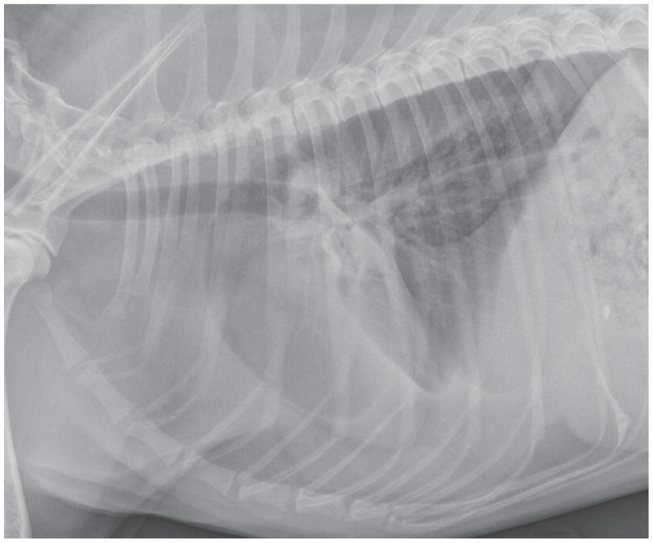
Some animals have a poor body condition score due to chronic depletion of nutrients and poor appetite associated with long-

standing inflammatory disease. Tachypnea and/or labored respirations are expected when fluid fills the pleural space. Heart and lung sounds are muffled ventrally or unilaterally; chyle can plug mediastinal fenestrae and result in unilateral effusion. Harsh or adventitious lung sounds are common in dorsal lung regions. Careful cardiac auscultation should be performed to detect a murmur, gallop, or arrhythmia that might suggest heart disease as an underlying cause of chylous effusion, and jugular veins are assessed for abnormal distention or pulsation. The latter could indicate restrictive pericardial physiology.

Diagnostic Findings

In chylothorax, unilateral or bilateral effusion can be present and rounding of lung margins is relatively common due to an inflammatory, fibrotic effect of chyle or due to atelectasis (Figure 7.13).

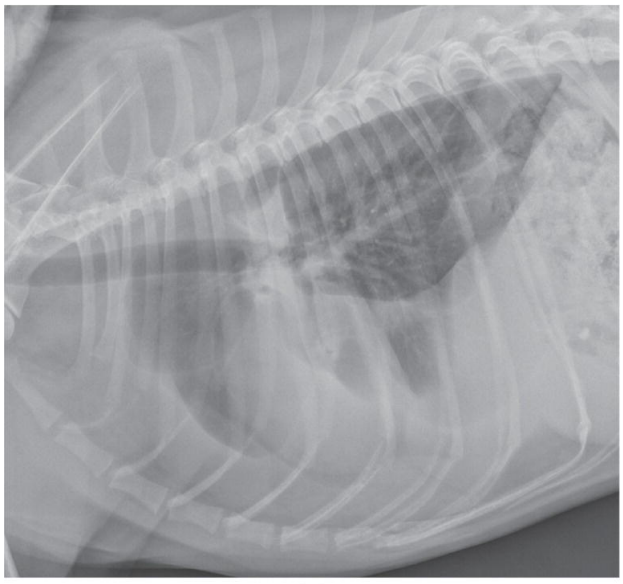
Radiographic, ultrasonographic, or physical examination evidence of pleural effusion generally indicates that thoracocentesis should be performed, and this typically yields a characteristic white or pink opaque fluid (Figure 7.14). Chylothorax is diagnosed by performing cholesterol and triglyceride analysis on pleural fluid and serum. Because chyle is lymphatic fluid, triglyceride levels in pleural fluid are significantly higher than in serum, and cholesterol levels are lower than in serum. A cholesterol/triglyceride ratio of <0.2 in pleural fluid is considered diagnostic for chylothorax. Once the diagnosis of chylothorax has been established, further diagnostic tests are performed to determine whether an underlying cause can be identified. Such tests include pleural fluid cytology to rule out neoplasia, heartworm testing, echocardiography to rule out congenital disease, cardiomyopathy, and pericardial disease, thoracic ultrasound to screen for masses, and abdominal ultrasound to investigate potential systemic lymphatic abnormalities, although intestinal lymphangiectasia is more often associated with hydrothorax due to low oncotic pressure rather than chylothorax.



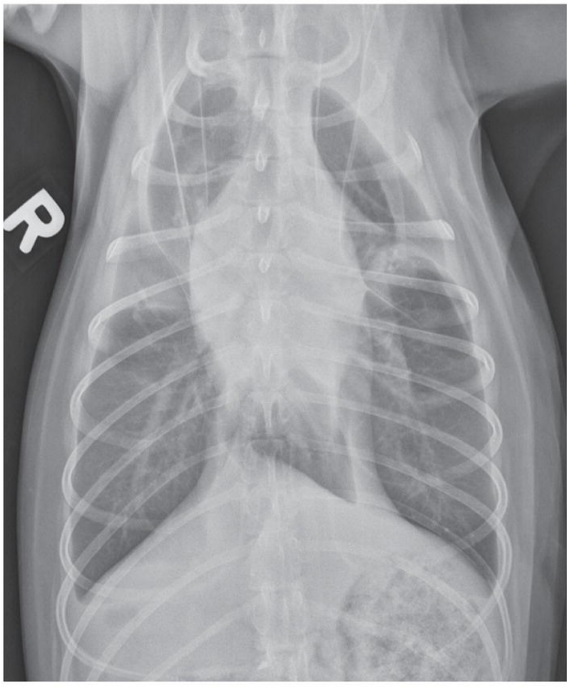
(a)



(c)



(b)



(d)

Figure 7.13 (a) Right and (b) left lateral radiographs show rounding of the lung margins, which is a typical finding in chylous effusion. Dorsoventral (c) and (d) ventrodorsal radiographs demonstrate the value of obtaining additional views in animals with pleural effusion. In the ventrodorsal view, pleural fluid pools in the paraspinal gutters and is hidden under the heart. This allows better assessment of the cardiac silhouette and lung fields.

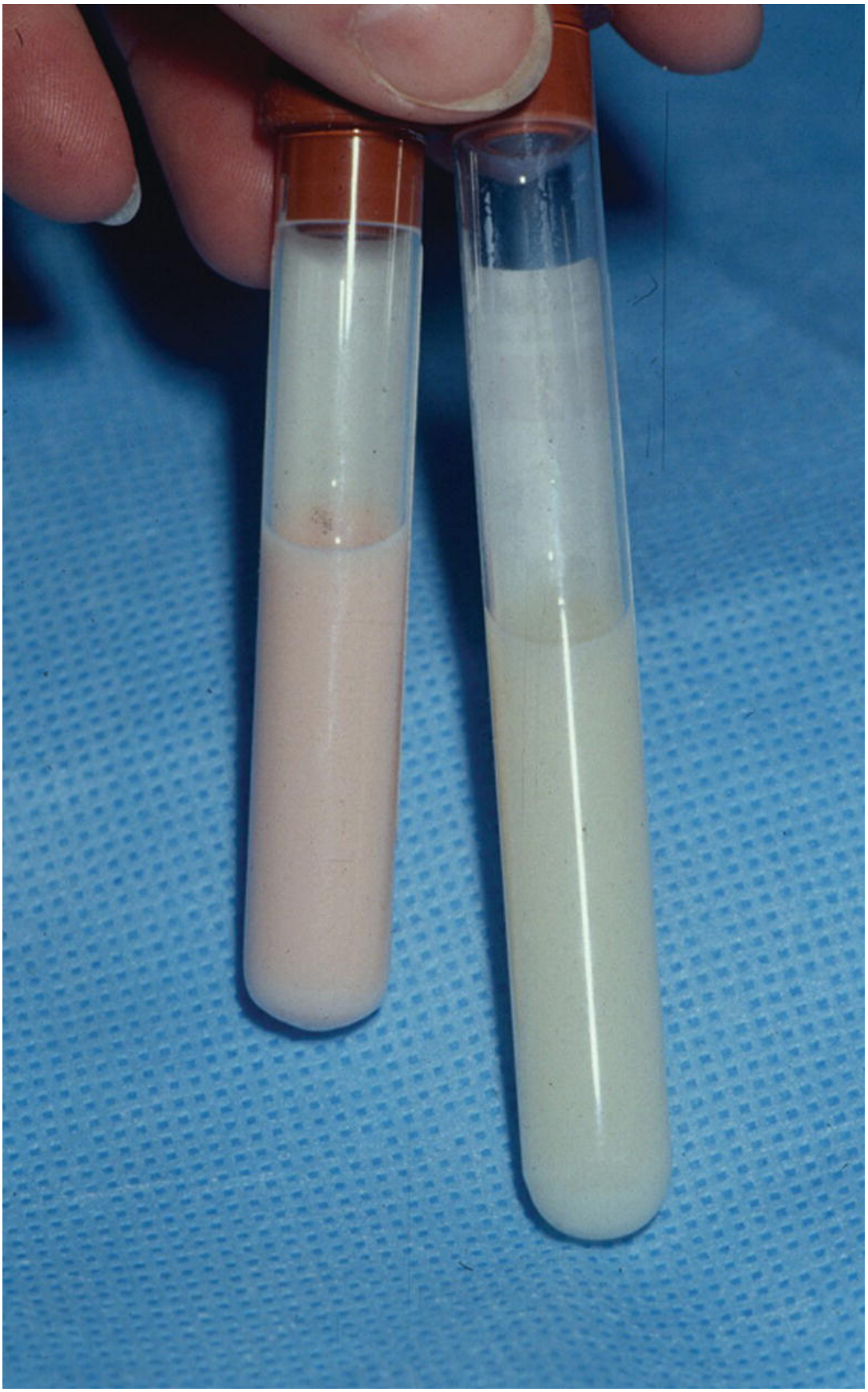


Figure 7.14 Chylous effusion is typically opaque due to the presence of chylomicrons and can be white or pink, depending on whether blood contamination has occurred.

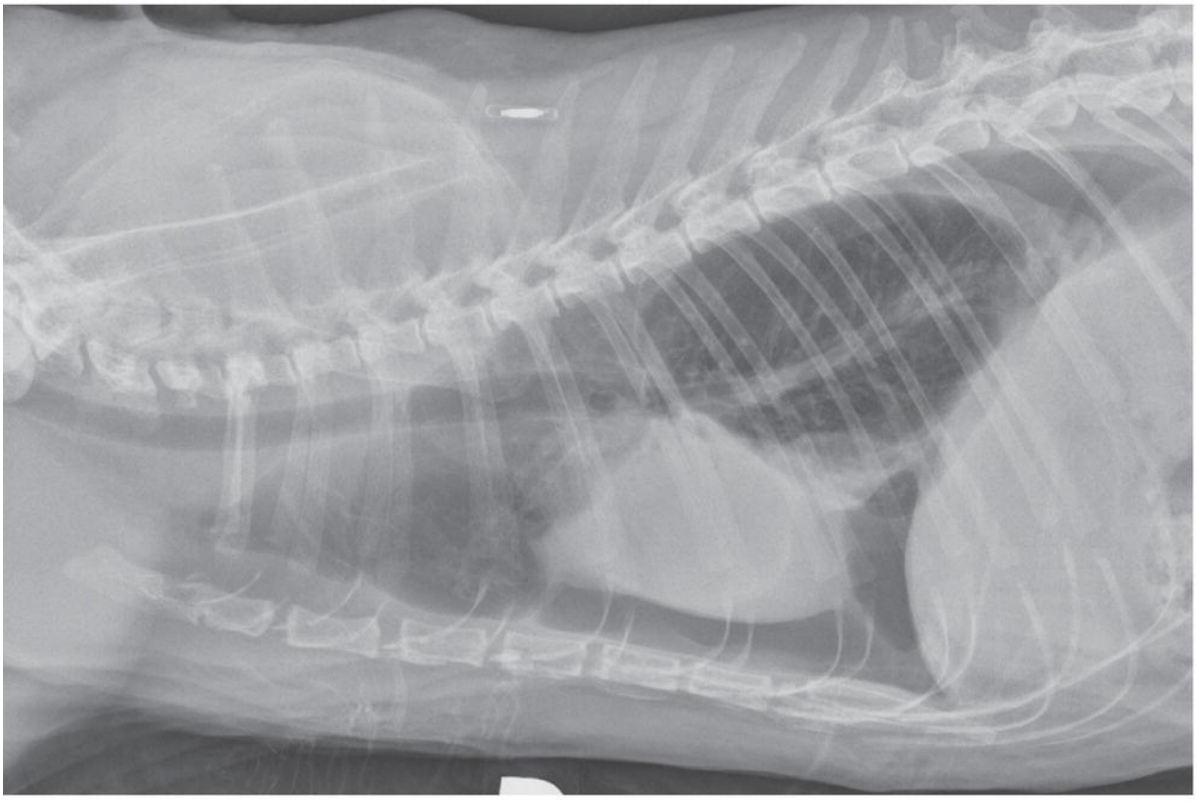
Treatment

Initial therapy for chylothorax should be directed at the cause when identified. Thoracocentesis should be performed whenever the animal develops respiratory difficulty. Dietary therapy with reduced fat and supplementation with medium-chain triglyceride oil has historically been the mainstay of treatment, because it was thought that these changes would reduce lymph flow. Some dogs might benefit from this therapy, but clinical studies have not confirmed that it substantially decreases lymph flow. Adjunctive dietary therapy with the nutraceutical rutin, a benzopyrone, at 50 mg/kg PO TID has had some success in reducing chyle accumulation in occasional animals with chylothorax, and relatively few side effects have been reported. The mechanism of action is unknown, but this agent appears to have some venoactive effects to decrease leakage of fluid from blood vessels, it may be anti-inflammatory, or it could enhance proteolysis and removal of protein from tissues.

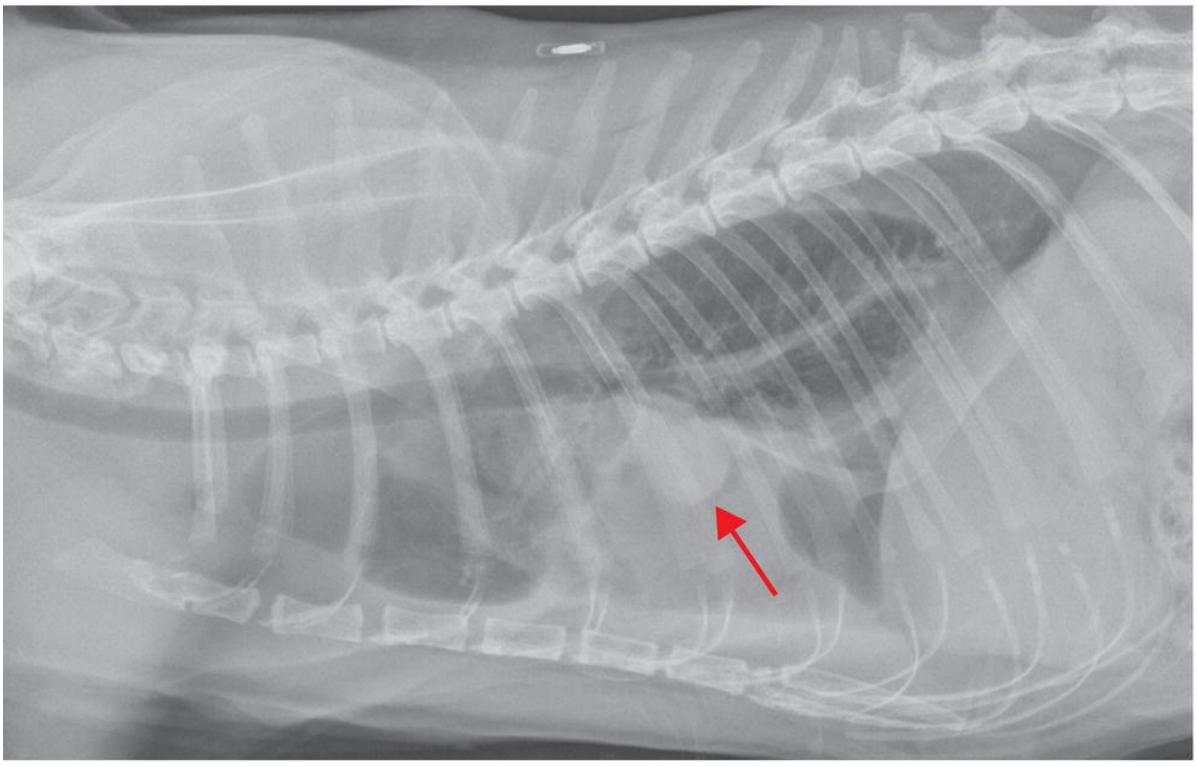
When thoracocentesis is required more often than once per week to keep the animal comfortable, surgical options should be strongly considered. Advances in diagnostic imaging and surgical techniques have resulted in markedly improved prognosis for this disease. CT-guided injection of the mesenteric lymph node or liver improves visualization of the thoracic duct and avoids the need for an abdominal surgery (Johnson et al. 2009; Korpita et al. 2022). Surgical therapies include thoracic duct ligation, cisterna chyli ablation, and pericardiectomy in various combinations, with thoracoscopic surgery considered by some to be the gold standard of therapy. In the absence of constrictive pericarditis, pericardiectomy appears to be of limited benefit in improving outcome (Mayhew et al. 2023). Success rates in dogs approach 90% whereas less information is available on cats and resolution of disease appears to be closer to 40% (Reeves et al. 2020; Mayhew et al. 2023). Eligible patients with motivated owners should be referred to a board-certified surgeon as soon as possible to avoid development of secondary fibrosing pleural or pericardial disease.

Prognosis

Fibrosing or restrictive pleuritis is a debilitating condition that can occur after long-standing high-protein pleural effusion, such as occurs with chylothorax or pyothorax. Chronic inflammation of the pleura results in metaplasia of mesothelial cells with production of collagen, and the presence of pleural fluid decreases fibrinolysis, resulting in a collagen network within the pleura. Pleural effusion may or may not be present in later stages of disease. The radiographic or tomographic appearance of fibrosing pleuritis is characterized by persistently unexpanded and rounded lung lobe margins (Figure 7.15).



(a)



(b)

Figure 7.15 (a) Right and (b) left lateral radiographs from a cat with chylothorax and concurrent fibrosing pleuritis. Note rounding of the lung margins. Collapse of the right middle lung lobe (red arrow) is visible in (b).

Thickened pleura restricts lung expansion (Figure 7.16). Therapy for fibrosing pleuritis involves surgical removal of the pleura. This procedure has been beneficial in humans if less than two lobes are affected; however, most affected animals have generalized pleuritis, which is not easily treated with surgery. Complications of the surgery include pneumothorax and hemorrhage. If surgery is performed, steroids should be considered for 2–3 weeks postoperatively. Lung function may improve over 2–3 months.

