Chicago Veterinary Medical Association
Shaping the Future of Veterinary Medicine - Promoting the Human-Animal Bond

Presents:

RESPIRATORY MEDICINE

With:

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The main function of the respiratory system is obviously gas exchange, yet this system also participates in thermoregulation, the metabolism of endogenous and exogenous chemicals and mediators, and protection of the animal against inhaled substances. Oxygen is brought from the ambient air to the alveoli where it diffuses across the capillary membrane, into the blood and then is distributed to the tissues throughout the body as carbon dioxide moves in the opposite direction. The delivery of $O_2$ into, and the transport of $CO_2$ out of, the body varies with the animal’s metabolism but it must be performed with minimal energy cost to the animal. The energy expended to breathe is referred to as the work of breathing ($W_b$).

Protection against inhaled particulates and gases is provided by a variety of pulmonary defense mechanisms. Changes in the function of these mechanisms can be caused by environmental as well as microbiologic agents and may lead to respiratory disease, which reduces the efficiency of gas exchanges and eventually the animal's performance. Our treatments can also impact these defense mechanisms and we must be aware of these potential interactions when initiating any treatment. Both inappropriate management and/or therapeutics can adversely affect normal pulmonary defenses.

1. **Upper airways** – the nasal turbinates/air passage-ways.
   In the nasal cavity, the epithelial surface over the turbinates is extensive, serving to warm and humidify air, as well as filter large particles from the incoming air stream. With nasal breathing, warming & humidification of inspired air is essentially complete before it reaches the lower airways.

2. **Protective reflexes** - The particular response (sneezing, reverse sneezing, coughing or airway narrowing) depends less upon the type, strength, intensity and duration of the stimulus applied to the irritant receptors, but rather to their location within the respiratory tract. Receptors may be stimulated by chemical, inflammatory or mechanical stimuli.

3. **Mucociliary tree** – Cilia beat in a coordinated motion to propel secretions out of the airways.
   - **Mucous layers** - The epithelial cells of the respiratory tract are covered by a periciliary fluid of low viscosity (the sol layer) in which the cilia beat in a coordinated fashion. The gel layer, which may be continuous or in plaques, consists of viscous mucus that protects the sol layer from desiccation and also entraps inhaled particles.
   - **Cilia** - beat in nose & trachea and mucus flow is towards the oropharynx.
   - **Tracheal mucus transport rates (TMTR)** - in the normal individuals are approximately 20 mm/min in the trachea; secretion clearance decreases to between 2-5 mm/min in chronic bronchitis.

Mucus secretion and ciliary activity are controlled under autonomic regulation. Stimulation of sympathetic nerves also causes secretion, alpha-receptors apparently being responsible for serous secretion and beta-receptors for mucin secretion (as well as increased ciliary beat frequency). Vagal stimulation, e.g., following inhalation of an irritant substance increases mucus secretion by submucosal
glands. Some inflammatory mediators, particularly the lipoxygenase products of arachidonic acid metabolism (leukotrienes), are potent mucus secretagogues (caution, there are significant species differences).

In the presence of chronic airway irritation (e.g. by dusts or chronic inflammation), submucosal glands hypertrophy and produce increased quantities of mucus. Secretions like this are a common finding in some of the chronic nasal and lower airway cases that I encounter. Chronic irritation may also lead to goblet cell hyperplasia in peripheral airways so that mucus is secreted into bronchioles which are poorly equipped for mucus removal. The overall effect is one that can lead to mucus accumulation/obstruction of peripheral airways and ventilation to perfusion (V/Q) inequalities, as well as common presenting complaints of coughing and nasal discharge.

4. **Bronchus associated lymphatic tissue (BALT)** - located in the epithelium of the respiratory tract, analogous to the Pyer's patches of the intestinal tract; very important in Agn processing. One grossly visible example of BALT is in the clinical condition of follicular pharyngitis.

5. **Pulmonary macrophage (MO)** - Particles deposited on the alveolar surface are cleared by phagocytic alveolar macrophages. These cells normally constitute approximately 70-85 percent of the cells in fluids washed from the lung periphery, i.e. in a bronchoalveolar lavage (BAL).

Alveolar macrophages form the first line of defense against bacteria and particulates that are deposited in the lung. When large numbers of particulates are inhaled, the macrophage is assisted by other phagocytic cells that enter the alveolus from the blood under the influence of chemotactic stimuli. Neutrophils migrate into the lungs more quickly and in larger numbers than monocytes. Phagocytic cells break down particulates by means of toxic O2 radicals and proteolytic enzymes, both of which may leak from the cells and damage the lung tissue. Protease inhibitors such as alpha-1 antitrypsin, and antioxidants such as glutathione peroxidase and superoxide dismutase (SOD) protect the lung from its own defense mechanisms (i.e. help prevent autodigestion). Therapeutically we sometimes use other antioxidants such as oral N-acetylcysteine, selenium and Vitamins A, C and E.

Once phagocytized, particles may be digested by the macrophage or transported up & out of the lung. Suppression of alveolar macrophage function is important in the pathogenesis of respiratory disease. Macrophages have adapted to the high O2 levels within the alveolus, their phagocytic ability may be depressed by hypoxia. Corticosteroids suppress the bacterial-killing ability of macrophages and may be the cause of the impaired function described after the transportation of animals. Viral infections are another common cause of decreased macrophage function.

Owners usually seek veterinary assistance because of changes in their animal's performance or behavior (typically exercise intolerance, signs of respiratory distress at rest, an unusual sound breathing or it is coughing/sneezing excessively). **The clinical signs of respiratory disease (an owner's presenting complaint what you detect on examination) represent the animal's expression of the functional changes secondary to that particular disease.**

**Dysfunction** of one portion of the respiratory system leads directly to many of the presenting signs we commonly recognize in our patients…a simple example would be a coughing after eating/drinking or a change in an animal’s voice pointing us to laryngeal disease and the need for a more thorough laryngeal evaluation.
Most organs have considerable reserve before signs become apparent, and this is also true in the lung, where there must be considerable obstruction of small airways or flooding of alveoli before clinical signs are apparent – especially when the animal is a not particularly active one. As there are few quantitative pulmonary function tests in veterinary medicine, the *objective* evaluation of respiratory disease may be difficult (more on this later when diagnostics are discussed). Understanding the four classical components of respiratory physiology will help recognize these functional changes and the pathology that might have caused them.

1. **Ventilation** - Ventilation is simply the movement of air into and out of the lungs. Ventilation is usually "set" at a sufficient level to supply O\(_2\) and remove the CO\(_2\) produced by the tissues (and sensed by central and peripheral chemoceptors). In order to do this, ventilation must increase whenever metabolic activity increases, obviously for example, during exercise. Approximately 33% of ventilation goes to dead space ventilation. Measuring arterial PaCO\(_2\) levels can objectively assess the actual adequacy of ventilation. Increases in PaCO\(_2\) (*hypercapnea*) are uncommon in awake dogs due to their extensive collateral ventilation. If this is encountered it is an ominous clinical finding in my experience. Hypercapnea is also one of the main clinical indicators in the decision process of whether to place an animal on a ventilator.