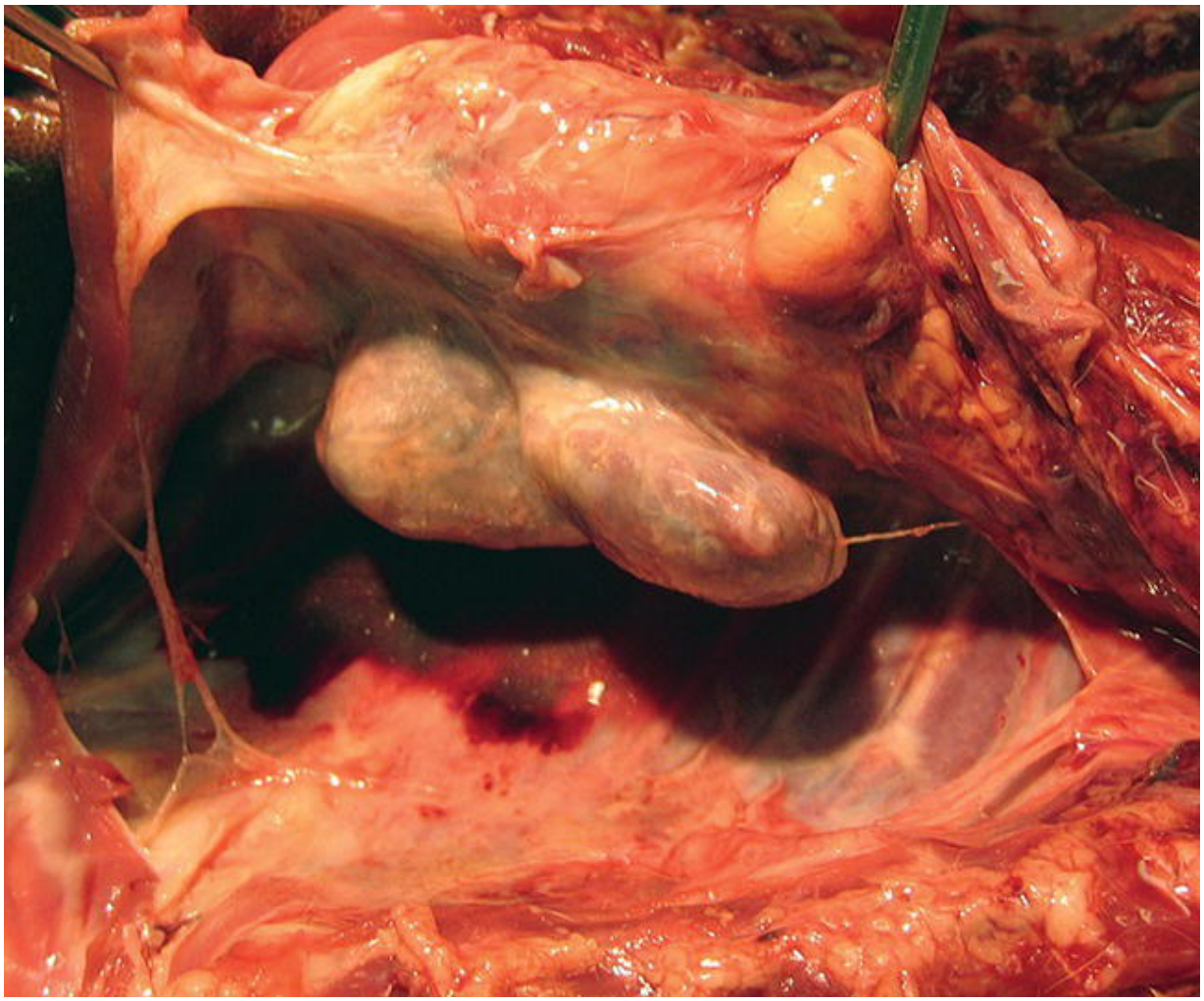


Figure 7.16 Necropsy image from a 5-year-old spayed female domestic short hair (FS DSH) that had chylothorax for at least 2–3 months. The lungs did not collapse after the chest was opened, and fibrin was evident surrounding the right lung lobes. Both the parietal and visceral pleura were markedly thickened.

Clinical Case

A 3-year-old castrated male (MC) Golden-doodle was presented to the emergency room for evaluation of a 3 week history of breathing abnormally. Physical examination revealed severe respiratory distress with inspiratory and expiratory effort and tachypnea. Lung sounds were absent on the left side and muffled

on the right. A single lateral radiograph revealed pleural effusion and a thoracocentesis was performed.

Approximately 3 l of pleural fluid was removed and submitted for fluid analysis. Total protein was 3.7 g/dl and total nucleated cell count was 700, comprised primarily of lymphocytes (92%) with a smaller percentage (8%) of neutrophils. Lymphocytes were all small with quiescent nuclei. Given the appearance of the fluid, triglyceride levels were assessed and were markedly elevated at 1120 mg/dl (RI 20–150 mg/dl). Thoracic radiographs taken after thoracocentesis were reviewed by a board certified radiologist and revealed a normal size and shape to the cardiac silhouette, normal lung fields, and persistent but small volume pleural effusion.

Differential diagnoses for chylothorax included heartworm disease, pericardial disease, right-sided heart disease (cardiomyopathy, congenital lesions), neoplasia, and possibly lung lobe torsion, although it is unclear whether chylothorax precedes lung lobe torsion or occurs because of the torsion. A point of care assay for *Ehrlichia*, Lyme disease, Heartworm and *Borellia* was negative. Abdominal ultrasound revealed normal liver, spleen, and GI tract. Echocardiography demonstrated normal cardiac structure and function as well as normal appearance to the great vessels. There was no evidence of constrictive pericarditis.

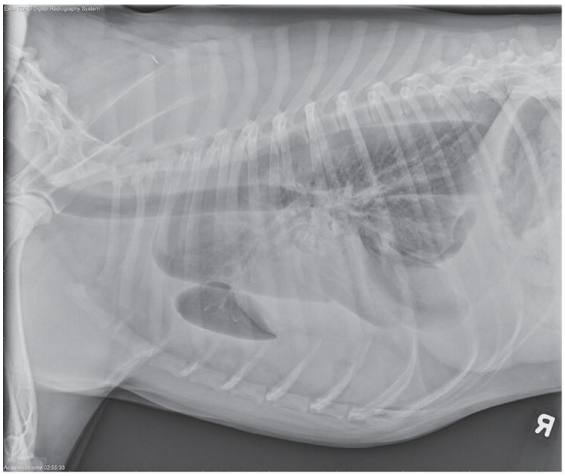
In the absence of a specific cause, chylothorax was deemed idiopathic. The dog was started on a low fat diet and Rutin therapy at 50 mg/kg PO BID, but effusion rapidly returned. After two more chest taps within 1 week, the dog was referred to a surgeon. Physical examination revealed a temperature of 103.2°F (39.6°C), pulse ranging from 130 to 220, and tachypnea with increased respiratory effort and superficial breaths.

Thoracic radiographs revealed moderate pleural effusion and were remarkable for narrowing and malpositioning of the right middle lobar bronchus. Radiographs also revealed a vesicular gas pattern in that lobe suggestive of lung lobe torsion (Case Figure 1). The dog was anesthetized for CT and video-assisted thoracoscopic surgery. CT confirmed torsion at the proximal

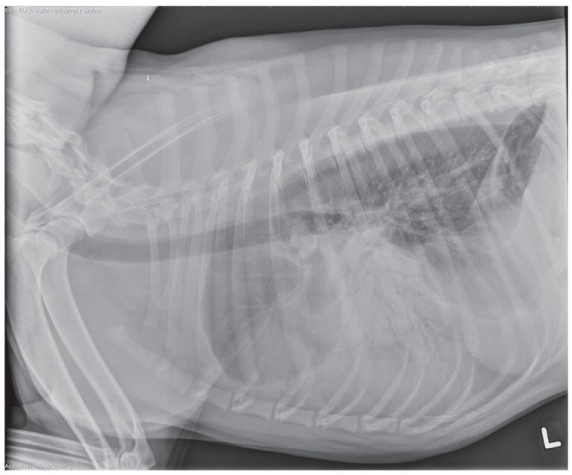
bronchus of the right middle lung lobe. CT was repeated following administration of contrast material into a mesenteric lymph node. The mesenteric lymphatics and the cisterna chyli filled with contrast, revealing a single lymphatic vessel directly dorsal to the aorta until the level of the 11th thoracic vertebra. At this point, a plexus of lymphatics appeared (Case Figure 2).

A Robert Shaw double lumen endobronchial blocker was placed in the left mainstem bronchus using a Karl Storz Flex XC 2.8 mm videoendoscope. During endoscopy, a twist was noted at the entrance to the right middle lobar bronchus.

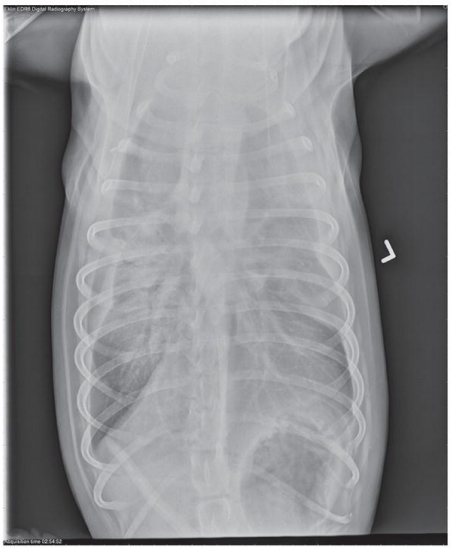
Thoracoscopic ports were placed at the 8th, 9th, and 10th intercostal spaces and the lung lobe torsion was visualized but deemed too large for thoracoscopic removal. An 8 cm thoracotomy was performed at the fifth intercostal space on the right side and the lung lobe was removed with a thoracoabdominal stapler. Using thoracoscopic-guidance through the intercostal portals, the thoracic duct was identified using near-infrared fluorescence imaging after perineal injection of indocyanine green. After dissection of the thoracic duct, multiple hemoclips were placed to seal the duct.



(a)



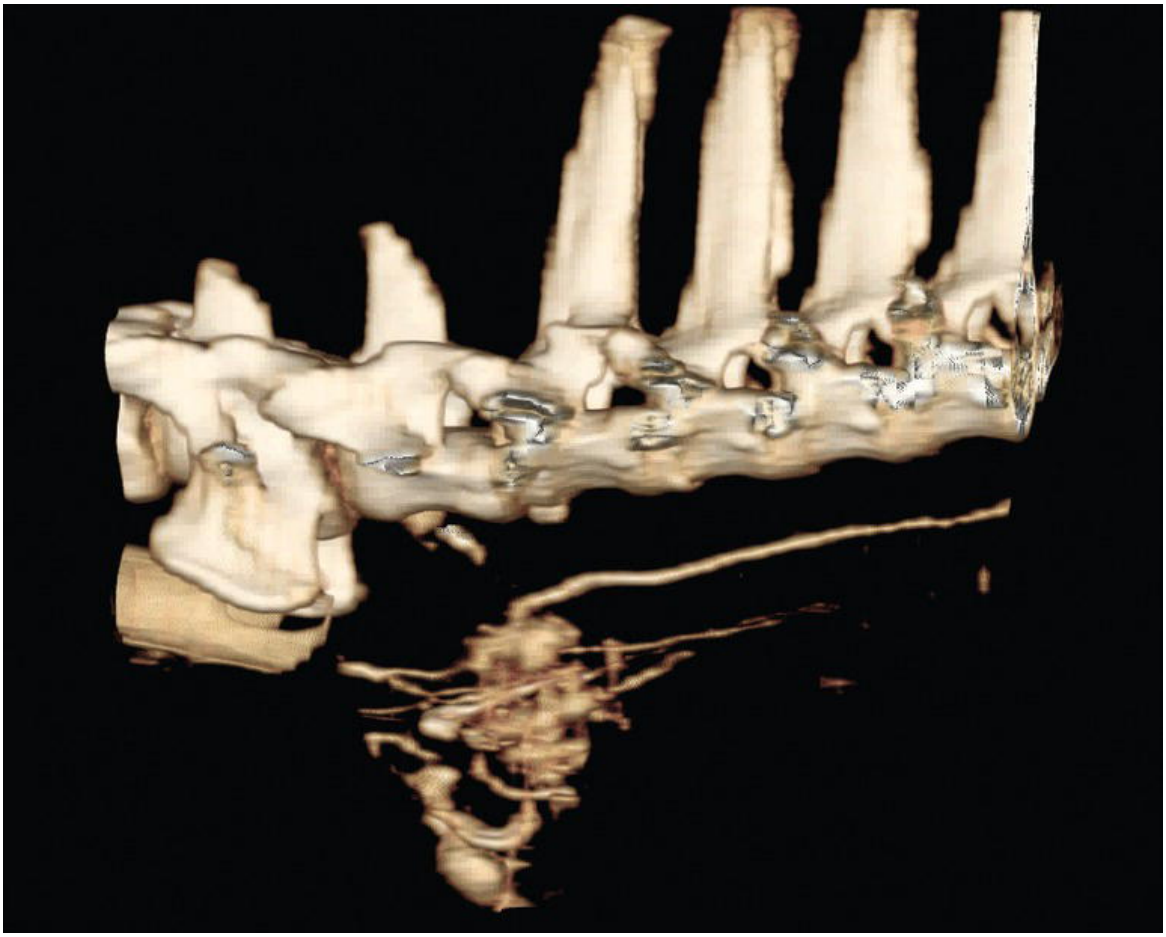
(b)



(c)

Case Figure 1 Thoracic radiographs.

A chest tube was placed for post-operative management and the dog recovered from anesthesia uneventfully. Histopathology of the right middle lung lobe was consistent with subacute hemorrhagic infarction and neutrophilic pleuritis.



Case Figure 2 Lymphoscintigraphy.

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8
Vascular Disorders

Structural Disorders

Pulmonary Thromboembolism

Pathophysiology

Systemic diseases that result in stasis of blood flow, hypercoagulability, and disruption of the endothelial layer in the vasculature can result in the complication of pulmonary thromboembolism (PTE). In dogs, immune-mediated hemolytic anemia, sepsis, neoplasia, amyloidosis, hyperadrenocorticism, and dilated cardiomyopathy are associated with increased risk for PTE, while neoplasia and cardiomyopathy are found most often in cats with PTE (Johnson et al. 1999b; Norris et al. 1999). Pancreatitis is a risk factor for hypercoagulability with venous embolization in humans, and this is likely the case in dogs also.

PTE results in multiple pathophysiologic events that affect gas exchange. Physical obstruction of large pulmonary arteries by clot material increases intravascular pressure, and release of clot-associated vasoactive factors (e.g. thromboxane) causes reactive pulmonary vasoconstriction. Elaboration of humoral mediators (e.g. serotonin, histamine, calcium, and growth factors) from platelets results in bronchoconstriction and increased airway resistance. Surfactant is a phospholipid compound comprised of hydrophilic and hydrophobic proteins that develop the surface tension-lowering properties within the alveolus to stabilize the gas exchange region. Large surfactant aggregates are more active in lowering surface tension, and embolization reduces the ratio of large to small aggregates at the alveolus, potentiating alveolar collapse and increasing shunt fraction. Capillary leakage of plasma into the alveolus further inhibits surfactant activity through a dilutional effect. These changes contribute to loss of elastic recoil and

atelectasis, decreased pulmonary compliance, and increased right-to-left shunting. Alveolar dead space is increased with PTE because of non-perfused lung regions, and this leads to increased work of breathing.

History and Signalment

PTE affects any age or breed of animal because it is secondary to underlying disease processes that affect animals of different signalments. Immune-mediated hemolytic anemia (IMHA) tends to occur in young to middle-aged female dogs and cardiomyopathy is more common in younger cats, while pancreatitis tends to affect middle-aged to older dogs. Therefore, the underlying disease process will determine the age of an affected animal. History and clinical signs reflect the underlying disease process, however the acute onset of respiratory distress and tachypnea in a seriously ill animal should trigger suspicion for PTE. Recent trauma or surgery might also lead to PTE.

Physical Examination

Animals with PTE often display relentless tachypnea and breathlessness that is refractory to supplemental oxygen administration. Harsh lung sounds or loud bronchovesicular sounds can sometimes be detected; however, crackles or wheezes are less common. PTE can result in mild pleural effusion and rarely, dampened heart and lung sounds might be encountered. General physical examination findings usually reflect the underlying disease process. For example, pale mucous membranes are present in animals with IMHA, a heart murmur, arrhythmia, or gallop sound would be anticipated in the patient with cardiac disease, or a pot-bellied appearance could be found in the dog with Cushing's disease.

Diagnostic Findings

Diagnostic testing is directed at determining the underlying cause for embolization and assessing the severity of gas exchange abnormalities. A complete blood count (CBC), chemistry panel, and urinalysis are indicated to evaluate systemic health, while pulse oximetry or arterial blood gas analysis can be used to document

hypoxemia and hypocapnia. Cardiac biomarkers such as troponin have not proven helpful in the diagnosis of pulmonary embolization (Goggs et al. 2014). A coagulation panel is generally indicated in the work-up of suspected PTE to assess the intrinsic pathway (activated partial thromboplastin time: APTT; activated clotting time: ACT), the extrinsic pathway (one-stage prothrombin time: OSPT), and fibrin degradation products or D-dimer (see Figure 2.1). D-dimer, a breakdown product of cross-linked fibrin, has some utility in assessing the risk of embolization in humans, but unfortunately this assay performs poorly in dogs, with multiple disease processes leading to an elevated D-dimer (Epstein et al. 2013; Goggs et al. 2014). A very low or negative D-dimer is sensitive for ruling out PTE in humans, but a normal value can sometimes be found in affected dogs (Epstein et al. 2013). Antithrombin levels are also measured in animals at risk of PTE, because loss of this anticoagulant enhances the risk for clot formation. Thromboelastography, a coagulation test that can identify hypo- and hypercoagulable states by assessing the speed, efficiency, and strength of clot formation, has questionable value in documentation of PTE (Goggs et al. 2014), but might prove useful in management of patients at risk for PTE and for monitoring anticoagulant therapy.

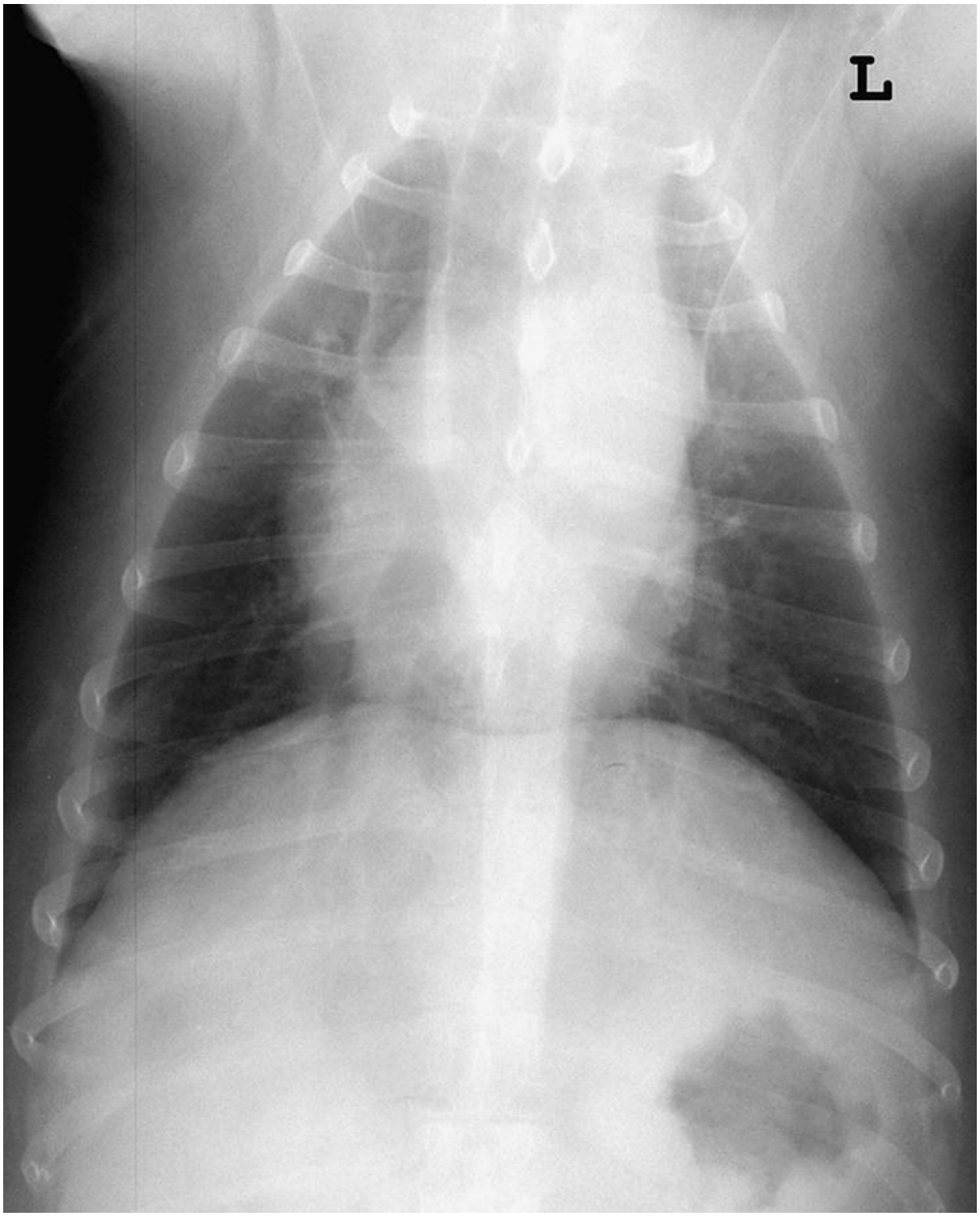


Figure 8.1 Dorsoventral film radiograph from a dog documented to have a pulmonary embolus in the lobar artery to the right caudal lung lobe. Note the lack of pulmonary infiltrates, pleural effusion, or any other vascular abnormalities.

Thoracic radiographs can be relatively unremarkable (Figure 8.1) and a variety of pulmonary infiltrates have been reported in dogs with thromboembolization, as well as mild pleural effusion. Review of thoracic radiographs will sometimes reveal pulmonary vascular abnormalities such as uneven distribution of perfusion or blunted pulmonary arteries. Detection of these abnormalities would facilitate early diagnosis in an animal with risk factors for PTE.

Confirmation of embolization is difficult and requires perfusion scanning with 99- technetium-labeled macroaggregated albumin (Figure 8.2), ventilation/perfusion scanning, or computed tomography pulmonary angiography (CTPA). Perfusion scanning could be a valuable clinical tool because it can be done in the awake animal; however, it is only available at specialty hospitals and requires radiation isolation after the scan, which could compromise care in an unstable patient. This technique has documented that pulmonary embolization is common in dogs after cemented total hip replacement (Liska and Poteet 2003); but it has not been evaluated for use in animals with cardiopulmonary disease or other risk factors for PTE. CTPA is used commonly in human medicine and has been employed in veterinary patients to establish filling defects in the pulmonary vasculature consistent with PTE (Goggs et al. 2014) but CT is not widely used because anesthesia is required to obtain a detailed, high speed helical scan with contrast injection. Echocardiography might be helpful in increasing suspicion for the diagnosis of PTE because a clot could be visible in the right atrium or pulmonary artery, or indirect evidence of right ventricular overload might be seen, such as right ventricular dilation, flattening of the right ventricular septum, or a high probability of pulmonary hypertension (PH).

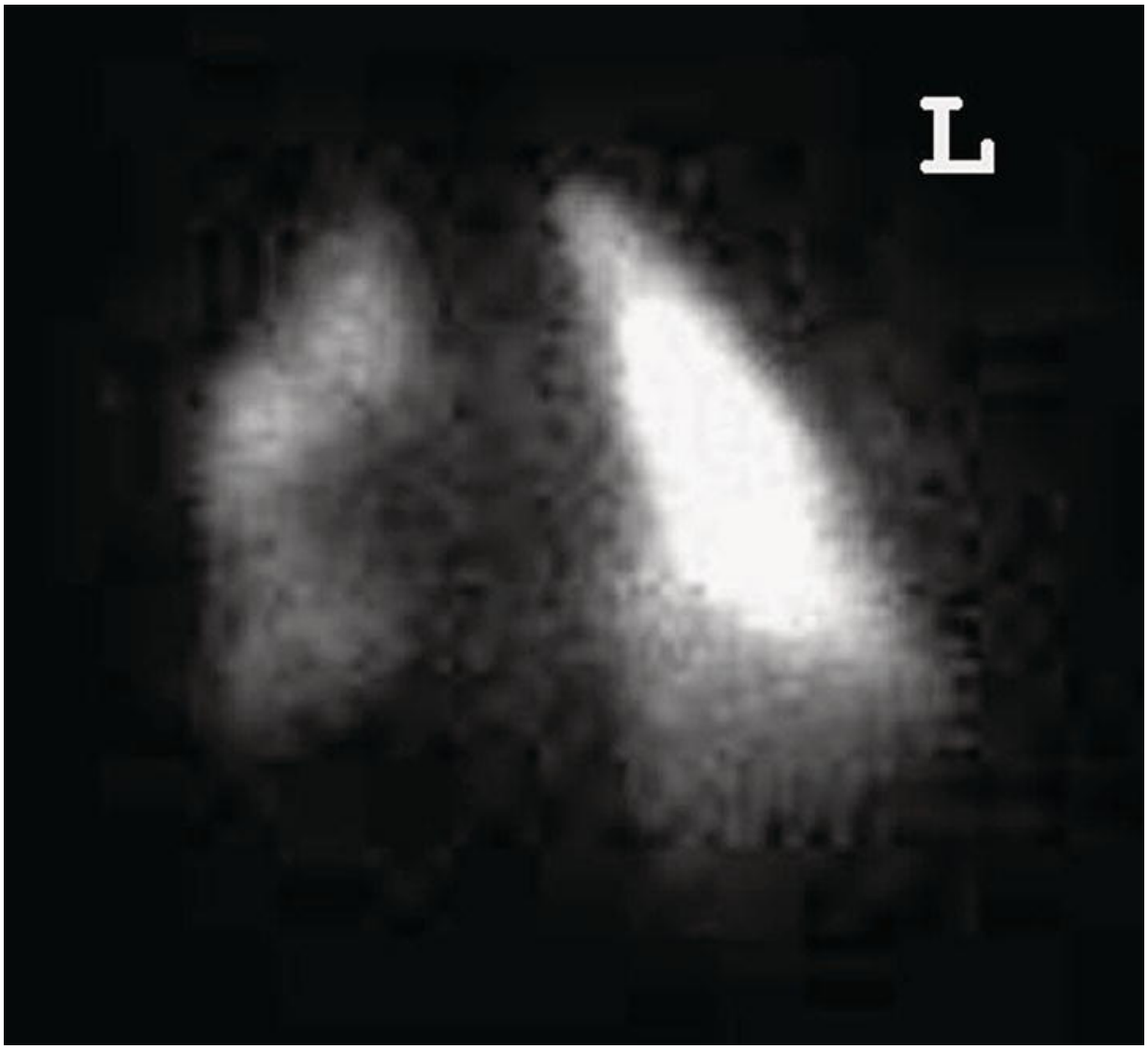


Figure 8.2 Perfusion scan from the dog depicted in Figure 8.1 indicates a lack of perfusion in the right caudal lung lobe, consistent with a major pulmonary embolus affecting the blood supply to that lung lobe.

Treatment

Control of the primary disease process is essential in managing PTE. Oxygen therapy is recommended for all animals initially, although the respiratory pattern may not improve dramatically because of alterations in central respiratory control, associated either with the physiology of embolization or due to central infarcts. Animals that do not have intrapulmonary shunting will show improved hemoglobin

saturation with oxygen while on supplementation; however, not all dogs with PTE are oxygen responsive (Johnson et al. 1999b).

Classically antiplatelet drugs would be indicated for venous clots such as PTE, while anticoagulants would be used for arterial emboli. Thromboembolism results in hypercoagulability due to both tissue factor activation of clotting and platelet activation, therefore multi-pronged treatment is utilized to reduce clotting and limit further deposition of fibrin on existing clots. Selection of specific medications often depends on the availability of drugs in an appropriate formulation and dose, the method of delivery preferred, side effects of the medications, and client finances.

Heparin bound to antithrombin inactivates some clotting factors – thrombin factor (IIa), factors Xa, IXa, XIa, and XIIa – and prevents further accumulation of fibrin on a clot. Subcutaneous heparin at an initial starting dose of 200–300 U/kg subcutaneously (SQ) two to three times a day (BID–TID) is administered to prolong the APTT two to three times the normal value, and dosing is tailored to the individual for maximal efficacy in clot reduction. However, in most hospitals, the use of heparin has been supplanted by administration of low-molecular-weight heparins (LMWH). Examples of LMWH agents include enoxaparin (Lovenox®, Sanofi-Aventis, Bridgewater, NJ) and dalteparin (Fragmin®, Pfizer, New York). This class of drug acts similarly to heparin in inhibiting further clot formation, but has greater inhibition of factor X versus factor II, and therefore does not prolong the APTT or theoretically result in hemorrhagic tendencies. Monitoring of drug efficacy requires an anti-factor Xa assay. Experimental studies in dogs have revealed improved antithrombotic efficacy of LMWH over unfractionated heparin, and use of enoxaparin (0.8 mg/kg SQ TID) in dogs with IMHA was well tolerated (Panek et al. 2015), although the extent to which embolization was prevented is unclear. In cats, LMWH given at standard doses (enoxaparin at 1 mg/kg SQ BID) resulted in plasma levels that approach the human therapeutic range 4 hours after dosing, while administration of dalteparin (100 IU/kg BID) resulted in less predictable levels (Alwood et al. 2007; Vargo et al. 2009). Enoxaparin was rapidly cleared, suggesting that more frequent administration could be required for effective anticoagulation in cats.

Rivaroxaban (Xarelto®, Janssen Pharmaceuticals, Beerse, Belgium), an oral direct-acting anti-Xa anticoagulant, is another agent that has been utilized in management and prophylaxis of PTE. In dogs with IMHA administered rivaroxaban at 0.9 mg/kg PO daily, no adverse effects were noted, although no differences were detected in rate of thrombosis or survival in comparison to those treated with clopidogrel and aspirin (Morassi et al. 2016). Apixaban, another direct factor Xa inhibitor, did not result in clinical bleeding when used in combination with clopidogrel in healthy Beagle dogs (Gagnon et al. 2021); however in sick, hospitalized patients, close clinical monitoring is advised in dogs administered any factor Xa inhibitor to avoid life-threatening gastrointestinal hemorrhage. Rivaroxaban was assessed as safe and well-tolerated in healthy cats when administered at 1.25–5.0 mg/day (Dixon-Jiminez et al. 2016), although studies in cats with embolic disease are lacking.

Antiplatelet therapy could also reduce the risk of clotting. A low dose of aspirin is used to inhibit cyclooxygenase activity without reducing endothelial cell production of prostacyclin. However, some dogs are genetically non-responsive to aspirin, which could impact the efficacy of this drug. Aspirin does not appear to be very effective in cats and it is difficult to dose. Drugs in the thienopyridine class are irreversible adenosine diphosphate (ADP) receptor/P2Y12 inhibitors that reduce platelet activation. One such drug, clopidogrel (Plavix®, Sanofi, Paris, France) is safe and effective at inhibiting platelets in *healthy* cats at oral dosages of 18.75–75 mg once daily (Hogan et al. 2004), and various experimental studies in dogs at 2–4 mg/kg/day have shown that it reduces clotting. The efficacy of these drugs to treat or prevent embolization in animals with clinical disease remains uncertain.

With increasing certainty of the diagnosis of PTE or worsening condition of the patient, more aggressive therapy with a fibrinolytic agent such as tissue plasminogen activator (TPA) can be considered, and TPA has proven effective in limiting physiologic derangements associated with systemic embolization (Diaz et al. 2022). The efficacy of this therapy has not been fully established in animals with PTE, and in human medicine, fibrinolytic therapy is reserved for patients with hemodynamic instability.

Prognosis

Development of PTE is associated with a guarded prognosis, and mortality is high. Because of poor success in the treatment of PTE, prophylactic anticoagulant therapy should be considered in animals with diseases that have been shown to predispose to the condition. Clopidogrel is advised for platelet inhibition. LMWH and rivaroxaban are more costly but can also be used for prophylaxis when the risk of embolization is high.

Infectious Disorders

Canine Heartworm Disease

Pathophysiology

Canine heartworm disease is a condition with essentially worldwide distribution, depending on the presence of the mosquito vector. It is most common in warm, humid environments, with the highest infection rates along the east coast of the USA, Gulf States, and Mississippi river valley. Southern Europe, Japan, China, India, South America, and Southeast Asia also have a large number of heartworm cases, as do other regions of the world where preventative medications are not widely used. Mosquitos deposit third-stage larvae of *Dirofilaria immitis* under the skin. The larvae migrate into the right heart and pulmonary arterial system, where they develop into adult worms and begin producing microfilaria 5–7 months after infection. High worm burden is common in infected dogs, and disease results from obstruction of pulmonary arteries followed by right ventricular failure due to pressure overload. Heartworms also trigger pulmonary endothelial damage that can stimulate clot formation, with subsequent thromboembolization. Physical damage to the adult worm or death of the adult can lead to worm embolization. Heartworms also trigger a pulmonary hypersensitivity response that results in eosinophilic inflammation in the parenchyma. Antigen–antibody complex deposition in the kidneys can lead to a protein-losing nephropathy, and heartworm infection can also cause hepatocellular damage.

Dirofilarial organisms commonly harbor the endosymbiont bacterium *Wohlbachia*, which helps the tissue larvae develop and survive and also aids adults in reproduction. This Gram-negative, intracellular organism is thought to contribute to the inflammatory response of heartworm infection through activation of neutrophils and monocytes, and it could play a role in the pulmonary vascular pathology induced by heartworm infection. Thus, treatment of *Wohlbachia* is often employed to lessen the inflammatory response to death of dirofilarial organisms during heartworm treatment.

History and Signalment

Heartworm disease can be detected in dogs with no clinical complaints, or owners may note coughing, exercise intolerance, or an abnormal breathing pattern. Dogs with severe infections develop hemoptysis and signs of right-sided heart failure, PH, or pulmonary embolization that can include respiratory distress, abdominal distention, and syncope.

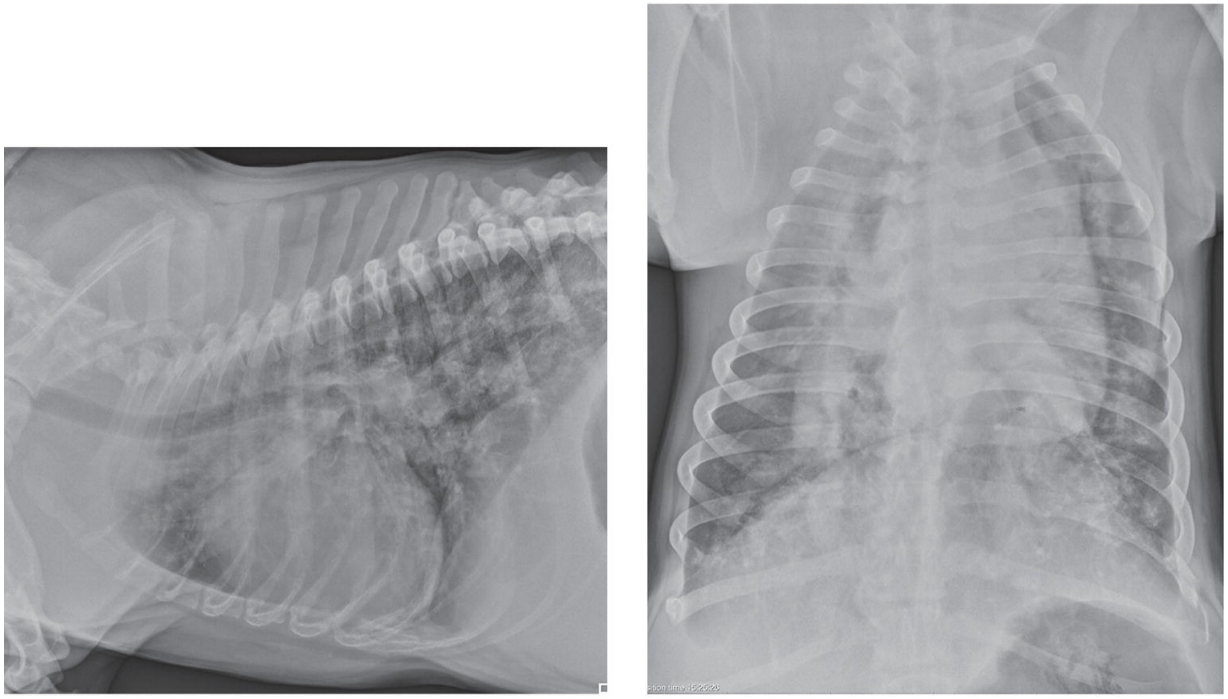
Physical Examination

Dogs sometimes lack any physical evidence of heartworm disease. In dogs with mild disease, tracheal sensitivity can be present. With progressive severity of infection, dogs can appear cachectic and display manifestations of right-sided heart failure, including ascites or hepatomegaly, icterus, jugular venous distension, a heart murmur or gallop sound, loss of lung sounds due to pleural effusion, or crackles associated with parenchymal disease.

Diagnostic Findings

Peripheral eosinophilia is commonly detected on a CBC in infected dogs. Chemistry panel and urinalysis should be closely scrutinized for evidence of liver dysfunction (indicated by an increase in alanine transaminase) and renal involvement (indicated by elevated blood urea nitrogen, increased creatinine, or the presence of proteinuria). When proteinuria is detected, a urine protein-to-creatinine ratio is recommended to gain an appreciation of the severity of glomerulonephritis.

Microfilaria can be detected by a modified Knott's or filter test; however, microfilaremia will be found only in infected dogs that are not on heartworm-preventive medication. Therefore, because most dogs are on some form of preventive, an antigen test is the recommended screening test. The test will be positive 6–7 months after infection, although a false-negative antigen test can be encountered with infection by immature worms or by all male worms. In addition, formation of an antigen–antibody complex can interfere with identification of heartworm antigen in point-of-care tests. These immune complexes might be related to the inherent immune response of the individual dog or might result from administration of avermectins or doxycycline. A heat-precipitated antigen test should be performed when there is a high suspicion of heartworm disease in a dog with a negative antigen test. When a positive antigen test is obtained, whole blood should be assessed for microfilaria.



(a) (b)

Figure 8.3 (a) Right lateral and (b) dorsoventral radiographs from a 4-year-old castrated male (MC) Pitbull Terrier with class 3 heartworm disease. There is severe enlargement of pulmonary arteries, and they are tortuous as well as blunted. A diffuse, nodular interstitial pattern is present. Right-sided cardiomegaly is present along with distention of the caudal vena cava. Diffuse pulmonary infiltrates are noted along with mild enlargement of the liver.

Radiographic findings in canine heartworm disease vary depending on the severity of disease. Pulmonary arteries become progressively enlarged, blunted, and tortuous, parenchymal infiltrates progress, and right ventricular enlargement develops (Figure 8.3). Echocardiography detects the walls of the heartworm as parallel lines (Figure 8.4) and can demonstrate signs of right ventricular overload, including right ventricular dilatation, tricuspid regurgitation, and PH.

Treatment

Prior to adulticidal treatment, the severity of disease should be staged and clinical signs stabilized as indicated. Class 1 dogs are mildly affected, with few clinical signs and normal radiographic and

laboratory findings. Class 2 dogs are moderately affected with cough or respiratory difficulty, have right heart enlargement on radiographs, and have abnormal laboratory values such as anemia or elevated liver enzymes. Class 3 dogs are severely affected with signs of right heart failure, severe radiographic abnormalities, and marked laboratory abnormalities. Class 4 dogs are those with caval syndrome.