   Observing an animal breathe at rest is a very important diagnostic skill (observe from a distance, not after he is excited after being placed on an exam table for instance).

   **Inhalation is normally an active process**, occurring as the result of contraction of the diaphragm and to a lesser degree the external intercostal muscles.

   During exercise, or when there is increased respiratory drive, or airway obstruction the "accessory muscles" of respiration may be used. These accessory muscles of respiration are located in the upper airway, where they dilate the nares, pharynx and larynx as well as in the neck and thorax, where they assist in enlarging the rib cage size. A classic example is seen in the nostril flaring of a racing horse, another would be thoracic inlet "retraction" in an animal with upper airway obstruction. Another example in the horse is "heaves" where there is small airway obstruction and marked expiratory effort – we see this as well in dogs and cats with extensive small airway disease. Your observation of accessory muscle activation at rest is a clear sign of severe respiratory disease.

   **Exhalation is normally a passive process**, and occurs as a result of the elastic recoil of the lungs and rib cage that were "stretched" (by the work of breathing) during inspiration.

   During inhalation, the respiratory muscles must work to overcome lung elasticity and frictional resistance to airflow in the airways. (Tissue and gas inertia is minimal – it is usually ignored.) The elastic recoil of the lung is a result of the collagen and elastic tissue in the alveolar septa as well as the surface tension of the fluid lining the alveoli.

   The elastic recoil of the lung is measured as **lung compliance**
\[ C = \Delta V / \Delta P; \text{ the units are volume/pressure e.g. } \text{ml/cmH}_2\text{O}; \]
▲ indicates the difference or change in the particular parameter, for instance ▲ in V<sub>T</sub> or tidal volume for a given ▲ in P or pressure. In disease, there can be an increase in the amount of collagen within the lung or there can be an increase in surface tension, both of which increase the elastic recoil of the lung (stiffens the lung), reducing compliance and making it more difficult to inhale. Many diseases, such as pneumonia, fibrosis and pulmonary edema, stiffen the lung causing a decrease in lung compliance. Animals with low lung compliance have difficulty breathing because the lung is more difficult to stretch/expand; these animals will classically breathe more rapidly and more shallowly than normally.

The second factor to be overcome during inhalation is the frictional resistance of the airways to airflow. In normal animals, approximately 50-70% of total resistance is in the upper airways (what must it be in our brachycephalic patients?!).

In the tracheobronchial tree, the majority of resistance is in the central airways (larynx, trachea and bronchi) with the small airways, the bronchioles, contributing very little. For this reason, obstructions of the upper airway or of the trachea and bronchi cause much more severe respiratory distress than obstruction of the bronchioles. Obstruction of the bronchioles must be extensive and severe to cause a major increase in the work of breathing, especially in dogs.

In respiratory disease, the resistance of the air passages may be increased:
• by the presence of obstructions, such as mucus, a FB or a mass,
• by the contraction of airway smooth muscle as a result of allergic responses or alterations in autonomic regulation, or
• as a result of edema in the walls of the airways,
• or by a combination of these – all effectively leading to a narrowing of the lumen.

**Airway resistance** can be measured clinically in the anesthetized animal \( R_L = \frac{\Delta P}{\Delta V} \); its units are pressure (P)/flow (V), or cmH<sub>2</sub>O/ml/s). Recent advances in respiratory physiology have allowed for the measurement of airway reactivity in healthy awake cats using a barometric whole-body plethysmograph, a technique that clinicians at Tufts University are working on developing and hopefully will become available for clinical use in the future.

2. **Distribution** - Inhaled air must be distributed throughout the air passages to all alveoli within the lung. The distribution of airflow is determined by a combination of the frictional resistance of the air passages and by local changes in lung compliance. Uneven distribution of ventilation is a major cause of abnormal gas exchange in lung disease. Maldistribution of inspired gas results in an inequality of ventilation (V) to perfusion (Q) (referred to as a **V/Q abnormality**), and clinically to hypoxemia, exercise intolerance and tachypnea for instance.

3. **Diffusion** - The transfer of gas between the alveolus and the capillary blood occurs by a process of diffusion. Diffusion is a passive process, depending on a number of factors including partial pressure differences of a gas on either side of the large surface area of the alveolar-capillary membrane. In disease, these factors can be altered because (for example) the alveoli are flooded with exudate or because of changes of the distribution of blood flow (e.g. pulmonary emboli). Carbon dioxide, because of its greater solubility, diffuses much more readily than O<sub>2</sub>. Lung disease, therefore, is more likely to
cause hypoxemia than it is to cause an increase in CO$_2$ tension; when I do encounter an increase in CO$_2$ in dogs it carries a grave prediction.

The efficiency of gas exchange in the lung is determined by the matching of ventilation to blood flow. In normal alveoli, the ratio of ventilation to blood flow is close to 1, but even in normal lungs there exist regions that have more ventilation than blood flow (more dorsal regions) and some that receive more blood flow than ventilation (the more ventral regions). In small animals these differences are probably of minor importance. In disease, a wide variety of ventilation to blood flow ratios can exist in the lung. Low V/Q ratio regions of the lung occur as a result of airway obstruction or flooding of the alveoli with exudates. These low V/Q ratio units are extremely common in lung disease and give rise to clinical hypoxemia. Although V/Q is not readily measured, the overall efficiency of gas exchange in the lung can be calculated by measuring the difference between the partial pressure of O$_2$ between arterial (A) blood and alveolar (a) gas, the DA-aO$_2$ or simply the “A-a gradient”.

4. **Perfusion** - The blood flow to the gas exchange region of the lung is delivered by the right ventricle, and must be matched to ventilation if a normal V/Q ratio is to exist. When pulmonary vascular disease exists, (e.g. pulmonary hypertension secondary to chronic bronchitis, canine heartworm disease), or when there is a low pulmonary artery pressure, (e.g. shock), the distribution of blood flow can be abnormal and can lead to signs of respiratory disease.

If there is some degree of airway obstruction (bronchospasm, edema, secretions etc.) then airway resistance will increase. The animal may attempt to facilitate exhalation by increasing intrapleural pressure via active abdominal contraction (mostly due to contraction of the external abdominal oblique muscles phenomenon which can easily be palpated). As intrapleural pressure increases in the face of expiratory airway narrowing, the pressure within the airways rostral to the obstruction begins to decrease and the point at which these pressures are equal (the equal pressure point or EPP which is normally near or at the thoracic inlet) begins to move upstream towards the alveolus. Any additional intrapleural pressure (active abdominal contraction/expiratory effort) will only further dynamically narrow the airways and results only in peak expiratory flow but overall a decrease in overall expiratory flow. If there is any structural weakening the increasing airway pressure upstream (caudal to the obstruction) may result in complete airway collapse (closure). Exhalation said time increases and exhalation is referred to as being “flow limited”.