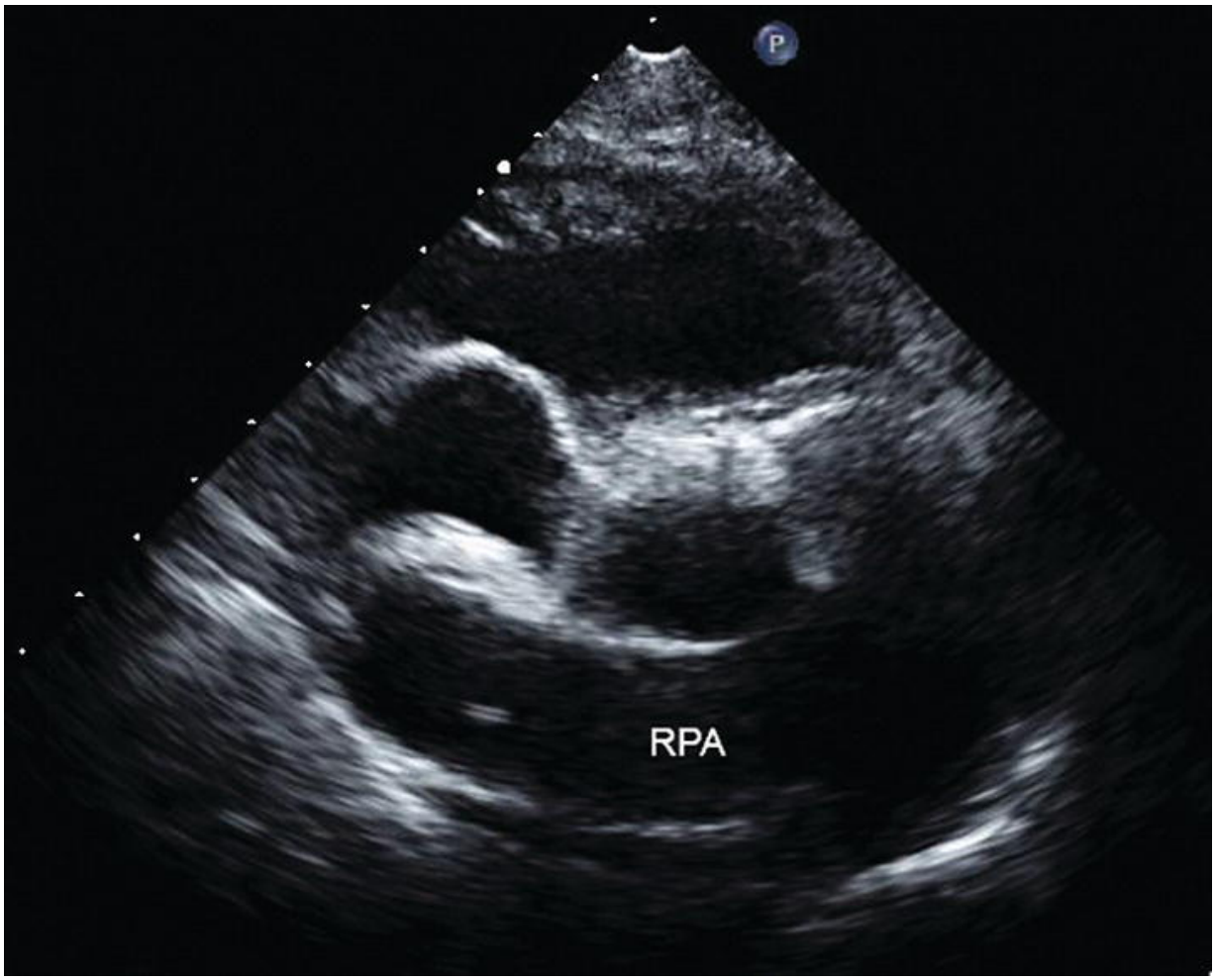


Figure 8.4 Echocardiographic image from the dog depicted in Figure 8.3 demonstrates parallel lines in the right pulmonary artery (RPA) characteristic of heartworm infection.

Melarsomine dihydrochloride is the approved adulticidal treatment for canine heartworm disease. The American Heartworm Society recommends use of doxycycline (10 mg/kg PO BID) for 1 month and a macrocyclic lactone for 2 months (an avermectin or milbemycin) prior to a split-dose protocol. This protocol entails administration of

one deep intramuscular injection followed 1 month later by two intramuscular injections on alternate sides of the spine 24 hours apart. To perform the injection, a region on the spine between the third and fifth lumbar vertebrae is clipped and prepared with a surgical scrub. Following injection of melarsomine (2.5 mg/kg), the dog is confined in the hospital, with monitoring of respiratory rate and effort as well as for any other adverse effects. For dogs with persistent clinical signs and a positive antigen test after the set of two injections, a second treatment can be given in 4 months. Class 3 dogs appear to be at higher risk for embolization and can require further stabilization with oxygen, diuretics, vasodilators, inotropes, and corticosteroids as indicated prior to adulticidal treatment. Use of anticoagulants is controversial. Class 4 dogs are those with caval syndrome, and melarsomine is not recommended for these dogs. Stabilization and physical removal of worms by an interventional cardiologist are required.

All owners should be cautioned about the possibility of embolic disease following treatment and should understand the need for cage confinement for 1–2 months after treatment to limit the occurrence of this complication. Monthly preventive medication is continued in dogs with occult infection. If microfilaria are present, the initial dose of preventive medication should be given to the dog while hospitalized to monitor for adverse effects. Treatment recommendations for canine heartworm disease are continually updated and can be found at www.heartwormsociety.org.

A non-arsenical treatment option that can be pursued utilizes topical 10% moxidectin/2.5% imidacloprid twice monthly for 3 months and then monthly along with doxycycline (10–15 mg/kg/day for 15 days) for *Wohlbachia* (Ames and Atkins 2020). Using this protocol, most dogs had converted to heartworm antigen negative status within 13 months and lacked detectable microfilaria. Exercise restriction is also warranted when using this slow kill protocol.

Any circulating microfilaria or developing larvae (L3 and L4) are eliminated over 6–9 months through administration of heartworm-preventive medications. Ivermectin and milbemycin oxime are oral preparations given monthly and administered year round to help limit the spread and expansion of heartworm in the environment.

Milbemycin is preferred for Collies or any Collie-type dogs that might have the deletion mutation of the *mdr1* (multi-drug-resistance-1) gene. Selamectin and moxidectin are topically administered drugs that prevent heartworm disease. Moxidectin is also available as an injectable product that provides 6 months of prevention.

Prognosis

Dogs with mild to moderate heartworm disease have a good prognosis for uneventful treatment and full recovery, although melarsomine can be associated with various toxicities, including injection site reaction and neurologic signs (Hettlich et al. 2003). Dogs with class 3 and 4 disease are at increased risk for embolization during and after treatment and can develop long-term cardiopulmonary disease associated with pulmonary arterial damage.

Heartworm-preventive medications remain highly efficacious against heartworm infection, although they are not always 100% effective and emerging resistance to medications is becoming increasingly apparent (Snyder et al. 2011; Blagburn et al. 2016). Lack of owner compliance or failure to ingest the appropriate dose plays a role in development of infection despite use of preventative medication. This might be reduced by use of extended-release injectable formulations, however, inherent resistance of new strains of heartworm cannot be completely ruled out.

Feline Heartworm Disease

Pathophysiology

The initial life cycle of heartworm in the cat is similar to that in the dog, with deposition of L3 larvae under the skin, followed by development into adult worms in the pulmonary artery approximately 4 months after infection. However, in the cat, infection with only one to two or up to six adult worms is typical and single-sex infection is common. This feature, along with an augmented host response to the microfilaria, might explain the lack of microfilaremia in most cats. Antibody production can be detected

within 2–3 months of infection, and heartworm antigen is present from 6 to 8 months post-infection.

Arrival of immature adult worms in the pulmonary circulation has been proposed to stimulate an immune response within the vasculature that leads to clinical signs of cough or respiratory difficulty (Dillon et al. 2017). This has been referred to as heartworm-associated respiratory disease (HARD), and clinical signs diminish as the worms mature. Similar to the dog, *Wohlbachia* species could play a role in the development of pulmonary pathology and resultant clinical signs in cats.

Cats do not attract mosquitos to the same extent as dogs and only 15–25% of cats develop infection after injection with *D. immitis* larvae. Many infected cats display no clinical signs and will self-cure within 2–3 years; however, serious consequences have been reported with feline heartworm disease. Sudden death might result from an anaphylactic response to internal filarial antigens released with worm death (Litster et al. 2008). Interestingly, aberrant migration of heartworm larvae is relatively common in the cat, and cerebral infection is another potential cause for sudden death in cats.

The prevalence of heartworm disease in the cat relative to the dog is difficult to assess because documentation of disease remains elusive due to features of the tests themselves as well as the lack of routine screening. In an endemic area of Italy, prevalence of heartworm infection in cats was approximately 10% that of dogs (Venco et al. 2011), while in southern Florida in the USA, the ratio was approximately 1 case in cats for every 7 in dogs (Hays et al. 2021). The difficulty in confirming a diagnosis of heartworm disease in the cat was acknowledged in both studies. A recent serosurvey of heartworm exposure reported antibody positivity in 3.5% of healthy cats lacking clinical signs of disease, with the highest seropositivity in the western United States (Murillo et al. 2023). Seroprevalence of antigen positivity in North America also varies with geographic location. The highest number of positive results on a standard point-of-care enzyme-linked immunosorbent assay (ELISA) was found in cats from the Hawaii, central west region, and southern USA (up to 1.6%) and the lowest (0%) in cats from Canada (Levy et al. 2017).

History and Signalment

Both indoor and outdoor cats can be infected with heartworm through mosquito exposure, although outdoor cats are at higher risk. Young to middle-aged cats are affected most commonly, but cats of any age can be infected. The majority of cats do not develop disease associated with heartworm, but it has been recognized as a cause of a multitude of clinical signs, including chronic cough, acute respiratory distress, chronic tachypnea, vomiting unrelated to eating, neurologic signs related to aberrant migration, and lethargy. Unfortunately, sudden death can also occur, and in some cats respiratory or gastrointestinal signs are noted immediately before death.

Physical Examination

There are no specific physical examination findings that characterize feline heartworm disease. Cats could display tracheal sensitivity or adventitious lung sounds associated with airway or pulmonary disease but these are non-specific.

Diagnostic Findings

Diagnosis of feline heartworm disease remains difficult. Peripheral eosinophilia is present in <50% of cases. Radiographic findings in feline heartworm disease are reflected by enlargement of caudal pulmonary lobar arteries to greater than 1.6 times the size of the ninth rib (Figure 8.5). However, in some cases pulmonary infiltrates can obscure visualization of the vasculature, and in one study of naturally infected cats, abnormalities in the pulmonary vasculature were uncommon (Venco et al. 2008). Unlike dogs, cardiac chambers are unlikely to be changed by heartworm infection. Focal or diffuse bronchointerstitial infiltrates are the most common parenchymal changes in cats with heartworm, but the presence and type of infiltrates depend on the stage of disease (Venco et al. 2008).

Heartworm antibody positivity indicates only exposure to heartworm, and false-negative tests are unfortunately common. The antigen test can detect a single female heartworm, but can be falsely negative when no females are present or when only a few live males are present. Also, antigen–antibody complex formation appears to be more problematic in cats than in dogs, and heat-treating serum leads

to a substantial increase in positive antigen tests in infected cats (Little et al. 2014). This methodology is not advised as a screening test however, because of an increase in false-positive results. Heartworm disease can be diagnosed on echocardiography by the presence of two parallel hyperechoic lines in the right ventricle or pulmonary artery, as in the dog depicted in Figure 8.4.

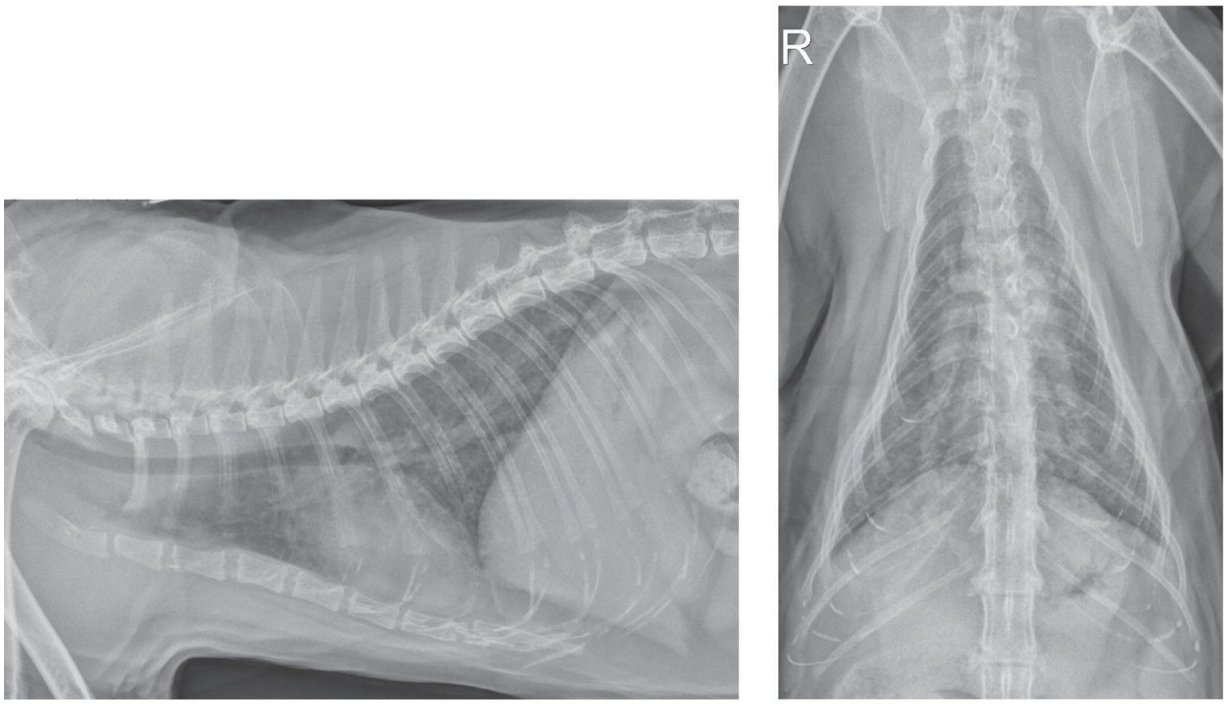


Figure 8.5 (a) Right lateral and (b) dorsoventral radiographs from a 5-year-old male castrated domestic short hair (MC DSH) presented for a 4-day history of non-productive cough. Radiographs reveal a diffuse, marked bronchial pattern, with a subtle nodular component. The caudal lobar pulmonary arteries are enlarged with respect to the corresponding veins and mild cardiomegaly is present. This cat was antibody positive, antigen positive, and positive on echocardiography for heartworm disease.

Treatment

Treatment of feline heartworm disease is based on control of clinical signs. Monthly ivermectin (24 μg/kg) for 2 years might help reduce the worm burden by inducing a slow kill of heartworm, and use of doxycycline for 1 month is effective in controlling *Wohlbachia*

infection and the inflammation this endoparasite induces. The pulmonary hypersensitivity response can be treated with prednisolone as required while waiting for the heartworms to die (generally within 2–4 years). In an acute presentation of respiratory distress, intravenous corticosteroids, terbutaline, and oxygen therapy should be provided. Use of aspirin is not advised because its role in preventing embolic disease has not been established, and it should not be administered concurrently with steroids. For potential embolic complications, clopidogrel would be recommended.

Adulticidal therapy is not recommended in cats because melarsomine has not been fully evaluated and it is likely toxic to cats. For cats with severe signs associated with pulmonary artery obstruction, physical removal of worms from the heart through jugular venotomy and use of intravenous snares or baskets can be performed when the worms are accessible. Caution is warranted to prevent breakage of the worm during removal and possible anaphylaxis.

Radiographs and serology should be repeated every 6–12 months until pulmonary lesions have resolved and the antigen test is negative.

Prognosis

Many cats appear to tolerate infection with heartworm without development of clinical signs and the immune system will clear the infection over several years. Some cats develop severe refractory clinical signs, and feline heartworm disease can cause sudden death in 20–30% of cats with clinical signs. For cats at risk of infection, monthly ivermectin (24 μg/kg orally [PO]), milbemycin oxime (2 mg/kg PO), selamectin (6–12 mg/kg topically), or 10% imidacloprid/1% moxidectin (applied topically) given year-round can afford protection against feline heartworm disease. Treatment can start at 8 weeks of age. Preventive treatment may also reduce worm burden in cats that are already infected. Updated guidelines on feline heartworm disease are available from the American Heartworm Society website.

French Heartworm Disease

Pathophysiology

Vascular infection with the metastrongyloid worm *Angiostrongylus vasorum* is responsible for the disease known as French heartworm disease. The worm is endemic in certain parts of the UK, Europe, Africa, and South America and has spread to Newfoundland, Canada (Chapman et al. 2004; Bourque et al. 2008). *Angiostrongylus* has been characterized by progressive spread across the world. The red fox is likely an important reservoir of infecting organisms (Elsheikha et al. 2014). *Angiostrongylus* infects dogs and foxes as its definitive host and is spread through ingestion of intermediate or paratenic hosts, including slugs, snails, and frogs that contain infective third-stage larvae. Larvae are released in the dog's intestine, migrate to intra-abdominal lymph nodes, and gain access to the portal circulation. L4 travel to the pulmonary artery, right heart, or pulmonary arterioles, where development into the adult stage is completed. The pre-patent period is typically 40–60 days but can be in excess of 3 months. Adults produce eggs that hatch to first-stage larvae, penetrate the alveoli, are coughed up and swallowed, and then pass in the feces to be taken up by the intermediate host. Maturation into infective L3 then occurs in the intermediate host.

Respiratory disease results from the inflammatory response induced by migration of the larvae, which causes granulomatous interstitial pneumonia and thrombotic disease (Bourque et al. 2008). Right heart failure appears to be less common than that seen with *D. immitis*, perhaps because of the smaller size of *Angiostrongylus* (1.5–2 cm). A hemorrhagic diathesis has also been reported with *Angiostrongylus* infection, resulting in epistaxis, hemoptysis, petechiae, and ecchymoses. The precise mechanism for this is unclear, but it may be related to a consumptive coagulopathy. Neurologic signs have also been reported (due to hemorrhage or infection by *A. cantonensis* or other species), and granulomatous lesions can occur in the liver and kidneys, reflecting systemic infection by the parasite.

History and Signalment

Outdoor dogs and those that hunt are exposed to possible infection more commonly than other dogs; however, both urban and rural dogs can be affected (Chapman et al. 2004). Infection seems more common in younger dogs (<1 year of age) and dogs are presented for a combination of signs, including coughing, exercise intolerance, respiratory distress, evidence of hemorrhage (ecchymotic hemorrhages, hemoptysis, gingival bleeding), and/or syncope. Non-specific findings such as lethargy, anorexia, and weight loss are also common.

Physical Examination

Dogs with a bleeding diathesis will display ecchymotic hemorrhage in the subcutis, conjunctiva, sclera, or mucous membranes. Overt bleeding from mucosal surfaces may be present. With severe bleeding, anemia can develop, resulting in pale mucous membranes. Pneumonia is responsible for tachypnea and respiratory difficulty. Abnormal or harsh lung sounds may be auscultated. Rarely cardiac failure, PH, or myocarditis can develop resulting in a murmur or gallop sound or an arrhythmia.

Diagnostic Findings

Eosinophilia or neutrophilia can be detected on a CBC and hyperglobulinemia is relatively common (Chapman et al. 2004). A platelet count should be assessed in dogs suspected of angiostrongylosis, because thrombocytopenia is common and can be as severe as that encountered in immune-mediated thrombocytopenia. A coagulation panel (OSPT, APTT) is recommended given the possibility for infection to result in a coagulopathy, and a thromboelastogram can be helpful for identifying a hypocoagulable state. Thoracic radiographs generally show a bronchoalveolar pattern that is often concentrated in the caudodorsal lung fields. The pulmonary pattern depends on the duration of infection and reflects the pulmonary hypersensitivity response to larval migration. Fibrotic lesions can develop over time. Right ventricular enlargement can be found when severe pulmonary

artery obstruction occurs, but this is rare. Echocardiography is useful for identifying PH (see later).