*Careful observation and examination of an animal (performed while breathing at rest) may detect this increased expiratory effort (by visual inspection or by manual palpation), and a diagnosis of diffuse small airway obstruction made. This is a very simple yet critically important and powerful clinical technique and diagnostic tool.*
Nasal, Nasopharyngeal & Laryngeal Diseases

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Signalment: Nasal, nasopharyngeal (NP) and laryngeal disorders are common causes of upper airway respiratory distress. Airflow obstruction is the problem in all these conditions. Laryngeal disease is perhaps more common than you realize in small animal practice, and includes such problems as the brachycephalic airway syndrome, laryngeal paralysis (in both dogs and cats!), and neoplasia. Clinical signs associated with these regions however are fairly similar.

History: There are a variety of presenting complaints that are associated with upper airway problems, including:

- Sneezing and reverse sneezing (also the "aspiration reflex," a normal response to any irritation of the dorsal nasopharyngeal mucosa).
- Nasal discharge: determine type (serous, mucoid, purulent, bloody etc.), amount, frequency, whether (when it was first noticed) unilateral or bilateral, if the character has changed, and if it is worse at any specific time of the day. Not uncommonly, the discharge may sometimes be due to chronic pneumonia or vomiting (secretions are thrown or coughed into the nasopharynx, and then noticed as a nasal discharge).
- Respiratory sounds/noise: does the animal make any sound while breathing (with exertion or while sleeping)? Sounds which are new or only recently noted are likely important indicators of airway obstruction. Ask if there are any voice (bark, meow/purr) changes (laryngeal disorders?). Sounds discussed include:
  - Stertor, a snoring sound, due to an intermittent physical obstruction usually heard on inspiration (e.g., soft palate, NP mass).
  - Snorting, found with obstructions due to accumulated secretions (e.g. nasal).
  - Stridor, an inspiratory wheeze or noise, typically associated with high cervical tracheal/laryngeal airway narrowing lesions. Listen specifically here with your stethoscope. Many subtle lesions may be detected this way.
- Exercise intolerance – do the owners play or walk their pet daily? If so, has there been a change in distance or time with activity? It is usually accompanied by an increased inspiratory effort and often with pronounced stridor if the problem is laryngeal or tracheal.
- Open mouth breathing – may indicate bilateral nasal or nasopharyngeal obstruction. Interrupted sleeping ("fitful" sleeping) is often confirmed if the owner is asked.
- Cheek puffing – often noted on expiration with NP obstruction (e.g. masses).
- Coughing after eating or drinking.

Physical examination: I test for airway patency through, and estimate airflow from, each nostril separately – often using the bell on my stethoscope to listen to airflow. At rest, a healthy animal should be able to breathe without distress through one nostril when its mouth is held closed. If there is any change in effort or noise associated with single nostril breathing, I assume there is some degree of obstruction.
Look at the type of discharge and ask the owner how this may have changed over time (response to previous treatments etc.). Facial deformity and/or periosteal pain may be indicative of bony or periosteal involvement—often associated with tumor, fungal infections, or occasionally abscessation of a tooth. Signs of pharyngeal disease usually are associated with airflow interference and/or the presence of a nasal discharge. Open mouth breathing (without difficulty) in the face of bilateral nasal obstruction is typical.

Specific **diagnostic tests** include:

- **For epistaxis**: look at platelet numbers and function (mucosal bleeding time), PT/PTT as well as arterial blood pressure (for systemic hypertension); check medication history for aspirin and/or the use of alpha agonists.
- **For feline calici virus (FCV)**: usually only by virus isolation.
- **For feline herpes virus (FHV), Chlamydia and Mycoplasma**: PCR tests are available to help diagnose these agents. The test may be performed on either a conjunctival scraping or tissue (conjunctiva or nasal) biopsy; transport media is required (sterile saline often works).
- **For nasal fungal disease**: canine aspergillosis - fungal serology is not very sensitive; for feline cryptococcosis the Latex agglutination test has good sensitivity.
- **Dental evaluation** – under anesthesia do complete periodontal probing and dental radiographs (focal distance to 16” with standard digital radiographic equipment).
- **For any nasal, NP or laryngeal disorder** – the best tests include:
  - radiography (skull and dental radiographs as well as CT/MRI which have particular application to nasal and sinus disease), and especially
  - complete periodontal / dental examination
  - anterior/posterior rhinoscopy, laryngoscopy including the use of doxapram HCl.

**Rhinoscopy** is the visual assessment of the anterior nasal cavities, the posterior nasopharynx (NP) and when there has been turbinate loss it is possible to examine some of the paranasal sinuses. General anesthesia and specialized endoscopic equipment are required. Indications for performing rhinoscopy include complaints of sneezing, reverse sneezing, nasal discharge, epistaxis, abnormal sounds and/or some degree of airflow obstruction. Animals with epistaxis should have a coagulation profile (platelet count, PT/PTT and/or buccal mucosal bleeding time) performed and their blood pressure checked prior to starting as these patients may have an increased risk of bleeding.

For a complete evaluation of the nasal cavity, sinuses and nasopharynx the assessment should include skull radiographs (or CT), rhinoscopy and complete periodontal probing. Due to strong airway protective reflexes (sneezing and gagging), rhinoscopy requires a deep plane anesthesia (with a fully inflated entotracheal tube cuff), especially for posterior rhinoscopy. Topical lidocaine, sprayed on the mucosal surfaces, may help blunt these reflexes. The patient is placed in sternal position, chin supported (avoid pressure under the pharyngeal area as this interferes with posterior rhinoscopy) and mouth held open with a mouth gag. I use both flexible and rigid endoscopes in doing a complete rhinoscopy. The size of the patient will determine the size of flexible endoscope that can be retroflexed around the palate and into the NP – I normally use the 5mm diameter bronchoscope. Anteriorly most people use the rigid pediatric cystoscope, although in larger animals the flexible endoscope can also be used to view at least the anterior nasal cavities.
Some degree of patience and practice is required to maneuver a flexible endoscope around the soft palate and into a position to clearly visualize the NP. Care must be taken to not force the scope – trauma to the patient and damage to the scope are possible if care is not taken. When properly positioned the following structures will be visible: the free edge of the soft palate, soft palate, mucosa of the dorsal nasopharyngeal wall, opening to the Eustachian tubes (on the dorsal, lateral walls), choanae, and some of the ectoturbinates in either nasal cavity as well as the vomer bone and the nasal septum. The mucosa should be pink and not friable; there should be minimal secretions, the choanae should be patent; turbinates should not protrude into the NP.

Typical lesions and abnormalities that I have encountered in the NP include:

- Mucosal abnormalities: inflammation, hyperemia, increased mucosal fragility or friability, and lymphoid follicle development (follicular pharyngitis - an indicator of chronic irritation) or mucosal proliferative lesions (caution - lymphoma in cats can look grossly similar).
- Decreased amount of space in the NP: due to tumor, polyp, foreign body, stricture, web, excess secretions or even “ectopic” (NP) turbinate development (brachycephalics).
- Miscellaneous: nasal mites, eustachian tube drainage, NP wall abscess.

Once the NP has been examined, the mouth gags can be removed and anterior rhinoscopy performed. The endoscope should initially be directed dorsally and medially (to bypass the bulbous alar cartilage) and then straightened out and advanced into the nasal cavity (be careful to remain parallel to the nasal septum). This will ensure that the scope enters the common meatus and minimizes the potential of trauma to the tissues at the entrance of the nasal cavity. With a small scope and a larger sized animal (or if there has been turbinate destruction) it may be possible to traverse the length of the nasal cavity and enter into the NP.

The following structures may be visible during anterior rhinoscopy:

- Opening to the nasolacrimal duct - ventral edge of the alar cartilage.
- Nasal septum (vertically aligned, opposite of turbinates).
- Turbinates (dorsal and ventral chonchae), all arise from lateral aspect.
- Four meatii (dorsal, middle, ventral and common) - it is important to note the size of the meatus!
- Ethmoidal labyrinth caudally, a smoother, more tan appearing mucosa.
- Maxillary, frontal and sphenoid sinuses - only viewed when there has been significant turbinate destruction/loss.

Anterior rhinoscopy can be made very simple if the size of the air channels (the meatii) or simply the amount of visible space is carefully evaluated. The amount of visible space can only be: 1) normal; 2) increased; or 3) decreased. As in the NP, the anterior respiratory mucosa should be pink, not friable with minimal secretions present.

Typical lesions or abnormalities encountered during anterior rhinoscopy include:

- Mucosal abnormalities: inflammation, hyperemia, increased mucosal fragility or friability, lymphoid follicle development (less commonly found than in the NP).
- Increased amount of visible space: turbinate loss, chronic inflammation (usually associated with such conditions as canine nasal aspergillosis or secondary to bacterial infections, e.g., due to tooth abscess, FB or feline viral infection).
• **Decreased amount of visible space:** the normal air space (meatus) is filled by secretions, tissue (tumor, granuloma, polyp), or foreign material.

• Secretions: all types (note: nasal mites do not cause thick nasal secretions)

• Miscellaneous findings: parasites (nasal mites), fungal plaques.

Cultures from the nasal cavity, although frequently positive, are not beneficial as these are thought to be secondary to another problem and usually clear up with minimal treatment if the underlying and primary problem is resolved (e.g., tooth root abscess, foreign body). Pinch biopsy forceps may be passed through the endoscope (rigid and flexible) or alongside the scope to biopsy a lesion in question using direct visual guidance. Care should be taken to obtain multiple biopsies and to get samples deep within the tissue (to avoid sampling the necrotic edge of a lesion). In the study by Lent and Hawkins 83 of 94 cases (88.3%) had a definitive diagnosis made using gross rhinoscopy and rhinoscopic assisted biopsy. Touch imprints for cytology should be reviewed in your practice while awaiting histopathology results. Recently forceful hydropulsion has proven useful in obtaining large biopsy samples as well as in at least temporarily relieving nasal obstruction in both dogs and cats.

**Laryngoscopy** is the gold standard for assessing laryngeal disease as it allows for the evaluation of both anatomic lesions but also importantly disorders of intrinsic laryngeal function/motion. Although routine equipment may be used (tongue depressor, light source), I firmly believe that using an endoscope allows for a more detailed evaluation of the larynx as well as allowing you to look into the NP and down into the trachea for any co-existing problems. Prior to anesthetizing the animal, be sure to evaluate for any loss of sensory function (gag reflex) in the oropharynx as this may be associated with an increased risk of future aspiration (especially important if laryngeal surgery is anticipated).

Classically, a light plane of anesthesia (ideally so the animal is still gagging) has been recommended when evaluating the larynx. Following assessment of the laryngeal anatomy I recommend using the respiratory stimulant doxapram HCl, (Dopram-V, 2.2 mg/kg BW IV) to overcome concerns about anesthetic depth and to maximize intrinsic laryngeal motion; the onset is fast, usually within 15-30 sec, with a duration of 2-3 minutes. The use of doxapram has allowed for a deeper plane of anesthesia initially and a better assessment of subtle anatomical abnormalities while still being able to assess intrinsic laryngeal function.

**Typical lesions that I have observed in the pharynx/larynx during laryngoscopy include:**

• Elongated soft palate: this should be anticipated and resected at the time of scoping if possible.

• Laryngeal mucosal edema: this can be severe in animals with a chronic history of upper airway noise (again, anticipate this in the brachycephalic breeds)

• Edematous/everted laryngeal saccules (lateral ventricles): eversion can be very dynamic (and historically intermittent) so look closely both at rest as well as following doxapram administration!

• Laryngeal paralysis: may be unilateral or bilateral, is cats as well as in dogs!

• Laryngeal collapse: a life threatening complication of chronic airway obstruction may be missed (not apparent) unless doxapram stimulation is used.

• Laryngeal neoplasia, most common types: lymphoma, squamous cell carcinoma

• Epiglottic entrapment: secondary to other inspiratory problems; may be intermittent.

Biopsies may be taken under direct visualization. Edema may result from vigorous laryngeal manipulation (especially in cats) and I frequently give corticosteroids following completion of the
procedure. Severely obstructive lesions may require the placement of a temporary tracheostomy to maintain a patent airway while ancillary measures are taken to treat the obstruction (corticosteroids for edema, laser resection of mass lesions, or perhaps definitive surgery for laryngeal paralysis).

**Examples of upper airway problems** that often present in respiratory distress include:

**Reverse sneeze:** this is a normal reflex to the irritation of the dorsal wall of the nasopharynx, and characterized by the sudden onset of forceful and paroxysmal inspiratory efforts. Although not a serious problem for the animal, it is a common cause of concern to owners! There is no specific treatment (except for an underlying cause if found – nasal mites are a common cause in my experience). NP inflammation (including severe follicular pharyngitis) is associated with reverse sneezing. Any irritant can be the trigger for this reflex. If no trigger can be found I will often prescribe a trial therapy of an anti-inflammatory (steroids or piroxicam).

**Nasopharyngeal stenosis or webbing:** A problem in cats (primarily) of any age; this is a transverse scar tissue (of variable width) formed above the soft palate which obstructs the flow of air through the NP. Typically there is a small pinhole size opening for airflow. Webbing is believed to result during the healing process after various injuries to the air passages (infectious, traumatic). Scar tissue has also been observed within the nasal cavities. Diagnosis is best made via CT or direct visualization (rhinoscopy). Surgical resection of the lesion, usually via splitting the soft palate, removing the web and closing the palate has been used. Complications include dehiscence of the palate and reformation of the web. Recently success has been reported using a ballooning technique to break the web down +/- using a stent to maintain an airway during the healing process. The difficulty with any of these procedures is to prevent the scar tissue (web) from reforming again.

**Nasal foreign bodies:** in my experience, the majority of these cases involve material that the animal has mouthed and then when trying to get rid of it has thrown it up into the NP; caudal (flexible) rhinoscopy is needed to identify and deal with these cases. Vigorous nasal flushing with sterile saline may be helpful in removing material.