Infection with this helminth can be confirmed through the use of a fecal Baermann analysis for L1 stages. However, larvae will not be present in the pre-patent period and a single fecal test has poor sensitivity for documenting infection. Pooling of feces over 3 days has been advised. FLOTAC, a flotation-based fecal examination that uses a high-specific-gravity solution, has improved sensitivity for documenting parasite eggs and larvae (Schnyder et al. 2011). An antigen-based serum ELISA is sensitive and specific, and this test will be positive approximately 5 weeks post-infection. Dogs with *D. immitis* can cross-react on this test. Serologic assessment of antibodies to *Angiostrongylus* is available and can be of use in select cases. Quantitative polymerase chain reaction on bronchoalveolar lavage fluid can be used to confirm the diagnosis when other tests are negative (Canonne et al. 2016), although dogs might not always be stable enough for collection of an airway sample.

Treatment

Successful treatment of *Angiostrongylus* infection has been reported with a single dose of 0.1 ml/kg imidacloprid 10%/moxidectin 2.5% spot-on solution or with fenbendazole (25–50 mg/kg PO for 20 days; Chapman et al. 2004; Willesen et al. 2007). Milbemycin oxime combined with praziquantel is also effective when administered orally PO for 4 weeks. Moxidectin and milbemycin can be used monthly to prevent *Angiostrongylus* infection. Depending on the severity of clinical signs and pulmonary infiltrates, additional therapy with corticosteroids, intravenous fluid support, and oxygen can be required. Cases with serious coagulopathies can require fresh frozen plasma or blood transfusions.

Prognosis

Dogs with low worm burdens can remain sub-clinical. Animals with severe radiographic changes, marked respiratory difficulty, or syncope have a guarded prognosis for recovery. It appears that dogs surviving to discharge experience few residual effects of disease.

Miscellaneous Disorders

Pulmonary Hypertension

Pathophysiology

PH is defined by a peak pulmonary arterial systolic gradient that exceeds 32 mmHg. Typically, probability of the diagnosis is based on echocardiographic interrogation of the velocity of a tricuspid regurgitant jet along with subjective changes in the right ventricle and pulmonary artery (Reinero et al. 2020). Classifications of PH include pulmonary arterial hypertension (usually of idiopathic origin), pulmonary venous hypertension associated with increased left atrial pressure, PH associated with respiratory disease, PH associated with thrombosis, PH caused by parasitic disease, and miscellaneous causes of PH. Idiopathic pulmonary arteriopathy resulting in PH has been reported rarely in the veterinary literature (Glaus et al. 2004; Zabka et al. 2006). Pulmonary venous hypertension associated with left heart disease is relatively common, although the elevation in pulmonary artery pressure (PAP) is often mild to moderate. PH associated with respiratory disease results from increased vascular resistance and occurs with a number of disease processes.

In veterinary medicine, the most well-recognized cause of PH is canine heartworm disease, which represents a form of embolic or vascular obstructive PH. PH has been described in association with a variety of respiratory diseases, including pneumonia in young dogs, chronic tracheobronchial disease, and suspected interstitial lung disease (Johnson et al. 1999a; Pyle et al. 2004; Jaffey et al. 2019; Johnson and Stern 2020). It also occurs in some dogs with brachycephalic obstructive airway disease. The proportion of dogs with these primary conditions that develop PH is unknown, although it has been estimated that greater than 40% of West Highland White Terriers with presumed idiopathic pulmonary fibrosis and ~40% of dogs with mitral valve disease causing increased left atrial pressure and pulmonary venous hypertension will have elevation in PAPs (Schober and Baade 2006; Borgarelli et al. 2015). It seems likely that

genetic and environmental influences play a role in the generation of vascular injury and subsequent PH in these common conditions.

PH also occurs in cats although it is not as clinically recognizable in cats as it is in dogs, perhaps because cardiac chambers are not often visibly enlarged radiographically or because syncope is less commonly witnessed in cats. Similar underlying disease processes can result in PH in cats, including congenital heart disease (VSD, PDA, ASD) and chronic left-sided congestive heart failure due to cardiomyopathy (Vezzosi and Schober 2019) as well as pulmonary fibrosis, thromboembolic disease, infectious or parasitic pneumonia, and feline bronchial disease.

PH has also been described as pre-capillary, resulting from a disease in the pulmonary arterial bed, and post-capillary, which relates to pulmonary venous hypertension. Pre-capillary PH occurs in conditions associated with normal left atrial pressure, while post-capillary PH develops when left atrial pressure is high, such as in mitral valve disease or cardiomyopathy. This categorization suggests active (arterial) versus passive (venous) influences on pulmonary vascular pressures; however, some conditions are associated with both pre- and post-capillary influences.

History and Signalment

PH develops most commonly as a secondary condition and any age or breed of dog can be affected. Young animals with congenital cardiac shunts or mitral stenosis are at risk, and puppies or kittens with severe pneumonia (bacterial or parasitic) can also develop PH. Adult animals with mitral insufficiency, cardiomyopathy, or chronic pulmonary disease can develop PH at any stage during the course of disease. West Highland White Terriers with interstitial lung disease are particularly predisposed to develop PH. A history of acute or chronic heartworm disease places an animal at increased risk for pulmonary vascular disease.

Clinical signs and historical complaints generally reflect the underlying cardiac or pulmonary conditions; thus, the majority of animals have non-specific complaints of cough, respiratory distress, or lethargy. Interestingly, syncope appears to be a relatively common

finding in dogs and should raise suspicion for the presence of PH. The mechanisms surrounding syncope are poorly understood and multiple factors could play a role. Reduced cerebral blood flow could lead to collapse. Low cardiac output caused by poor filling of the left ventricle or by development of an arrhythmia from myocardial ischemia could be important. A baroreceptor reflex causing inappropriate bradycardia during times of exertion might occur in PH, potentiating collapse. Also, respiratory disorders resulting in PH are commonly associated with cough, which can cause vagally-mediated syncope. It is not uncommon for syncope to be mistaken for a seizure disorder. Seizures can be differentiated from syncope by the presence of pre- and prodromal behavioral abnormalities and prolonged recovery from the collapsing event whereas collapse due to PH is more spontaneous and animals recover almost immediately.

Physical Examination

Abnormalities on physical examination usually reflect the cardiopulmonary disease responsible for development of PH. Cyanosis can be present in animals with severe respiratory disease. Auscultation can reveal harsh crackles and possibly expiratory wheezes with tracheobronchomalacia or pneumonia, or perhaps fine crackles, tachypnea, and tachycardia with pulmonary edema of congestive heart failure. A left or right-sided apical systolic murmur is common in older animals with myxomatous valvular disease or cardiomyopathy and generally represents a non-specific finding. Cats tend to have loud heart murmurs with congenital disorders. A prominent second heart sound is occasionally heard as the pulmonic valve closes against elevated pressure. Animals can develop right heart failure from PH and display jugular venous distention or ascites. Heart and lung sounds can be muffled when pleural effusion is present.

Diagnostic Findings

Laboratory evaluation is directed toward identification of underlying disease conditions that could be associated with PH. A neutrophilic leukocytosis could be related to the primary disease process or might reflect a stress response. The presence of immature neutrophils on a CBC can suggest infectious pneumonia, and peripheral eosinophilia

indicates that heartworm disease and eosinophilic or parasitic pneumonia should be considered. An occult heartworm test is always recommended when PH is suspected and, if negative, a heat-treated heartworm test is advised. Urinalysis might reveal proteinuria related to primary or secondary glomerular injury. When a urine protein-to-creatinine ratio exceeds the normal value (1.0), loss of antithrombin through the urine should be investigated, because this could lead to a hypercoagulable state. Thus coagulation testing is advised in most cases of PH, including OSPT, APTT, D-dimer, and antithrombin levels. Thromboelastography should also be considered to assess the kinetics of clot formation. Pulse oximetry or an arterial blood gas analysis would support hypoxemia or acidosis as factors contributing to PH. Additional diagnostic testing would be focused on identifying specific underlying conditions.

Thoracic radiographs show a variety of abnormalities in PH, but none that are pathognomonic for the condition. Cardiomegaly, particularly right ventricular enlargement, pulmonary infiltrates, and large pulmonary arteries are expected, particularly in dogs with PH (Figure 8.6), although these changes are non-specific. Cats with enlarged caudal pulmonary arteries and pulmonary veins in combination with pulmonary infiltrates are commonly diagnosed with left congestive heart failure rather than PH (Diana et al. 2022). An electrocardiogram (ECG) might reveal a right-axis deviation pattern (deep S waves in leads 1, 2, 3, and aVF) if right ventricular enlargement is severe, although detection of electrocardiographic changes is also variable. Both atrial and ventricular arrhythmias can occur in dogs with PH and are related to the primary cardiac disease or secondary cardiac injury from hypoxia.

Definitive documentation of PH requires catheterization of the right heart with an end-hole Swan Ganz balloon-flotation catheter, however this is rarely done in clinical practice due to the need for sedation or general anesthesia. Instead, Doppler echocardiography can be used for non-invasive prediction of the probability of PH when a high-velocity regurgitant jet across the tricuspid or pulmonic valve is detected. Pulmonic stenosis must be ruled out to utilize this methodology. Systolic or diastolic PAP is estimated by application of the modified Bernoulli equation (Eq. 8.1) to the maximal velocity of

regurgitant flow across the tricuspid or pulmonic valve. A peak tricuspid regurgitant velocity ≥2.8 m/s estimates a systolic PAP ≥32 mmHg (Figure 8.7) and a pulmonic insufficiency velocity ≥2.2 m/s estimates a diastolic PAP ≥20 mmHg, either of which is consistent with PH. Right atrial pressure can be estimated clinically and added to the Doppler-derived pressure gradient to provide a closer approximation of PAP, although this is not always performed because standards are not available for assessment of right atrial pressure.

$$\Delta P = 4 \times \left(\text{velocity}\right)^2 \tag{8.1}$$

where $\Delta P(\textit{systolic})$ is the right ventricular–right atrial pressure gradient when the velocity of tricuspid regurgitation is used, and $\Delta P(\textit{diastolic})$ is the right ventricular–PAP gradient when pulmonic insufficiency is used. Velocity is in meters per second. An estimated systolic PAP from 36 to 50 mmHg is often referred to as mild, while 50–75 mmHg is moderate PH, and >75 mmHg is categorized as severe PH (Johnson et al. 1999b). Echocardiography is subject to variability due to misalignment of the Doppler signal with flow and right ventricular systolic dysfunction as well as operator experience and patient characteristics. This is likely the reason that syncope and quality of life scores had no correlation with the estimated PA pressure, and tricuspid regurgitant velocity showed only a weak negative association with survival (Johnson and Stern 2020).

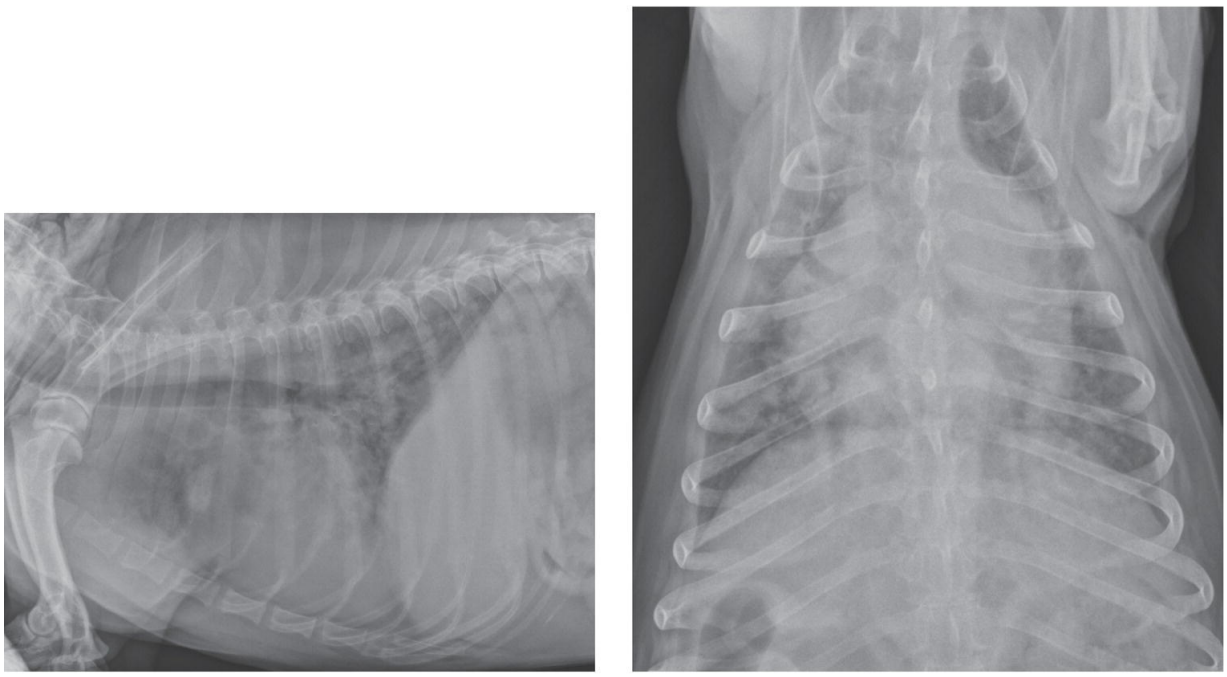


Figure 8.6 (a) Right lateral and (b) dorsoventral radiographs from a 13-year-old spayed female (FS) Terrier mix dog presented for tachypnea and collapse demonstrate diffuse, coalescing bronchoalveolar infiltrates throughout the lung regions. There is mild right heart enlargement and a prominent main pulmonary artery bulge at the 1:00 position. Doppler echocardiography revealed an estimated right ventricular-right atrial pressure gradient of 70 mmHg. Pulmonary hypertension (PH) in this case was thought to have developed secondary to interstitial fibrosis.

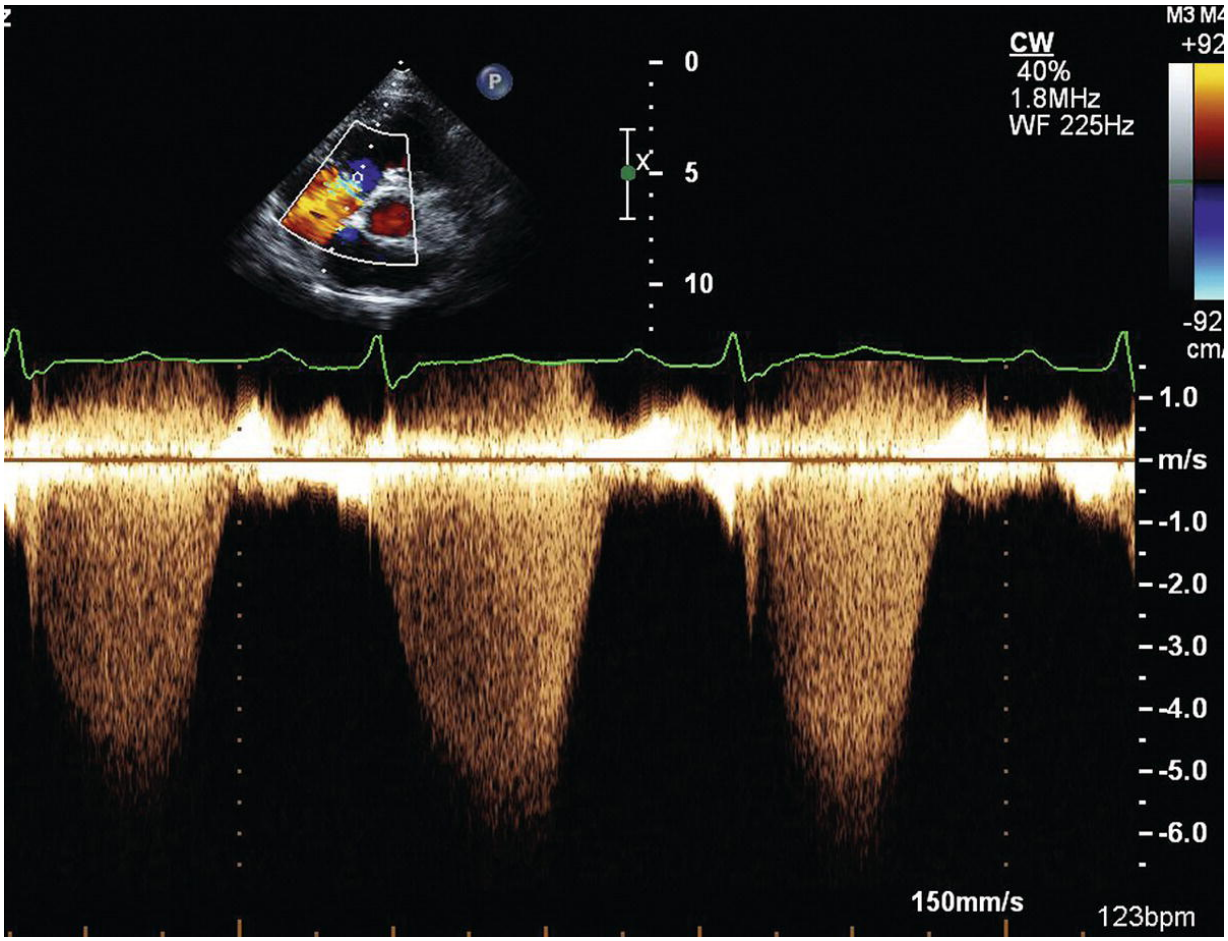


Figure 8.7 Doppler echocardiography reveals tricuspid regurgitation with an instantaneous maximal velocity of 5.1 m/s (right ventricular–right atrial pressure gradient of 104 mmHg).

The right pulmonary artery distensibility (RPAD) index is another echocardiographic parameter that can be used to assess the probability of PH and is particularly useful when tricuspid regurgitation is absent (Visser et al. 2016). The RPAD index calculates the percent change in diameter of the right pulmonary artery (RPA) between systole and diastole. A change of ~40% is found in normal dogs, while the value is decreased to ~27% in moderate PH and ~9% in severe PH (Visser et al. 2016).

Subjective echocardiographic parameters aid in assigning intermediate or high probability status of at least moderate PH (Reinero et al. 2020). When pulmonary pressures are elevated, the main pulmonary artery and RPA are typically dilated (Figure 8.8) and a distinctive change is noted in the velocity profile of blood flow

across the pulmonic valve, with an increased rate of rise in pulmonary pressure (Figure 8.9). The deceleration phase can be rapid, or a delayed deceleration with mid-systolic notching can be seen. Right ventricular dilatation and hypertrophy and right atrial enlargement can be encountered in dogs or cats diagnosed with PH. The left ventricle often appears small because of poor filling, and the interventricular septum is thick. Septal flattening or paradoxic septal motion is an indicator of increased right ventricular pressure (Figure 8.10).

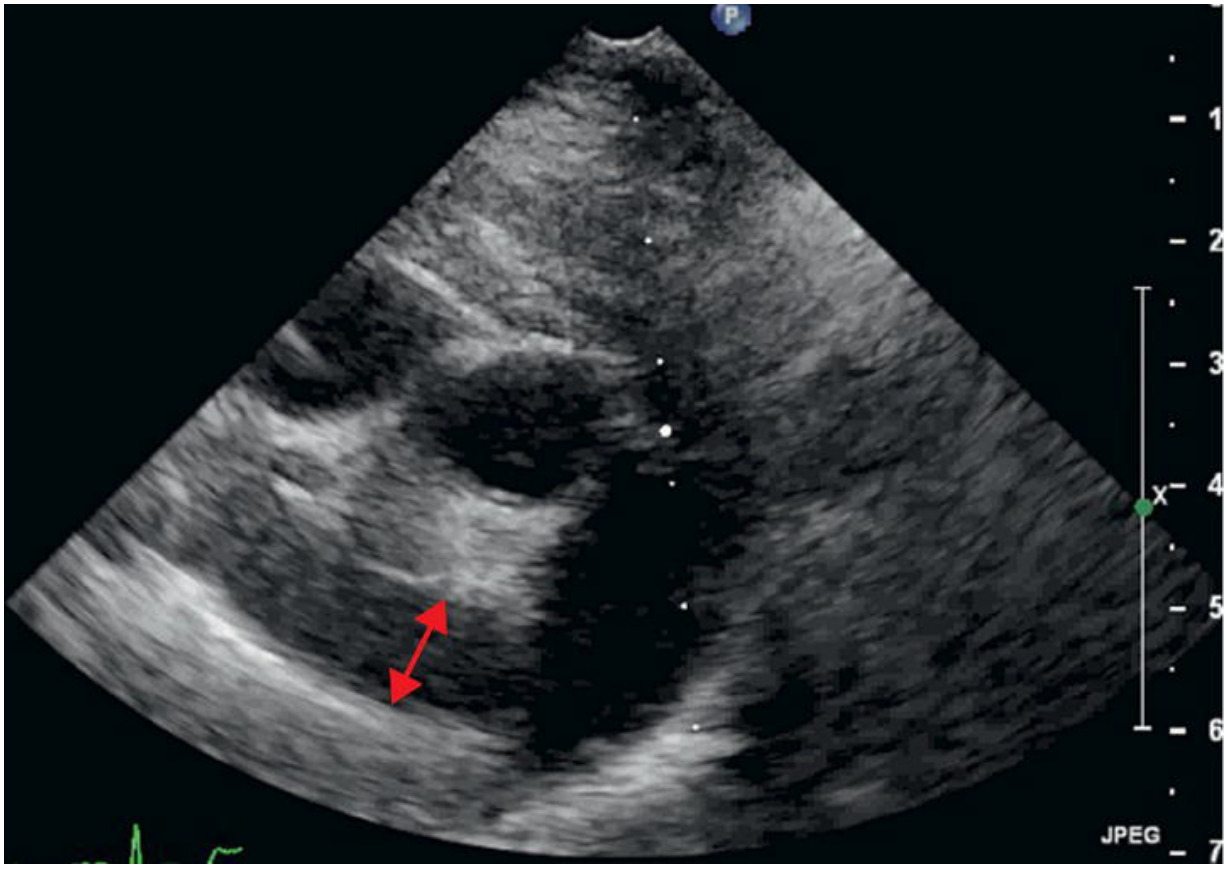


Figure 8.8 Two-dimensional Doppler image from the right parasternal short-axis basilar view shows a white cursor through a dilated main pulmonary artery, which would provide an assessment of the pulmonary velocity flow profile as seen in Figure 8.9. The dilated RPA is illustrated by the double-headed arrow. Changes in this dimension between systole and diastole can be used to calculate the RPAD index to estimate the severity of PH.

Treatment

Treatment of the primary disease condition is essential for the management of secondary PH. Dogs or cats with chronic tracheobronchial disease can show improvement in respiratory signs with judicious use of oral or inhaled glucocorticoids, extended-release theophylline, and weight loss. Dogs with congestive heart failure generally have mild to moderate PH and often do not have clinical signs specifically related to PH, such as syncope or right ventricular failure. These dogs are first managed with pimobendan and diuretics as indicated to control pulmonary edema, as well as angiotensin-converting enzyme (ACE) inhibitors and spironolactone in some cases. Specific management of PH would be instituted after determining response to heart failure therapy. Use of sildenafil in dogs with severe left atrial enlargement and heart failure could theoretically result in worsened pulmonary edema, because relaxation of the pulmonary vasculature could lead to increased pulmonary blood flow with increased venous return to the left atrium.

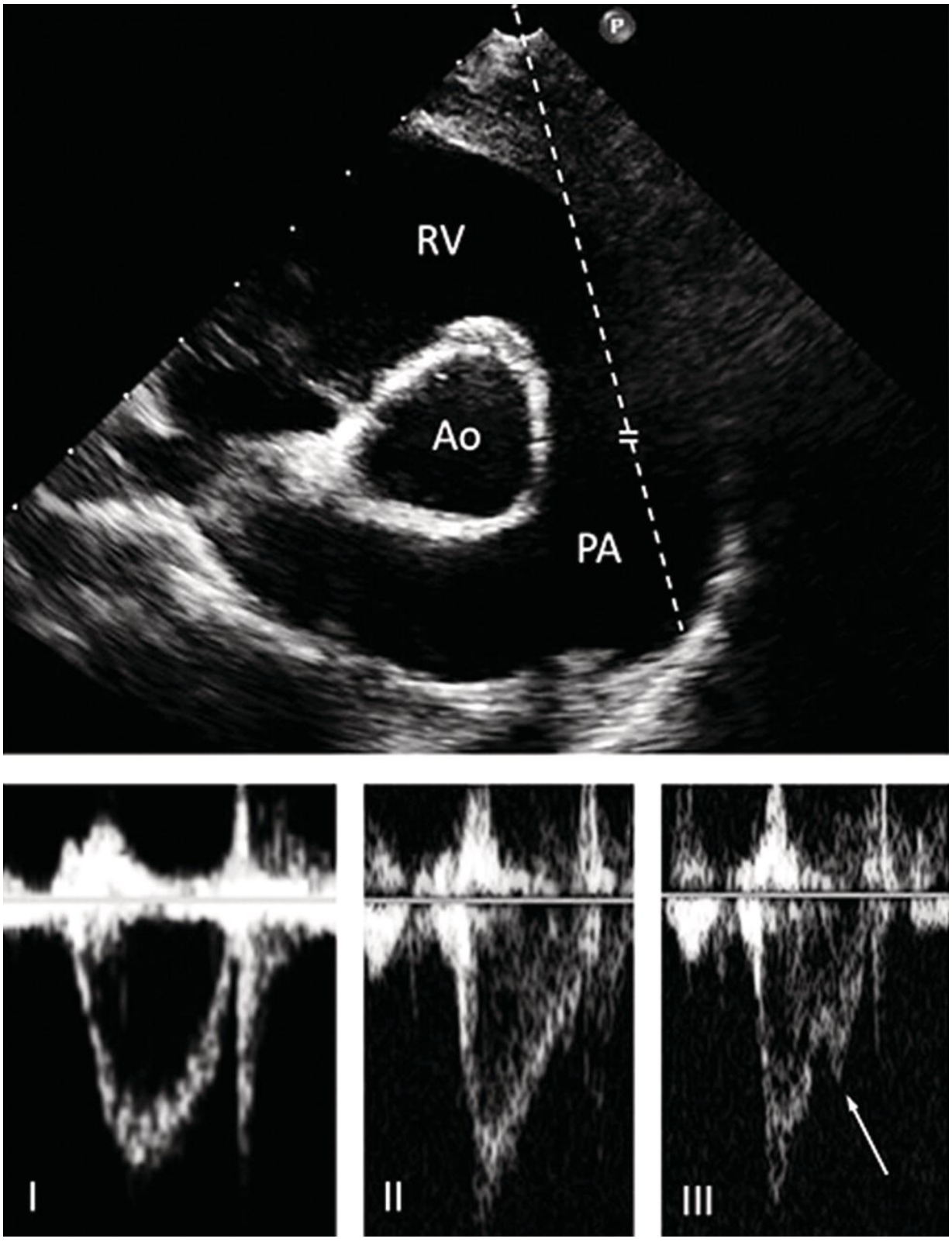

RV
Ao
PA
I
II
III

Figure 8.9 Type I (normal), type II, and type III pulmonary velocity profiles reflect progressive elevation of pulmonary vascular pressures. The arrow in the image of the type III velocity profile indicates reversal and then return of flow associated with very high vascular resistance. Ao, aorta; PA, pulmonary artery; RV, right ventricle.

Source: Courtesy of Dr. Lance Visser, formerly of University of California, Davis; currently at Colorado State University in Ft. Collins, CO.

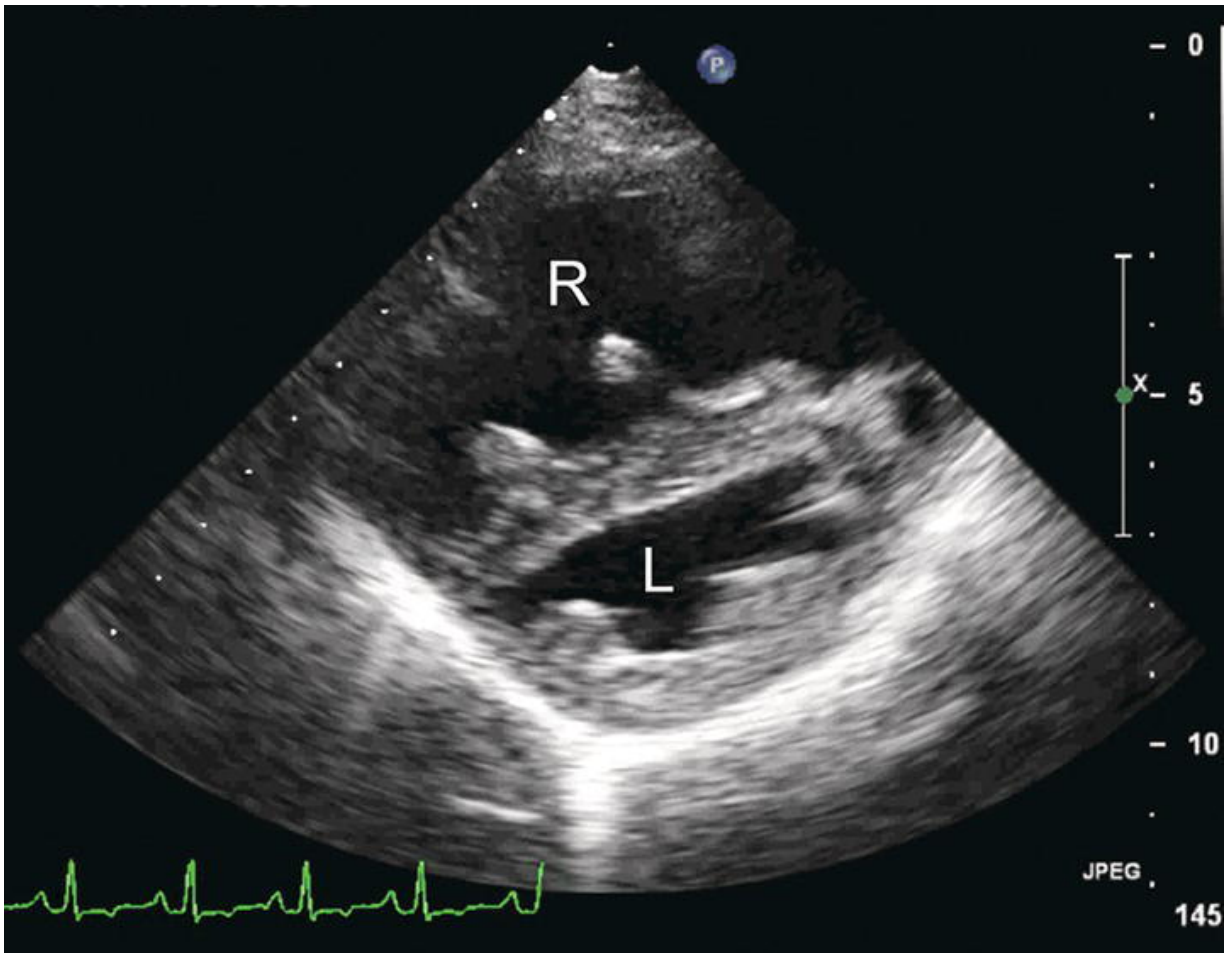


Figure 8.10 This right parasternal short-axis view through the left (L) and right (R) ventricles reveals flattening of the interventricular septum due to increased right heart pressure.

Phosphodiesterase-5 (PDE-5) inhibitors such as sildenafil and tadalafil have proven useful in management of PH. Inhibition of PDE-5 elevates cyclic guanosine monophosphate (cGMP), a selective

pulmonary vasodilator. Specific dosing regimens have not been established, but sildenafil is often started at 1.0–3.0 mg/kg BID–TID and tadalafil at 2 mg/kg daily. Echocardiographic monitoring for efficacy in reducing pulmonary pressure and blood pressure monitoring for hypotension can be performed, although studies have presented conflicting results on the effects of sildenafil on PAP (Bach et al. 2006; Kellum and Stepien 2007; Johnson and Stern 2020) and it is unclear that this impacts treatment. Nonetheless, sildenafil treatment is associated with improved quality of life. Arginine supplementation is considered in some dogs in an effort to increase the substrate used to create nitric oxide in pulmonary endothelial cells. In Japan and other regions of Asia, beraprost, a prostaglandin I_2 analog that has vasodilatory properties, has demonstrated efficacy in management of PH (Suzuki et al. 2022). Many dogs with PH are treated with anticoagulant therapy, including enoxaparin or clopidogrel to limit *in situ* thrombosis. Finally, pentoxifylline (15–25 mg/kg PO BID) can be considered in an attempt to improve blood flow through the capillary bed and enhance oxygen delivery. This drug is a xanthine derivative that is purported to reduce blood viscosity by improving red blood cell deformity.

Prognosis

Development of PH exceeding 55 mmHg secondary to mitral valve disease was associated with decreased survival (15 months) in comparison to 25 months, when PH was absent (Borgarelli et al. 2015). In one retrospective study of PH due to various causes, the magnitude of elevation in PAP had no direct impact on survival (Johnson et al. 1999a). A retrospective study of dogs with respiratory-related PH reported improved survival in dogs treated with PDE-5 inhibitors when estimated systolic PA pressure was <47 mmHg compared to those with pressures >47 mmHg (Jaffey et al. 2019). Finally, a prospective study of dogs with moderate to severe PH due to respiratory disease demonstrated 50% mortality at 6 months for all dogs treated with sildenafil, although those that survived beyond the first month of therapy reached 50% mortality at 1 year (Johnson and Stern 2020), demonstrating the marked improvement that a PDE-5 inhibitor conveys on survival.

Non-cardiogenic Pulmonary Edema and Acute Respiratory Distress Syndrome

Pathophysiology

Non-cardiogenic pulmonary edema (NCPE) results from over-expansion of extracellular fluid volume with leakage into the alveoli due to over-zealous intravenous fluid administration, decreased oncotic pressure, or from damage to the permeability of the alveolocapillary membrane. The most serious cause, permeability edema, results in flooding of the alveoli with protein-rich fluid. It can develop from respiratory insults including aspiration of gastric contents, severe upper airway obstruction, inhalant injury, re-expansion lung injury, or drowning, and from extrapulmonary disorders such as sepsis, electric shock, central nervous system disease, pancreatitis, or disseminated intravascular coagulation (Nemi et al. 2023; Unger and Martin 2023). This condition can progress to acute respiratory distress syndrome (ARDS) with refractory hypoxemia, decreased pulmonary compliance, hyaline membrane formation, and ultimately respiratory failure.

History and Signalment

NCPE should be considered in an animal with a history of a predisposing event or disease process that acutely develops difficulty breathing or tachypnea. In this way, it is similar to PTE. Any age, breed, or species can be affected depending on the underlying disease process.

Physical Examination

Thoracic auscultation is expected to reveal tachypnea and bilateral, moist, fine crackles or harsh lung sounds. Detection of upper respiratory stridor in conjunction with such lower respiratory signs would suggest upper airway obstruction (laryngeal paralysis or collapse), choking, or strangulation as a cause for NCPE. Severe cervical tracheal collapse could also lead to upper airway obstruction and subsequent NCPE. Signs of systemic disease are variably found depending on the cause of NCPE. External burns would support smoke inhalation as a cause, while burns around the mouth would

indicate electric cord bite injury. Abdominal pain would be consistent with pancreatitis, with development of NCPE as a result of cytokine release. Alternately, pancreatitis could result in vomiting, with NCPE due to aspiration pneumonia. Peripheral edema might suggest more widespread vasculitis resulting in permeability edema, while neurologic signs could support increased intracranial pressure as a cause for NCPE.

Diagnostic Findings

Stress-induced hyperglycemia and a stress leukogram are expected hematologic findings. Oxygenation is typically abnormal, with low hemoglobin saturation with oxygen found using pulse oximetry or hypoxemia and an increased alveolar–arterial oxygen gradient detected on arterial blood gas analysis. Thoracic radiographs typically reveal symmetric infiltrates (alveolar or interstitial-alveolar) that are concentrated in the caudodorsal lung fields (Figure 8.11) but can be diffusely distributed (Nemi et al. 2023).

Treatment

Aggressive treatment of the primary disease process is essential for control of NCPE. Oxygen supplementation is indicated to manage tachypnea and labored respirations, and generalized supportive care should be administered. Intravenous fluid therapy should be provided cautiously because breakdown of the alveolocapillary membrane can result in fluid extravasation into the alveolus. Diuretics, positive inotropes, anti-microbials, and corticosteroids have not been proven efficacious for specific treatment of NCPE, although they may be indicated to treat the primary disease process. Mechanical ventilation should be considered for patients with intractable respiratory difficulty and those that develop ventilatory fatigue.

Prognosis

Animals with fluid overload that have acceptable renal function usually respond to a decrease in supplemental fluids and diuretic therapy. Animals with upper airway obstruction, neurogenic-related causes of pulmonary edema, and those that survive drowning can

also have a relatively good prognosis if they do not require mechanical ventilation (Nemi et al. 2023). A guarded prognosis should be offered for animals with NCPE thought to be related to permeability edema. In animals ventilated for therapy of ARDS, survival to discharge was 10%, while 30% of animals mechanically ventilated for treatment of aspiration pneumonia survived (Hopper et al. 2007).

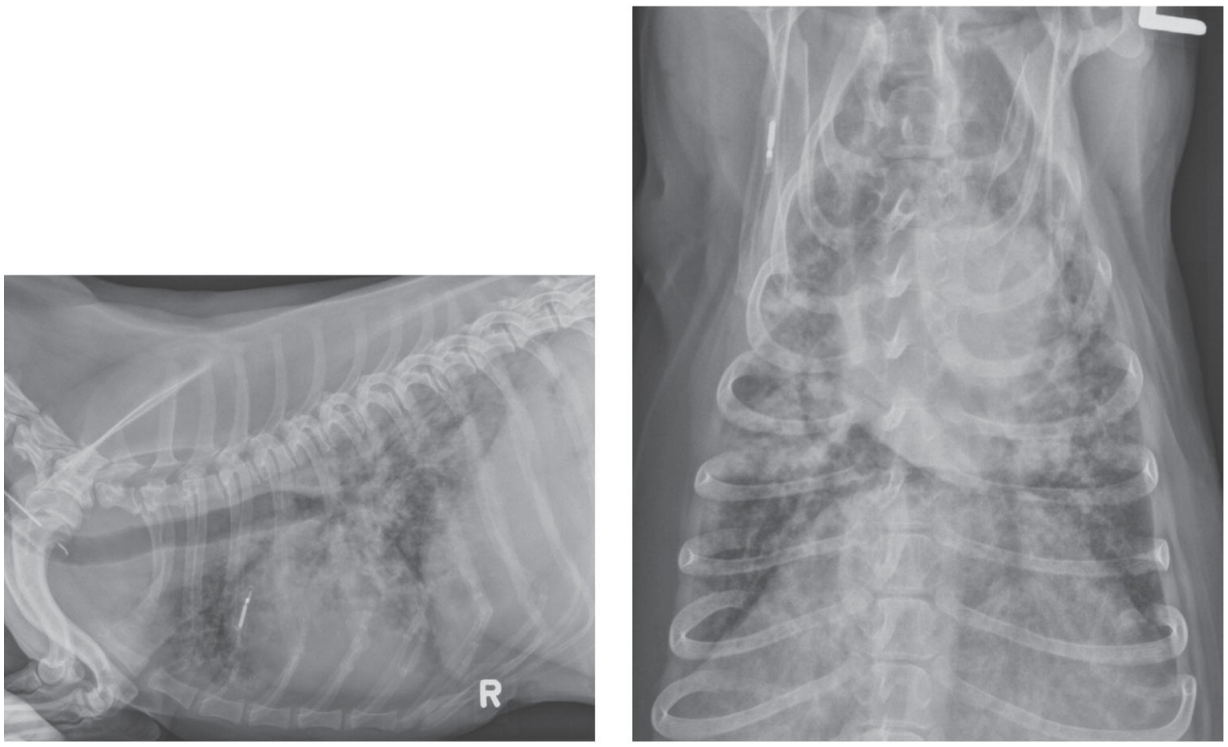


Figure 8.11 (a) Right lateral and (b) dorsoventral radiographs from a 10-year-old spayed female (FS) Dachshund show severe diffuse coalescing bronchoalveolar infiltrates. *Escherichia coli* bronchopneumonia progressing to acute respiratory distress syndrome was confirmed histologically in this dog by positive bacterial cultures as well as the presence of fibrin in the alveolar space, hyaline membrane formation, and type II pneumocyte hyperplasia.