**Laryngeal paralysis:** this is a common problem in large breed dogs (as an acquired, slowly progressive neuropathy), as well as in some breeds of dogs as a congenital problem (the Bouvier, Siberian Huskies, Dalmatians etc.). Cats can also be affected – I will see a number of these each year. Doxapram administration will assist in assessing intrinsic laryngeal function and should be a standard part of any complete laryngoscopy.

I have begun to evaluate these cases more critically at the time of diagnosis to include an evaluation of the site of obstruction (vocal cords or arytenoids?), the degree of arytenoid motion (fixed and rigid or easily abducted?) and the location of the upper esophageal sphincter in attempts to define criteria for selecting the best surgical technique for treating them. Laryngeal surgery is only recommended when respiratory distress is severe due to the high incidence of aspiration pneumonia that has been reported (approximately 15-25%). Surgical procedures include the standard arytenoid lateralization or “tie-back” surgery as well as laser procedures (vocalcordectomy and partial laryngectomy in cats). The risks of intra-laryngeal surgery have always been subsequent scarring (granulation tissue); the topical use of Mitomycin-C (an older chemotherapeutic agent) has shown promise in preventing this complication and we use it routinely.
Brachycephalic airway syndrome: we can do better! I am continually amazed at the severity of airway inflammation that is seen in these cases. The syndrome includes or is associated with a number of specific problems; these airway problems should be aggressively dealt with early in life (at the time they are neutered?) to minimize the chance of/or prevent the onset of irreversible airway changes.

There are at least 7 (maybe 8!) conditions I consider and evaluate for in these animals:

** Stenotic nares –** resect if they are narrowed and especially when there is paradoxical inspiratory motion.

** Elongated soft palate –** the most common problem, I recommend that all brachycephalic dogs have this corrected when they are neutered if not sooner as indicated (along with other abnormalities identified on examination).

** Laryngeal edema –** some degree (often severe) of edema will be present in almost every case; steroids are indicated following surgical correction of these problems but in many cases should be given prior to surgery in attempt to reduce airway inflammation. Chronic edema can lead to fibrosis over time (many dogs suffer from years of inflammation).

** Everted laryngeal saccules –** these are secondary to other problems but with time they can become fibrotic and not resolve following removal of the other (inciting) airway problems.

Laryngeal collapse – an end stage process caused by cartilage failure secondary to long standing inflammation and inspiratory effort; prognosis for these dogs is grave.

Tracheal hypoplasia – I recommend checking all brachycephalic dogs for this (a straight Rt. lateral chest radiograph) prior to any upper airway surgery.

Nasopharyngeal turbinates – normal nasal turbinates which extend into the NP during development and seem to act as another site of airway obstruction.

Enlarged tonsils – these can be quite large secondary to chronic irritation and should be removed if they contribute to airway obstruction when examined.

(** = most common conditions)

Signalment: Any brachycephalic dog (and sometimes cats despite some references which indicate to the contrary) may suffer from one or more of the above lesions. Common breeds include Pugs, English and French Bulldogs, Boston Terriers, Pekingese, Lhasa Apsos, Mastiffs, Boxers, Persian cats etc. Although typically presented during middle age (mean age in a couple of studies was about 2.5 years)
there is a tremendous range in ages encountered (quoted as from as young as 2-3 months upwards to 12 years. Frequently dogs less than 1 year of age are symptomatic and many of these may be severe with Grade II and III laryngeal collapse.

**History:** Looking back in time it is apparent that breeding selection favored the shorter nasal cavity appearance (compare current Google photographs of those from the 1800s or even early 1900s). This rostral-caudal skull shortening and upturning on the mandible resulted in overall crowding of the structures and therefore of the upper airways themselves. The resulting increased resistance to airflow increases the work of breathing, leads to hypoxemia and exercise intolerance, and eventually to additional structural changes including saccular eversion, laryngeal collapse, possible hiatal hernias and both lower airway collapse and gastrointestinal inflammation.

Presenting signs typically involve not only those of airway obstruction (stertor, stridor, exercise intolerance, inspiratory effort, cyanosis, syncope) but also commonly extra-respiratory signs (gagging, regurgitation, vomiting, hyperthermia). In many cases owners indicate that the animal has always made noise (for example) and frequently think it is normal or even cute. Clinical signs often are made worse following exercise, stress, heat exposure, during sleep and recovering from anesthesia.

**Physical Examination:** These are great dogs – energetic, happy, playful – but only to the degree that their airways permit! Obesity is of major importance in the well-being of these dogs, I always record body weight as well as body condition score in my patients and discuss diet and weight management with the owners.

Observing breathing patterns for these patients is important – I am looking at their BCS, effort (inspiratory especially), for evidence of paradoxical motion (nostrils), thoracic inlet or intercostal retraction and/or an abdominal expiratory push. Noisy breathing which is heard in the exam room is common (usually due to stertor associated with an elongated soft palate), but careful actual auscultation of the larynx with your stethoscope may reveal inspiratory wheezing (stridor) which indicates a more serious problem in my experience (indicates serious laryngeal narrowing – e.g. possible severe everted saccules, mucosal edema or laryngeal collapse). Lung sounds may be harsh and crackles are not uncommon. Fluid accumulating in larger airways is often encountered and coughing or coarse crackles (gurgling) can be noted on auscultation.

**Differential Diagnoses:** The main components of this syndrome are given above, only a full endoscopic evaluation in conjunction with chest radiographs (to measure for tracheal hypoplasia) will confirm the extent of disease in any given dog. Other causes of airway obstruction should be included in your list of differentials including ranula (lingual, pharyngeal), neoplasia (nasopharyngeal, tonsillar, laryngeal, tracheal, thyroid), polyp and possibly lung tumors. Tracheal and mainstem bronchial collapse has recently been reported as a common finding in brachycephalic dogs (>90% in pugs reported in one study).
Gastrointestinal disease is often present in conjunction with the BAS. While confirmed lesions in the esophagus, stomach and duodenum have been associated with the brachycephalic airway lesions (and significantly improve following treatment of the upper airway issues) other differentials for vomiting should be considered including primary GI (foreign body, IBD, neoplasia) and secondary GI issues (pancreatitis, liver or renal disease etc.).

**Diagnostic Tests:**

*Tracheal hypoplasia* is determined or defined based on the size of the trachea as seen on lateral chest radiographs. The normal tracheal diameter in brachycephalic dogs should be equal to or greater than the width of the 3rd rib where it crosses the trachea (Suter). Using the tracheal and thoracic inlet diameter Harvey established a TD/TI ratio for English Bulldogs, non-bulldog brachycephalic dogs, and non-brachycephalics – this is the technique that I routinely use. The figure at the right shows this; the reported TD/TI values from Harvey are:

- English Bulldogs – the TD/TI ratio should be $\geq 0.126$
- Non-bulldog brachycephalic dogs – the TD/TI ratio should be $\geq 0.160$
- Non brachycephalic dogs - the TD/TI ratio should be $\geq 0.210$

*Chest radiographs* are also taken to look for evidence of pneumonia or other lower airway parenchymal diseases.