Clinical Case

A 15-year-old spayed female (FS) Yorkshire Terrier cross was presented for evaluation of a 1 month history of worsening respiratory distress, intense coughing, and an episode of collapse. The dog was reportedly aware of her surroundings during the entire episode. Two similar episodes were noted during the past 3–4 weeks.

On physical examination, the dog had increased respiratory rate (40 breaths/minute) and effort, with a mild abdominal push on

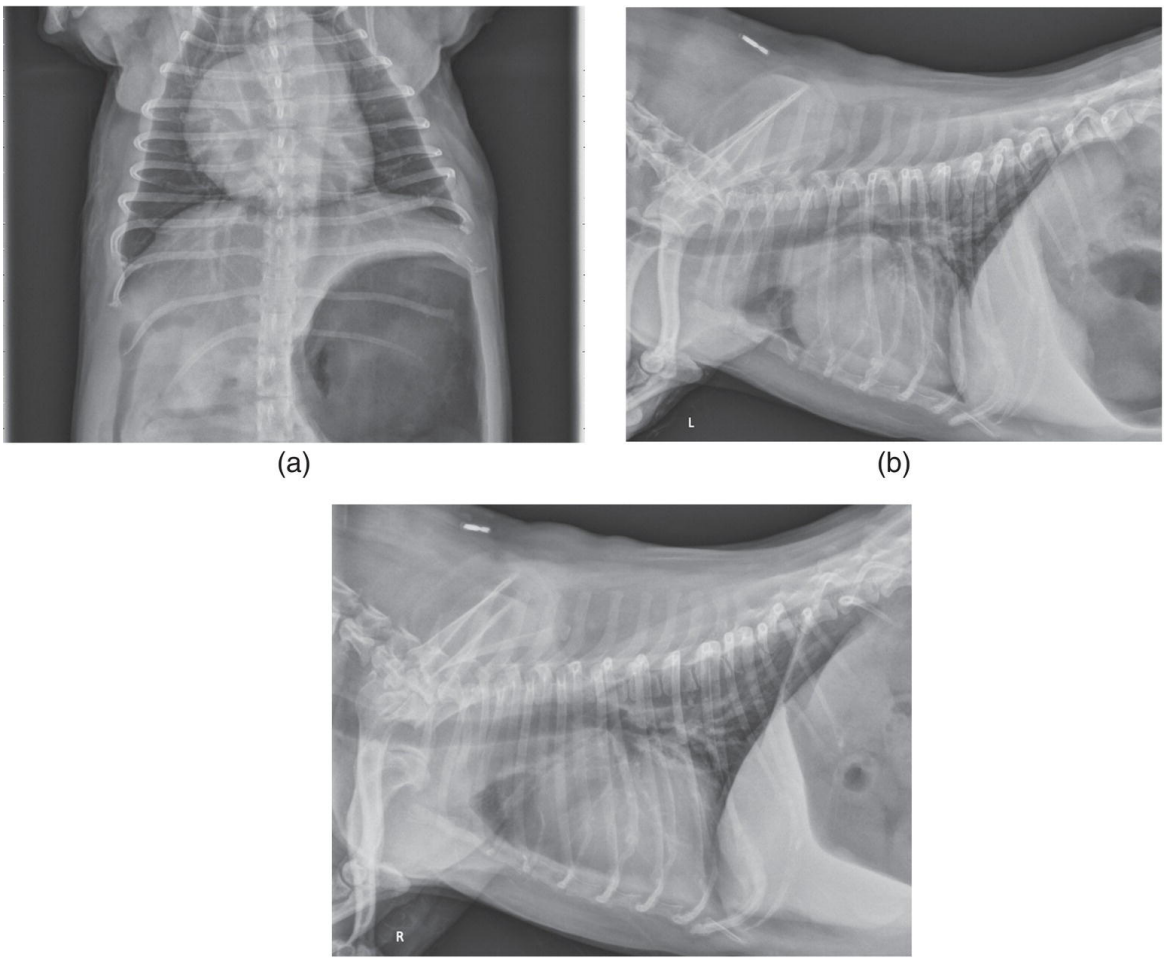
expiration. Temperature was normal (100.2°F, 37.9°C) and pulse was 82 beats/minute. A grade 3/6 apical systolic murmur was ausculted on the left and right sides of the thorax along with mild, diffuse inspiratory crackles. The abdomen was mildly distended with no fluid wave appreciated.

The problem list for this dog included collapse, a heart murmur, and crackles. Differential diagnoses for collapse include disorders affecting the respiratory tract (obstructive or restrictive diseases), cardiac diseases (congestive failure, arrhythmia, PH), metabolic/endocrine diseases (hypoadrenocorticism, hypocalcemia, hypoglycemia), hematologic diseases (anemia), and neuromuscular disease (seizures, myasthenia gravies, myopathy). For the heart murmur, the most likely differential diagnosis was myxomatous valvular disease although endocarditis, cardiomyopathy, and cardiac neoplasia remained on the differential list. Crackles were considered most likely to reflect tracheobronchomalacia or pulmonary fibrosis; pulmonary edema due to left-sided congestive heart failure was considered unlikely given the low heart rate.

Routine laboratory work was unremarkable, ruling out systemic causes of weakness or collapse. Thoracic radiographs (Case Figure 1) revealed mild rounding of the cardiac silhouette on lateral projections and a convex bulge at the left cranial margin of the cardiac silhouette on the DV projection suggesting pulmonary artery dilatation. The caudal pulmonary arteries were minimally dilated compared to the veins but tapered appropriately. There was a mild diffuse unstructured interstitial pattern throughout the pulmonary parenchyma, most pronounced on the lateral projections and complicated by hypoinflation. Marked aerophagia was also present.

Echocardiography (Case Figure 2) revealed severe pulmonary artery dilation with decreased distensibility of the RPA (between red arrows). Maximal tricuspid regurgitation velocity was 4.74 m/s, which translates to a right ventricular to right atrial pressure gradient of 90 mmHg (4 × velocity^2). There was no obvious thrombus formation and the left heart was under-filled. Findings

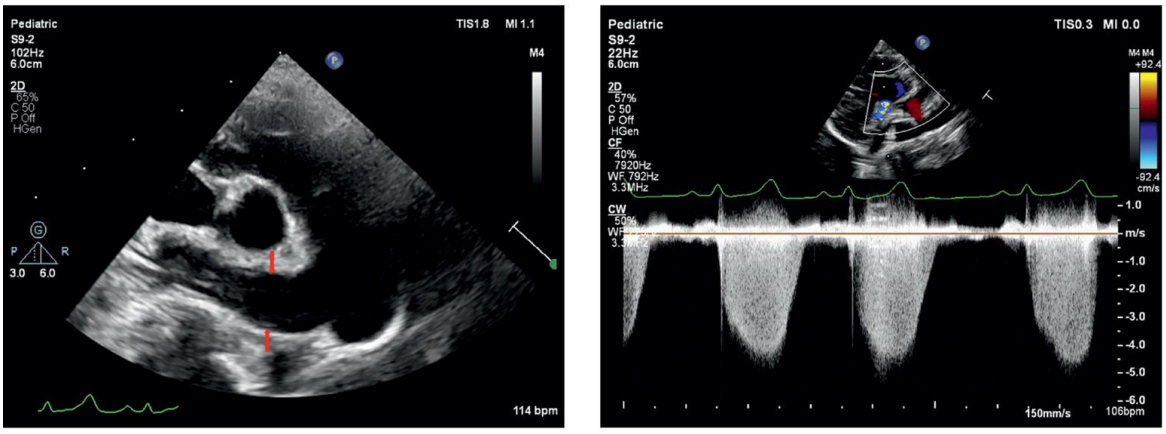
were supportive of a high probability of severe PH, likely secondary to respiratory disease.



(a) (b)

(c)

Case Figure 1 Dorsoventral (a) and lateral (b and c) thoracic radiographs.



(a) (b)

Case Figure 2 Echocardiography demonstrating the right pulmonary artery index (a) and the tricupsid regurgitant jet (b).

A heat treated heartworm antigen test was negative. Thromboelastography suggested hypercoagulability. Airway fluoroscopy, thoracic CT, and bronchoscopy were recommended for further evaluation of underlying respiratory tract disease, but these tests were declined in favor of palliative care. The dog was discharged on sildenafil (1.4 mg/kg PO q8h) and clopidogrel (5.3 mg/kg PO q24h) with recommendations to initiate oxygen therapy at home.

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Glossary

Alar fold
lateral ridge at the external opening of the nostril

Arytenoids
cartilage wings that form the lateral walls of the opening to the larynx

Bronchiectasis
irreversible dilatation of the airways

Bronchitis
non-specific airway inflammation

Bronchoalveolar lavage
instillation and aspiration of warmed sterile saline into an isolated lung segment to retrieve airway fluid for culture and cytology

Bronchomalacia
>50% collapse of one or more primary or segmental bronchi.

Bronchoscopy
endoscopic evaluation of the inner aspects of the airways, with a flexible or rigid, fiberoptic or video-endoscope

Carina
vertical ridge of cartilage separating the left and right principal bronchi

Choana
one of the caudal openings of the nasal cavity into the nasopharynx (plural: choanae)

Ciliary dyskinesia
defective ciliary motion, can be primary or secondary

Concha
thin bones within the nose (turbinates; dorsal, ventral, and middle within the nasal cavity and ethmoid system caudally)

Cribriform plate

bony separation between the nasal cavity and brain containing sieve-like perforations (part of the ethmoid bone)

Cyanosis
bluish discoloration of mucous membranes indicating the presence of >5 g/dl of deoxygenated hemoglobin; can be central or peripheral

Dynamic airway collapse
excessive opening (on inspiration) and closing (on expiration) of airways beyond the carina; often a sign of bronchomalacia

Dyspnea
the sensation of difficult or uncomfortable breathing; a *symptom* described to physicians by a human patient

Epistaxis
hemorrhage from the nose

Ethmoid bone
the bony structure comprised of the ethmoturbinates and the cribriform plate

Eupnea
normal respiration

Extrathoracic
refers to airways from the thoracic inlet to the nose

Hemoptysis
coughing up blood

Hypercapnea/Hypercarbia
increased arterial carbon dioxide content

Hyperpnea
increased minute ventilation due to increased depth +/– rate of respiration

Hyperventilation
increased alveolar ventilation in excess of CO_2 production

Hypoventilation
decreased alveolar ventilation characterized by increased arterial P_aCO_2

Hypoxemia

decreased arterial oxygen content (P_aO_2 < 80 mmHg at sea level)

Intercostal
between the ribs

Intrathoracic
refers to airways within the chest cavity, caudal to the thoracic inlet

Laryngeal ventricles (saccules)
mucosal folds found within the laryngeal crypts between the vocal fold and the arytenoid

Meatus
passageway within the nasal cavity between the conchal folds; dorsal, middle, ventral, and common (plural: meati)

Mediastinum
space within the central portion of the chest defined by the thoracic inlet cranially, the diaphragm caudally, the mediastinal pleura laterally, the paravertebral gutter and ribs dorsally, and the sternum ventrally. It contains the heart, great vessels, and esophagus and separates these structures from the left and right lung lobes. Fenestrae within the mediastinum allow communication between the two sides of the thorax (incomplete mediastinum)

Naris
one of the external openings of the rostral nasal cavity, i.e., nostril (plural: nares)

Nasopharynx
region of the pharynx above the soft palate. Bounded rostrally by the choana and extending caudally into the oropharynx; allows passage of air during nasal breathing

Oropharynx
region of the pharynx between the soft palate, base of the tongue and the epiglottis

Orthopnea
inability to breathe in the supine position

P_aCO_2
partial pressure of arterial carbon dioxide (mmHg)

P_aO_2
: partial pressure of arterial oxygen (mmHg)

Pleura
: serous layers of epithelium lining the thoracic wall (parietal pleura) and lungs (visceral pleura), responsible for producing and removing lubricating fluid within the pleural space

Pneumonia
: inflammation of the lung parenchyma

Reverse sneeze
: repeated efforts to inspire against a closed glottis; usually occurs with the head in a raised position and is a sign of nasopharyngeal irritation

Rhinoscopy
: endoscopic evaluation of the interior of the nasal cavity

SPO_2
: hemoglobin saturation with oxygen (%)

Staphylectomy
: soft palate resection

Stertor
: snoring or snorting sound due to soft tissue obstruction of the upper airway

Stridor
: high pitched inspiratory sound due to upper airway obstruction, typically within the larynx, nasopharynx, or cervical trachea

Tachypnea
: rapid respiratory rate

Thoracic inlet
: site of transition between atmospheric and intrapleural pressure effects on the airway, located anatomically at the level of the first thoracic vertebrae and first pair of ribs

Tracheobronchomalacia
: Tracheal collapse with concurrent collapse of one or more larger bronchi

Tracheostomy

creation of an opening into the trachea for insertion of a tube or for permanent respiration

Tracheotomy
incision through the skin and cervical muscles to access the trachea

Turbinate
thin bones of the nose (concha; dorsal, ventral, and middle within the nasal cavity and ethmoid system caudally)

Ventriculectomy
surgical removal of laryngeal ventricles

Xeromycteria
dry nose syndrome associated with loss of parasympathetic stimulation of serous secretions from the lateral nasal gland

Index

a

Activated clotting time (ACT) 17, 222

Activated partial thromboplastin time (APTT) 17, 210, 222, 223, 231, 233

Acute respiratory distress syndrome 20, 21, 59, 74, 176, 178, 237–239 *see also* Edema, non-cardiogenic

Adventitious lung sounds 9–11, 13, 162, 180, 212, 229

Aelurostrongylus abstrusus 42, 134, 137, 144

Air bronchograms 162, 163, 177

Airway collapse 8, 9, 12, 23, 25, 35, 57, 120–128, 138–140, 150, 244 *see also* Bronchomalacia; Tracheobronchomalacia

  in chronic bronchitis 142

  in eosinophilic bronchopneumopathy 172

Allergy 17, 18, 172, 174, 175

  and bronchitis 143

  and rhinitis 95, 100–102

  and rush immunotherapy 147

Alveolar-arterial (A-a) oxygen gradient 20, 21, 238

Alveolar hypoventilation 20, 21, 63, 115, 244

Amphotericin B (including lipid complex) 53–55, 59, 84

Anaerobe 43–45, 48–51, 98, 160, 164, 178, 202

Anemia 10, 18, 51, 115, 130, 167, 172, 200, 202, 210, 211, 226, 231, 240
immune-mediated 51, 221
Anesthesia
complications 21, 74, 79, 116, 119, 124, 148, 157, 176, 193, 196, 197
for laryngeal exam 26, 35, 116, 117, 120, 163
local 28, 30, 64, 66
use 5, 24–26, 34–36, 63, 74, 80, 94, 96, 106, 133, 138, 178, 180, 199, 223, 234
Angiostrongylus vasorum (French Heartworm) 230–232
Antibiotics
dosing 51
lower respiratory disease 49–52, 126–128, 130, 133, 142, 156, 164, 165, 178
nebulization 50, 59
pleural disease 202, 205
side effects 52
susceptibility 50
upper respiratory disease 41, 47–49, 76, 77, 80, 81, 89, 98, 100
Anticoagulant 17, 210, 222–224, 227, 237
Antifungal therapy 52–54
aspergillosis 87–89
cryptococcosis 83, 84
fungal pneumonia 53, 169
pneumocystosis 171, 172

Anti-inflammatory therapy 56, 60–62
canine bronchomalacia and chronic bronchitis and 126, 141
eosinophilic lung disease 174, 175
feline bronchial disease 146, 147
fungal pneumonia 53, 169
interstitial lung disease 180
nasal neoplasia 105
pneumocystosis 171, 172
upper respiratory tract disease 79, 94, 99, 102, 119
Anti-parasitic therapy 135, 136, 174 *see also* *Angiostrongylus vasorum;* Heartworm disease; eosinophilic lung disease (canine)
Antitussive 58, 124, 126, 142
contraindications 33, 130, 133
Arterial blood gas analysis
indications 18, 19, 63, 162, 173, 175, 177, 180, 222, 233, 238
interpretation 20, 21, 63, 115, 139, 165, 198
method 19
Ascites 10, 13, 14, 180, 198, 208, 225, 233
Aspergillosis, nasal 89, 90
canine 2, 3, 5, 31, 49, 52, 75, 84–90, 100, 102, 166
diagnosis 41, 85–87, 90
feline 2–4, 54, 78, 90–91, 100
treatment 52–54, 87–89, 91

Aspiration 7, 8, 10, 12, 15, 63, 113, 115, 118, 120, 122, 126, 161, 179, 181
clinical syndrome 175–179
complications of 74, 237–239
diagnosis 21–24, 42, 116, 177
treatment 127, 166, 178
Aspirin 224, 230
Asthma, feline 8, 9, 11, 17
clinical syndrome 142–147
diagnosis 22, 42, 144–146
treatment 59, 61, 146–147
Azalides/azithromycin 48, 50, 51, 98, 102, 130, 160, 200
Azoles
oral 52–55, 84, 89, 92, 102, 169
topical 87–89, 91

b

Bacteria, intracellular 42, 43, 122, 162, 164, 201, 202
Bacterial culture for infection
airway 43, 44, 124, 131, 132, 145, 146
aural 94
in bronchiectasis 128–130
nasal 32, 41, 47–49, 79, 80, 95, 97, 98, 102
pleural 44, 45, 200–202
in pneumonia 42–44, 49, 50, 52, 156, 159, 161–163, 165, 178
Bacteroides 45, 49, 98, 202, 205
Baermann 136, 231

Balloon dilation 79, 127
Blastomyces dermatitidis 52, 166, 169
Bordetella 2, 8, 15, 43, 48, 50
infection in dogs 131, 132, 139, 160, 164, 165, 173
infection in cats 79, 98, 144, 165
treatment 50, 59, 98, 133, 166
vaccine 134
Brachycephalic 1, 4–6, 8, 24, 35, 61, 122, 135, 205, 232
in aspiration pneumonia 1, 176
brachycephalic obstructive airway syndrome 71–75
in epiglottic retroversion 120
in lung lobe torsion 157
in sino-orbital aspergillosis 90
Bronchiectasis 8, 9, 15, 22, 25, 42, 51, 101, 128–130, 140, 142, 147, 156, 162, 173, 174, 180
causes of 118, 128, 130, 138, 147, 155, 161
medical therapy 58, 60, 130, 156, 165
surgical therapy 130
Bronchitis (chronic) 8, 11–13
canine 9, 12, 22, 122, 123, 128, 129, 138–142, 172, 179
diagnosis 22, 42, 139–141, 144–146
feline 130, 142–147
treatment 56–60, 63, 126, 141–142, 146–147, 180

Bronchoalveolar lavage
blind 25, 27, 28
bronchoscopic 21, 22, 35–38
cytology 42, 43, 124, 140, 141, 144, 146, 164, 173
indications for 21, 22, 124, 133, 135, 162, 171, 173, 231
Bronchoconstriction 58–60, 166, 175, 176, 178, 221
in feline asthma/bronchitis 9, 10, 28, 143, 144, 146, 147
Bronchodilators
beta agonist (terbutaline, albuterol) 28, 57–59, 165, 166, 175, 178
in feline bronchitis 146, 147
indications for 28, 36, 126, 144, 166, 175, 178
side effects 52, 57, 58, 165, 166
theophylline/methylxanthine 57, 181, 236
in canine tracheobronchial disease 126, 140–142
in feline bronchitis 57, 147
Bronchomalacia 8, 9, 11, 12, 36, 120–127, 138, 139, 141, 233 *see also* Airway collapse; Trachea, collapse
Bronchoscopy
complications 36, 124, 174
indications 21, 22, 27, 34, 123, 124, 126–129, 134, 140, 144, 148, 157, 161–163, 180, 203
technique 35–39
Bulla
osteotomy 94
pulmonary 193, 195
tympanic 93, 94