*Skull radiographs* can be very difficult to interpret (see above), radiographs of brachycephalics are even more difficult (but do not give information about functional or dynamic airway caliber changes. CT images have been recently employed to document the structural (developmental) abnormalities in the skull and turbinates of brachycephalic dogs.

The *nares* can be examined grossly, I look at the nostril size per se as well as any paradoxical motion on inspiration (nares should flare with exertion and not narrow further on inspiration).

**Endoscopy of the upper airway** is needed to asses all the other abnormalities.

The normal *soft palate* should not overlap the tip of the epiglottis (be careful not to pull the tongue out too far as this displaces the epiglottis farther rostral than normal. The laryngeal mucosa should not appear edematous, thickened, proliferative. Submucosal capillaries should be easily visualized on all respiratory mucosal surfaces.

*Laryngeal saccular eversion* (the mucosal lining of the lateral ventricles). These can result in dynamic (intermittent) episodes of airway obstruction and early on appear very pink and edematous. Over time, the chronic saccular eversion tissue becomes more fibrotic and firm, often turning a tan color.

*Laryngeal collapse* gradations of were published by Leonard about 50 yrs ago and include:

- Stage 1: eversion of the laryngeal saccules
- Stage 2: loss of rigidity and medial displacement of the cuneiform processes of the arytenoid cartilages
Stage 3: collapse of the corniculate processes of the arytenoid cartilages

Nasopharyngeal turbinates – once the bony outline of the skull is forming the turbinates (which develop at a later time) may have insufficient room to develop, “turn” caudally and grow into the nasopharynx ending up protruding from the choanae/into the nasopharynx resulting in a newly reported nasal obstruction in dogs and cats. Pugs are reported to have a very high incidence of this abnormality.

Tracheal hypoplasia – the shape of the trachea is usually abnormal and grossly apparently small or misshapened (angular rather than circular or cartilage edges rolling inward on themselves rather than forming an open “C” shape joined by the trachealis muscle.

Enlarged tonsils – in rare cases I have encountered tonsils that are extremely enlarged and appear to interfere with eating, oral breathing – or both. I have elected to perform a bilateral tonsillectomy in a few of these more severe cases.

Endoscopy of the upper gastrointestinal tract may be indicated. In one recent study of 73 French Bulldogs 98% of gastric biopsies showed evidence of chronic inflammation. Lesions encountered included hiatal hernia, gastroesophageal reflux, esophagitis, gastric and duodenal inflammation to list only a few. Significantly many of the clinical and histologic abnormalities resolved or regressed following surgery for the upper airway BAS.

Treatment: I firmly believe (and multiple articles recommend) that early diagnosis and surgical intervention is indicated in these dogs. Although there is concern that years of recurring “microtrauma” in these dogs may lead to progressive and potentially irreversible airway obstruction, it is not just middle aged and older dogs as puppies as young as 3-4 months of age may be severely affected.

There are three types of treatments that are employed to manage and treat these cases, often a combination of all three will be needed.

Management: Diet is critical (have them lose weight if overweight, counsel the owners on proper diet and recommended weight for the breed) - you can look up standard breed weights on the AKC web site, go to http://www.akc.org/breeds/index.cfm?nav_area=breeds. Keep these dogs thin! Lifestyle changes are needed; avoidance of triggers which can make their airway issues worse – excessive exercise, exertion, stress and heat are examples and real life risk factors.

Breeding – owners of severely affected dogs should be cautioned about the likely heritability of these conditions and warned against breeding.

Medical options: Corticosteroids are used to help reduce mucosal swelling. Sedation of the lab with laryngeal paralysis is most often done with acepromazine and this relieves the anxiety that makes these cases get progressively worse. I find however that the muscle relaxation with ace makes many brachycephalics worse as the oropharynx relaxes. Instead, I try to use narcotics to relieve the anxiety and subjectively seem to have less airway muscle relaxation.

Oxygen support is frequently needed and may be provided via an oxygen cage or nasal canula, the latter often placed as an animal is undergoing surgical correction for one or more of these problems.
If pneumonia has been identified then appropriate antibiotic therapy will be needed (best if based on cytology and culture/sensitivity).

If gastrointestinal problems are part of the clinical picture then specific GI medications (antacids, prokinetics, treatment for IBD if identified) may be required as well.

**Surgical options:**

**Stenotic nares** – procedures using a wedge resection of a portion of the alar fold or simple resection (sharp or laser) have been used. I prefer to remove a portion using the CO2 laser as it is fast, has less bleeding and heals nicely (pigmenting in within 1-2 months).

**Elongated soft palate** – again procedures to use scissors, laser or RF to remove the elongated portion of the palate have been used and at least one study indicated roughly equivalent outcomes. The palate should just barely touch the top of the epiglottis (some use the caudal aspect of the tonsillar crypt as a landmark).

**Everted laryngeal saccules** – removal of these is dependent on assessing the degree of obstruction as well as the chronicity of the problem (whether fibrotic changes have taken place in the tissues). Correction of the stenotic nares and elongated soft palate is often sufficient to improve (lower) airflow resistance and to allow the saccules to revert to normal without surgery (you can always do it later if needed). Sharp and laser techniques are available to remove the saccules. To minimize the potential for granulation tissue formation I have applied a Mitomycin-C soaked sponge (a chemotherapeutic that inhibits fibrosis) to the lasered surfaces for ~5 min.

**Laryngeal collapse** – this represents a serious and end stage development in the BAS, one that I caution owners is a critical development and that carries a very guarded prognosis. Most often I see the cuneiform processes of the arytenoid cartilage scissoring across and obstructing the glottic lumen. Using doxapram to stimulate ventilation is recommended to confirm collapse in suspected cases. Some have advocated a modification of the standard laryngeal tie-back procedure, others a partial laryngectomy (removing part of the cuneiform process).

A permanent tracheostomy is one way of dealing with severe laryngeal collapse or other severe obstructive upper airway lesions (granulation tissue formation in the larynx for instance). Although requiring a skilled surgeon and a dedicated owner this is usually a lifesaving procedure that studies have shown to be well accepted by owners.
AIRWAY DISEASE IN THE CAT AND DOG: WHAT WORKS?

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When I was sitting in class last century (!), it was questioned whether there was such a thing as naturally occurring chronic bronchitis (CB) in dogs…when I spoke at the WVC recently I was challenged by a recent graduate who said he was taught that there was no such thing as chronic bronchitis in dogs…trust me, chronic bronchitis does exist! It is a very common disease in dogs and cats with varying degrees of long term morbidity.

CB is the term initially applied by Wheeldon in 1974 in an article describing the pathology that was seen in dogs when chronic coughing which occurred for two or more consecutive months during the preceding year and which was not attributable to another cause (e.g. neoplasia, CHF). It also implies a non-reversible (indeed a slowly progressive) condition. Both dogs and cats develop CB, and the 2 month time course has been generally extended to apply to cats as well as to dogs.

Acute bronchitis (canine infectious tracheobronchitis, “kennel cough”) is typically reported to be caused by viral and/or bacterial agents. It is normally self-limiting (<2 months in duration with or without treatment). Immunocompromised animals (young, stressed, those in crowded housing etc.) are at increased risk. Various viral agents have been incriminated (including canine distemper virus, parainfluenza, adenovirus and recently canine influenza to name a few). Secondary bacterial infection is the main concern and common cause of secondary pneumonia. *Bordetella bronchiseptica* is the classic but not only bacterial agent recovered in these pneumonia cases – others include *E. coli, Pseudomonas* spp. and *Strep. zooepidemicus*.

A specific etiology for CB is rarely determined. Chronic airway inflammation leads to chronic coughing. The primary effects on the respiratory system are hypoxemia, exercise intolerance and respiratory distress. Recurrent airway inflammation (e.g. persistent infections, inhaled irritants) is suspected. Persistent tracheobronchial irritation results in chronic coughing and changes in the epithelium and wall of the tracheobronchial tree. Mucus production is increased due to changes in glandular structures as well as goblet cells. Other commonly reported changes include airway inflammation, epithelial edema, thickening and metaplasia. Airway narrowing (with the associated increase in resistance and decreased expiratory air flow rates) is the net effect of these changes. In severe cases the work of breathing increases and is detected as respiratory distress (an increase in breathing rate/effort, disproportionate to the patient’s level of exertion). Acute exacerbations may be superimposed on a chronic course.

Changes in the histochemical structure of the cartilaginous rings in the trachea and/or the plates in the bronchial walls result in a weakening of the wall and potential collapse of the affected airways, e.g. tracheobronchial malacia (note the collapse of the lobar bronchi during quiet breathing in the images to the right) or tracheal collapse when the trachea itself is affected. Secondary effects on the heart (*cor pulmonale*) may lead to pulmonary hypertension and may be severe. Syncopal episodes are frequently reported in dogs with chronic coughing due to decreased blood flow thorough
the brain. Hepatomegaly secondary to passive congestion may occur with elevated liver enzymes/bile acids.

CB is typically thought of as a small/toy breed dog problems, but it is also commonly observed in larger dogs. Bronchiectasis has frequently been observed in young to middle aged Cocker Spaniels following a long history of CB. Siamese cats have been reported to be more frequently and more severely affected than other breeds of cats. CB most often affects middle aged and older animals. Ciliary dyskinesia is usually reported in young dogs and results in chronic bronchial disease (including bronchiectasis) due to poor secretion clearance and recurrent infections. A female sex predilection has been suggested by some authors in feline CB, but not our studies. No sex predilection has been noted for canine CB. The patient's **body condition score (BCS)** should be determined as obesity is a common and significant morbidity factor in many diseases including chronic bronchitis.

**History:**
Coughing is the hallmark of lower airway disease. Tracheobronchitis (acute and chronic) typically has the dry, hacking, non-productive cough; post-tussive gagging is common and owners may misinterpret this as "vomiting". Pneumonia is associated with the moist, productive cough. Another major difference is that tracheobronchial disease usually has few if any systemic signs (lethargy, anorexia, fever, depression).

Coughing may occur at any time during the day but is common following exertion (exercise intolerance), at night (nocturnal coughing) as secretions accumulate, or when if the trachea is irritated – for instance with "leash pulling". Breathing with an expiratory effort (abdominal muscular contraction), expiratory wheezing, balloononing at the thoracic inlet, exercise intolerance, cyanosis and even syncope may be reported or noted on careful examination.

**Physical examination:**
With pre-existing tracheal irritation/inflammation, any additional irritation (by palpation or manipulation) of the trachea normally results in coughing; this "increased tracheal sensitivity" is a non-specific indicator of existing inflammation or irritation. The large inspiration required to generate a cough can be used to listen for crackles as they tend to occur on inspiration. An expiratory abdominal push (increased effort during quiet/resting breathing) and/or end-expiratory wheezing are characteristics encountered in patients with severe small airway disease.

Most CB animals are bright, alert and afebrile. Bronchovesicular lung sounds and end-inspiratory crackles are commonly heard. Wheezing may be noted, especially when airflow initially moves through airways obstructed by secretions or during a laryngeal brake maneuver. An end-expiratory “snap” may be heard in dogs with decreased cartilage rigidity (**malacia**), as the increased intrathoracic pressure generated with an active expiratory effort (cough) often collapses central airways (normal airways will narrow but do not collapse) and the airway walls literally “snap” together. Active abdominal (external abdominal oblique muscle contraction) during quiet breathing is both abnormal as well as an excellent indicator of diffuse small airway disease.

In cats with CB, lung sounds may be normal at rest but (post-tussive) crackles become prominent after coughing is induced and as secretions are loosened. Increased tracheal sensitivity should be evaluated
in all patients but especially in cats. Tachypnea is a more frequent primary complaint in cats than in dogs with CB.

A careful cardiac examination is important in order to differentiate heart disease from CB; in many cases this can be difficult to do. Murmurs secondary to valvular insufficiency are common in older, small breed dogs (but not in cats); these cases must not be misinterpreted as being in CHF. A simple but fairly accurate method of determining whether CHF or CB is present in the dog (less so in the cat) is to examine the resting heart rate; CHF is associated with an elevated heart rate while CB often results in a normal to slower heart rate due to vagal stimulation.

**Differential diagnoses** for an animal presented in respiratory distress and with a history of coughing, crackles, exercise intolerance and a murmur include: bronchitis, tracheobronchial malacia, pneumonia, bronchiectasis, aspiration secondary to laryngeal dysfunction, allergic lung disease, compression on a mainstem bronchus (LAE?, hilar lymphadenopathy), foreign bodies, pulmonary hypertension, HW or other cardiopulmonary parasites and primary cardiac problems.

**Diagnostic tests** for patients with lower airway disease/respiratory distress include:

**ABGs** – These are easy to do and provide the only functional assessment of overall lung function available in practice (using local human hospitals which are accessible to everyone or in house small portable blood gas units which are commonly available now).

**Parasite evaluation** – fecal exam(s) including Baerman, HW testing (endemic areas, dogs with a travel history). If cytology supports a possible eosinophilic airway infiltrate then prophylactic deworming (with ivermectin or fenbendazole) is indicated – regardless of fecal test results.

**CBC** – Useful in those with systemic signs (pneumonia cases primarily). Less than 40% of confirmed allergic airway cases (those with eosinophils on airway cytology) have an absolute peripheral eosinophilia. A word of caution – bacterial pneumonia can exist and be severe despite a normal CBC! (not all dogs read your Clinical Pathology book as to how to react)

**Radiography** - Thoracic radiography provides one of the most widely available method for evaluating the tracheobronchial tree and lung parenchyma. Bronchial disease normally demonstrates the thickened bronchi (“donuts”, “tram lines”). Parenchymal diseases usually cause an increase in interstitial density, which increases with severity to an alveolar pattern and eventually to lobar consolidation. Changes may be patchy, lobar or diffuse. Remember however that functional changes and visible structural changes do not parallel each other. Thoracic radiography should include views made in at least two planes; lateral and either the VD or DV position. I prefer to obtain 3 views of the chest, both right and left laterals and the VD view for the evaluation of lung disease. For optimal demonstration of parenchymal lesions, thoracic radiographs should be obtained at peak inspiration (for dynamic airway lesions both peak inspiratory and peak expiratory radiographs should be obtained).