C

Calicivirus, feline 2, 55, 79, 159

Cardiomyopathy 12, 13, 23, 24, 44, 212, 214, 221, 232, 233

Carina 9, 25, 27–29, 124, 135, 136, 148, 156

Caval syndrome, heartworm associated 227

Chemodectoma 206

Chest tube

- indications for 63, 195, 196, 202
- placement 63–68
- removal 202

Chlamydia felis 2, 48, 79–81, 91

Choana *see also* Nasopharyngeal

- abnormal 72, 77, 91, 94
- examination of 30

Cholesterol/triglyceride ratio 44, 214

Chorioretinitis 83, 132, 160, 167, 170, 211 *see also* Ocular, disease

Chronic bronchitis *see* Bronchitis (chronic)

Chyle, chylous effusion 13, 22, 44

- causes of 44, 157, 159, 212
- chylothorax 212–216

Ciliary dyskinesia 2, 3, 8, 51, 161

- with bronchiectasis 128, 130
- primary ciliary dyskinesia disease syndrome 155–157

Clotrimazole 52, 87–89, 91

Coagulopathy 1, 3, 44, 205, 209, 231
diagnosis of 16, 17, 205, 210, 231, 233
treatment 210, 232
Coccidioides immitis 52, 166–169
Colloid osmotic/oncotic pressure (COP) 209
Conidiobolus 166
Conjunctivitis or keratoconjunctivitis 52, 80, 81, 105, 132, 171, 202
Coronavirus
canine respiratory 2, 8, 130, 131, 159
coronavirus, feline 47, 56, 159
disease syndrome (FIP) 210–212
Corticosteroids 175, 227, 230, 232, 238 *see also* Glucocorticoids; Prednisolone or prednisone
Cough, reflex and receptors 7–9, 12, 24, 58, 114, 124
Coupage 27, 130, 142, 156, 166, 175, 178
technique 60
Crackles 9, 10, 13, 123, 126, 132, 139, 143, 144, 162, 167, 172, 176, 179, 180, 222, 225, 233, 238
Cranial lung herniation 123, 124
Cranial mediastinal mass 113, 203–206
Cranial vena cava syndrome 204, 206
Cribriform plate 24, 32, 53, 85–87, 95, 103, 104
Cryptococcosis 2–5, 41, 78, 96, 166
disease syndrome 82–84
treatment 52–54, 84
CT pulmonary angiography 223
Cyanosis 62, 114, 118, 122, 143, 146, 233

Cytokine 85, 100, 172, 238

d

D-dimer 17, 222, 233
Dendritic ulcer 132
Dental exam and probing 4, 5, 30, 34, 77, 94, 98
Dental radiography 96
Dental related nasal disease 1, 3, 34, 76, 77, 95
Dirofilaria immitis see Heartworm disease
Doxapram 35, 116
Dysphagia 93, 117, 148 *see also* Aspiration; Videofluoroscopy
Dysphonia 11, 34, 93, 135, 148

e

Echocardiography
  indications for 22, 44, 180, 198, 199, 214, 223, 226, 229, 231, 232, 234–236
Edema
  non-cardiogenic 21–23, 59, 175, 176, 237–239
  pulmonary 7, 9–13, 21–23, 233, 237
  re-expansion 199, 209
Electron microscopy 156, 160
Enilconazole 87, 89
Eosinophilic inflammation
  bronchial 17, 43, 78, 124, 136, 225
  feline specific 8, 15, 17, 42, 61, 142–147
  nasal 1, 3, 41, 97, 99, 172, 174

Eosinophilic lung disease (canine) 1, 3, 8, 15, 17, 43, 101, 128, 129, 172–175
treatment 56, 58, 174, 175
Epiglottis 35, 72, 73, 113
retroversion 6, 119–120
Epistaxis 3, 16, 75, 90, 91, 101, 103–105, 231
Esophagus 113, 123, 196
dysfunction 7, 24, 77, 117, 135, 161, 176, 204, 206 (*see also* Megaesophagus)
perforation or rupture 204
stricture 98, 117
Exercise intolerance 7, 11, 71, 114, 115, 118, 122, 138, 139, 143, 170, 172, 179, 198, 200, 225, 231
Exudate 13, 44, 159, 201

f

Facemask 37, 59–62, 99, 141, 146, 147
Facial deformity 103
Famciclovir 47, 55, 81, 99
Feline bronchial disease 12, 15, 232 see also Asthma, feline
disease syndrome 142–147
treatment 56–58, 146–147
Feline infectious peritonitis 13, 14, 44, 47, 56, 159, 210–212 *see also* Coronavirus
Fenbendazole 136, 174, 195, 205, 231
Fibrosis *see* Pulmonary, fibrosis

Fine needle lung aspiration or biopsy
complications 39, 40, 193
indications for 20–22, 162, 163, 171, 185
technique 39–41
Flora (normal respiratory) 15, 41, 43, 47, 80, 97, 173
Flovent® (fluticasone propionate metered dose inhaler) 61, 126, 175
Flow-vu indicator 62
Flucytosine 53, 54, 83
Fluoroscopy 79, 185
airway 22, 24, 123, 124
pharyngeal 72, 120, 161
videofluoroscopic swallowing 24, 116
Foreign body inhalation 2, 3, 8, 15, 22, 31, 33, 36, 43, 75, 76, 100, 160, 161, 163, 201, 202
complications of 2, 76, 77, 84, 95, 162, 203
French heartworm disease *see* *Angiostrongylus vasorum*
Frontal sinus 31, 84, 86–89, 97, 101–103
surgery 94
trephination 88, 166, 193, 194, 196, 200
Fungal culture 41, 86, 91, 92
Fungal granuloma or plaque 4, 33, 41, 52, 84, 86–89, 91, 93, 167

g

Glomerulonephritis or nephropathy 130, 208, 225
Glottis 35, 113, 114

Glucocorticoids 56, 57, 59–62, 79, 94, 99, 100, 102, 117, 119, 126, 130, 138, 141, 142, 146, 147, 169, 178, 180, 187, 236 *see also* Corticosteroid; Prednisolone or prednisone; Steroid

h

Heartworm disease (dirofilariasis) 22, 43, 44, 209, 212, 214
- canine 172, 193, 224–228, 232, 233
- feline 144, 228–230

Hemoglobin saturation (SPO_2) 18–20, 223, 238

Hemorrhage 216, 224, 231
- coagulation testing 16, 210, 231
- mediastinal 113, 203–205, 209–210
- nasal 1, 96 (*see also* Epistaxis)
- pleural 159, 198
- pulmonary 16, 21, 22, 40, 43

Heparin 223
- low molecular weight 223
- in pleural lavage 202

Hernia
- diaphragmatic 22, 44, 197–199
- hiatal 1, 71, 75
- peritoneopericardial 198–199

Herpes virus
- canine 2, 8, 130, 131, 159
- feline 2, 15, 47, 55, 79, 97, 159

Histoplasma capsulatum 52, 53, 166–170

Horner's syndrome 93, 94, 105, 204, 206

Hyaline membrane 238, 239
Hydrothorax 11, 22, 208–209, 214
Hyperadrenocorticism 162, 221
Hypercapnea/hypercarbia 115, 139
Hypercoagulable 71, 221, 222, 233
Hyperglobulinemia 15, 85, 211, 231
Hypersensitivity 18, 52, 100, 209
  pulmonary 179, 225, 230, 231
Hypoalbuminemia 15, 44, 167, 208–210
Hyposensitization or immunotherapy 100, 147, 175
Hypoventilation 20, 21, 63, 115
Hypoxemia/hypoxia 11, 15, 18–21, 28, 36, 63, 115, 123, 139, 162, 173, 176–180, 222, 233, 234, 238

i

Imidacloprid 136, 227, 230, 231
Immunocytochemistry 133, 211
Immunohistochemistry 160, 212
Influenza virus, canine 2, 130, 131, 133, 159
  vaccine 134
Interstitial lung disease 12, 21, 23, 25, 62, 179–182, 232, 233
Intradermal testing 18, 101, 143, 174, 175
Irish Wolfhound 3, 9, 161
Ivermectin 107, 136, 205, 227, 230

j

Jugular venous distention 13, 180, 208, 212, 213, 225, 233

k

Kennel cough (Canine Infectious Respiratory Disease Complex) 2, 7, 8, 56, 130–134
Keratoconjunctivitis sicca 52, 81, 171, 202

l

Laryngeal 5–7, 9, 10, 113, 119, 122
collapse 5, 6, 71, 73, 74, 118
examination 23, 24, 26, 34–35, 72, 73, 116–119, 163
inflammation 115, 125, 135–138
neoplasia 147, 148
paralysis or dysfunction 6, 8, 11, 12, 24, 28, 113–118, 122, 123, 126, 161, 176, 177, 204, 206, 238
stenosis or web 74
ventricles (saccules) 5, 35, 71, 73, 118, 119
Laser assisted turbinectomy (LATE) 74
Lingual ulcer 80
Lobectomy 135, 159, 166, 180, 186
Lung biopsy 21, 40, 41, 180
Lymphadenopathy 5, 76, 83, 92, 95, 96, 101, 103, 161, 167, 205
hilar 167–169, 181, 182, 184, 205–207
Lymphangiectasia 208, 209, 214
Lymphoma 208, 209
larynx 148
mediastinal 203, 204, 206
nasal or nasopharyngeal 42, 43, 103–105
pulmonary 43

Lysine 81

m

Mechanical ventilation *see* Ventilatory support
Megaesophagus 114, 117, 176 *see also* Esophagus, dysfunction
Melarsomine 227, 230
Mesothelioma 206, 207
Metaplasia 138, 141, 179, 180, 215
Metered dose inhaler 60–62, 98, 147
Methemoglobin 18
Metronomic chemotherapy 105, 187
Microfilaria 225–228
Milbemycin oxime 107, 136, 205, 227, 229, 231
Mite, nasal 2, 106–107
Modified Bernoulli equation 234
Modified transudate 44, 159, 208
Molecular test 2, 55, 132 *see also* Polymerase chain reaction (PCR)
Mucociliary clearance 3, 57, 142
Mucolytic 58, 59, 102, 142, 147
Myasthenia gravis 205–207

Mycoplasma spp.
diagnosis 8, 43, 123, 129, 133, 139, 141, 144, 146, 163, 173
as flora 43, 141, 146
in lower respiratory disease 8, 126, 131, 132, 156, 160, 163, 165, 178
in pleural disease 45
treatment 48–51, 58, 98, 126, 133, 142, 160
in upper respiratory disease 2, 48, 79

n

N-acetylcysteine
nebulization 58, 59
oral 58, 100, 102, 130, 142, 187
Narcotic cough suppressants 47, 58–59, 126
Nasal airflow 4, 7, 75, 76, 85, 90, 92, 93, 95, 96, 100, 101, 103, 172
Nasal depigmentation 5, 85, 90
Nasal discharge 1–5, 48, 49, 75–78, 80, 82, 83, 85, 89–91, 93, 95, 96, 100, 101, 103–106, 155
in lower respiratory disease 1, 23, 24, 41, 161, 162, 172, 173
Nasal flush 33, 34, 41, 79, 98, 99

Nasopharyngeal *see also* Choana
examination 4, 30, 77, 97
foreign body 30, 31, 33, 34, 75, 76, 118
mass effect 4, 5, 13, 42, 82, 90, 91, 103, 105
polyp 2–4, 92–95
regurgitation 1, 23, 24, 74
stenosis 6, 77–79
turbinates 71–73
Nebulization 59–60
indications for 130, 141, 142, 147, 156, 166, 175, 178
of medications 58, 59, 133
Nematode 205
Neospora caninum 170–171
Nonbronchoscopic bronchoalveolar lavage 28
Noncardiogenic pulmonary edema *see* Acute respiratory distress syndrome

O

Obesity 10, 12, 61, 72, 115, 119, 123, 124, 126, 139, 140
treatment of 63, 117, 125, 147
Ocular
discharge 55, 101, 106, 131, 160
disease 47, 80, 84, 99, 132, 166. 167 (*see also* Chorioretinitis; Retinochoroiditis)
retropulsion 4, 5, 95, 103
trauma 61
One stage prothrombin time (OSPT) 17, 210, 222, 231

Oronasal fistula 2, 3, 76–77, 98
Oslerus osleri 134, 135, 137
Otitis externa 93
Otitis interna 94
Otitis media 93, 105, 106, 155
Oxygen therapy 62–63
  complications of 62, 83, 178
  indications for 36, 37, 74, 116, 117, 124, 146, 160, 162, 166, 170, 172, 180, 195, 197, 210, 223, 227, 230, 232, 238
  nasal 62
  response to 18, 20, 21, 63, 175, 181, 222, 237
  tracheal 36, 148

p

Palate, soft 113, 119
  elongation 5, 7, 23, 35, 71–73, 118
  palpation 4, 5, 83, 93, 94, 103
  resection 74, 75 (*see also* Staphylectomy)
Paragonimus 43, 134–136, 193, 195, 196
Percussion 10, 135, 144, 194
Periodontal or dental probing 5, 34, 35, 76, 77, 98
PF or oxygenation ratio 20
Phosphodiesterase-5 inhibitor 237
Piroxicam 99, 102, 105, 187
Pleuritis, fibrosing or constrictive 203, 215, 216
Pneumocystis 52, 166, 170–172
Pneumomediastinum 196–197

Pneumonia *see* Specific type
Pneumonyssoides caninum 2, 106–107 *see also* Mite, nasal
Pneumothorax 193–196
clinical signs/examination 10, 135, 194, 197
as a complication 39, 40, 64, 134–136, 147, 183, 196, 216
treatment 39, 63, 64, 195, 196
Polycythemia 15
Polymerase chain reaction (PCR)
antigen receptor rearrangement 206
canine disease 131–133, 135, 160, 171, 173, 231
coronavirus 44, 211
feline disease 55, 80, 91, 93, 96, 135, 146, 160
Polyneuropathy 6, 113, 114
Posaconazole 52–54, 84, 89, 91
Prednisolone or prednisone 56, 102, 126, 141, 146, 175, 207, 230 *see also* Corticosteroids; Glucocorticoids
Propofol 26, 27, 36, 116
Protein electrophoresis 44
Proteinuria 209, 225, 233
Pulmonary
arteriopathy 232
fibrosis 9, 11–13, 21, 167, 179–182, 232, 234
hypertension 11, 13, 22, 62, 71, 122, 123, 179–181, 223, 232–237
Pulse oximetry 18–20 *see also* Hemoglobin saturation
indications for 28, 63, 162, 165, 173, 177, 180, 222, 233, 238
Pyothorax 13, 15, 22, 44, 63, 64, 68, 157, 200–203, 215

r

Regurgitation

atrioventricular valve 13, 180, 226, 235, 240 (*see also* Valvular insufficiency)

gastroesophageal 1, 3, 71, 77, 114, 116, 176, 198, 204

nasal or nasopharyngeal 1, 74, 77, 101, 123

Resting energy requirement 63

Retinochoroiditis *see* Chorioretinitis

Retroflex endoscopic examination 72, 73, 77, 91, 106 *see also* Nasopharyngeal

Reverse sneeze 1, 75, 101, 106, 107

Rhinitis, inflammatory or post-infectious

canine 2, 3, 9, 15, 49, 58, 89, 90, 100–102, 161

feline chronic rhinosinusitis 2, 3, 15, 49, 58, 79, 95–100

Rhinoscopy 30–34, 75, 77, 89, 96, 98, 102–104, 173

Right heart/ventricular enlargement 223, 226, 227, 231, 234, 235, 237

Right heart/ventricular failure 11, 13, 44, 212, 225, 226, 230, 233, 235, 236

Right pulmonary artery distensibility index (RPAD) 235–236

Rodenticide intoxication 3, 16, 43, 204, 209, 210

Rutin 214

s

Saccule, everted *see also* Laryngeal, ventricles (saccules)

Sedation 26, 28, 39, 63, 64, 73, 124, 125, 195, 210, 234

Seizure 82, 85, 103, 176, 233

Simonsiella 43

Situs inversus 155

Spacing chamber 60, 62, 146, 147

Spirocerca lupi 204–205

Staphylectomy 74

Stenotic nares 6, 71, 72, 74

Stent 25, 35, 79, 126, 127

Steroid *see also* Glucocorticoids; Prednisolone or prednisone

Stertor 3, 5–7, 71, 78, 82, 93, 95, 101, 103, 118

Stridor 5–7, 11, 34, 72, 74, 78, 115, 118, 120, 123, 135, 148, 177, 204, 206, 238

Subcutaneous emphysema 64, 197

Surfactant 39, 176, 221

Swan Ganz catheter 234

Syncope or collapse 62, 71, 114, 122, 123, 148, 179, 197, 198, 206, 231–233, 235, 236

t

Tachypnea 7–13, 51, 59, 62, 83, 123, 132, 134, 136, 143, 146, 157, 160, 167, 170, 176, 177, 179, 183, 194, 197, 198, 200, 204, 210–212, 221, 228, 231, 233, 238

Terbinafine 53, 54, 84, 89, 91, 92

Terbutaline *see* Bronchodilators

Theophylline *see* Bronchodilators

Thoracic duct 212, 214

ligation 215

Thoracocentesis 39–40
complications of 193, 200
indications for 22, 158, 195, 197, 198, 201, 210, 214
Thoracoscopy 180, 186, 195, 202, 206
Thoracotomy 159, 176, 180, 186, 195, 202, 206
Thromboelastography 17, 222, 231, 233
Thromboembolism 22, 43, 193, 221–225, 232
Thymoma 203, 205–207, 212
Tissue plasminogen activator 17, 224
Tooth root abscess 2, 3, 5, 35, 76–77, 100
Torsion, lung 22, 24, 157–159, 209, 210, 212
Toxoplasma gondii 170–172
Trachea
auscultation 5, 6, 8, 9, 148
collapse 5–8, 23, 25, 119–127, 139, 142, 238 (*see also* Tracheobronchomalacia)
hypoplasia 71–73
mass 148–150, 204, 206
nodules 134, 135 (*see also* Oslerus osleri)
ring prostheses 126–127
scintigraphy 22, 156
Tracheal wash 21, 22, 25–30, 129, 133, 140, 144, 162, 169
complications 28, 175, 196
culture 43, 141
cytology 42–43, 136, 144, 171
Tracheobronchitis, infectious 8, 15, 130–134

Tracheobronchomalacia 11, 13, 120–127, 233 *see also* Airway collapse; Bronchomalacia; Trachea, collapse
Tracheostomy 74, 75, 117, 118, 120, 126, 138, 148, 196
Transudate 44, 159, 208
Trematode 195
Trephination, sinus 88
Triglyceride 44, 214
Turbinate 32, 77, 86, 101, 105
  destruction of 31, 32, 49, 76, 84, 85, 87, 88, 90, 96–98, 101–103

V

Valvular insufficiency or regurgitation
  mitral 13, 123, 232, 233, 237
  pulmonic 233–235
  tricuspid 13, 180, 226, 232, 234, 235
Ventilation/perfusion
  mismatch 20, 176
  nuclear scanning 222, 223
Ventilatory support 63, 178, 193, 238, 239
Ventriculectomy (sacculectomy) 74, 119
Videofluoroscopy 24, 116
Vitamin K 17, 43, 205, 210
Vocal fold 35, 73, 117
  granuloma 135
Voriconazole 52–54, 89, 91

W

Wheezes 9, 13, 72, 132, 139, 143, 144, 148, 162, 172, 176, 180, 222, 233 *see also* Adventitious lung sounds

X

Xeromycteria 2, 105–106

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