**Airway cytology** is necessary to determine an etiologic diagnosis and in order to recommend the most appropriate/specific therapy. Samples should be examined both cytologically as well as by culture and sensitivity determinations. Extensive cytology experience is not required in order to differentiate between many of the common causes of coughing. Each technique has reasons pro and con as well as different risks associated with the procedure.
**Transtracheal aspiration biopsy** (TTA) is indicated in acute (when a culture is needed) or in chronic lower respiratory tract diseases when other routine tests have failed to establish a diagnosis. A large bore (e.g. 16ga), "thru-the-needle" type jugular catheter, 3 way valve, sterile saline, syringes and microscopic slides is required for a true transtracheal procedure. Lidocaine (2%) is sufficient for local anesthesia; general anesthesia should be avoided due to cough suppression. A sterile urinary catheter may be used through a sterile endotracheal tube if performing a trans-oral technique. Care must be taken if a trans-oral technique is used in order to avoid oral cavity contamination. With either technique, the tip of the catheter should be just proximal to the carina. The amount of fluid injected will vary with both the disease and the size of the patient. I typically inject 3-5 ml aliquots of sterile saline and, after the animal has coughed, aspirate the repeat as needed until a visible sample is obtained.

A **fine needle lung aspirate** (FNA) may be used when there is diffuse lung disease or when a large region of lung is diseased (e.g. lung mass or consolidated lobe). The aspirate should be obtained from a region identified by radiography, using a small gauge needle (typically a 1-1.5" x 22-25 ga. needle) and a 6 ml syringe. The needle should be inserted in front of the rib and (with respiration stopped) briefly thrust into the lung, aspiration applied and then the needle quickly withdrawn. Only a small sample (perhaps enough for 1 or 2 cytology slides) will normally be obtained although repeated samples can be used to obtain material for culture. Be careful performing a fine needle lung aspirate in an animal with an active expiratory effort as the risk of inducing a pneumothorax is increased.

**Bronchoscopy** - There is no question, when performed by an experienced endoscopist, that bronchoscopy is the gold standard for the diagnosis of lower respiratory tract diseases in small animals. Bronchoscopy has been an integral part of respiratory practice in veterinary medicine since at least the early 1970s. There is no question that bronchoscopy (which should always include bronchoalveolar lavage - BAL - for cytology and culture) is the gold standard for the diagnosis of lower respiratory tract diseases in small animals. Bronchoscopy may be used for diagnostic, therapeutic and prognostic purposes. Diagnostic bronchoscopy obtains visual information concerning the airways (e.g., compression, dynamic collapse, dilation) as well as samples (cytology, culture, and occasionally biopsy) to help establish a specific etiologic diagnosis and information regarding prognosis.

General anesthesia is necessary to control airway reflexes during bronchoscopy, thereby preventing trauma to the airways, and at the same time protecting the endoscope throughout the procedure. The ideal anesthetic should provide good patient restraint, have minimal cardiorespiratory effects, be either reversible or of short duration and allow for a smooth recovery period. The availability of newer, short acting and/or reversible injectable anesthetics has allowed bronchoscopy to be performed on patients with minimal concern.

My current anesthetic protocol utilizes either atropine or glycopyrolate, with either acepromazine or butorphanol for premedication; diazepam and propofol are used for the anesthetic procedure. I prefer not to intubate my patients until the recovery phase of the procedure. This form of anesthesia is very beneficial because it not only provides adequate anesthesia for the procedure, but also allows for rapid patient recovery, an important factor in geriatric patients. Oxygen should be administered prior, during and following the bronchoscopy while using O2 saturation monitoring to ensure adequate oxygenation throughout the procedure. Bronchodilators (injectable terbutaline is what I prefer) is recommended prior to performing a bronchoscopy – particularly in cats and smaller dogs to minimize possible bronchospasm.
The bronchoscopist must have a good understanding of normal endoscopic lung anatomy if s/he is to recognize subtle abnormalities and diseases. The differentiation (recognition) of normal from what is abnormal (and often only subtly so) is a subjective one. Experience, images in textbooks and practice greatly improve the clinician's ability to detect lesions at an early stage.

I routinely examine the larynx (anatomy and intrinsic function/motion if possible – use doxapram as outlined above if there is any doubt about intrinsic laryngeal function), the cervical and intrathoracic trachea and then the carina before sequentially evaluating all the lobar and finally as many segmental and/or sub-segmental bronchi as possible (the latter varies with patient and endoscope size). Changes in gross anatomy, fixed and dynamic lumen size, abnormalities in airway shape, mucosal/submucosal characteristics, and the presence of secretions should be noted. Experience and practice will improve an endoscopist's ability to detect early lesions. Samples obtained (cytology, culture, +/- biopsy) are then relied upon to establish a specific diagnosis.

**Bronchoalveolar lavage (BAL)** is essentially a washing of the distal airways and alveoli. Material obtained from this area is thought to be representative of the distal airways, alveoli, and the interstitium of the lungs. The bronchoscope is guided distally into the selected bronchus and into a gentle wedged position. Once positioned, 10-20ml of body temperature (warmed) sterile saline is flushed into the airways and immediately aspirated using gentle syringe suction (2ml/kg in small patients). Two aliquots per site will improve the return and two lobes/sites per animal gives a better overall representation of the animal's lower airways. The sites are evaluated individually with total cell counts and a cytospin for differential cell counts but I combine the fluid from these 2 BAL sites and do a quantitated culture.

A “blind” BAL is also done at times and although this procedure lacks the information that might be gained from a visual assessment of the respiratory tract, it is preferable (and usually more successful) than a transtracheal (or transoral) wash. A small (5-8Fr) red rubber feeding tube is usually adequate. An approximate measurement should be made from the incisors to the last rib so as to know the farthest point of insertion. The tip of the catheter should be cut off to avoid side hole suction being applied. The catheter is passed through a sterile entotracheal tube and gently down into the lower airways until resistance is felt, then pulled back slightly and the lavage performed. The technique is “blind” since a specific lobe cannot be selectively examined as with the bronchoscopy BAL technique. Most often the catheter will end up in one of the caudal lung lobes.

Difficulties with the procedure (poor returns) may be expected when a proportionately large endoscope prevents wedging into a smaller bronchus, or when the airways are malacic. In the former situation, the fluid is dispersed into too large an area to be easily retrieved, and in the latter, the airways collapse (even with gentle suction), preventing the return of any significant volume of the infusate. The predominant cell in all species should be the alveolar macrophage (70+%), with approximately 3-8% of all other cell types (except the cat which may have up to 20+% eosinophils and still be considered healthy). Many pathologists interpret the high numbers of macrophages in the BAL cell differential as...
“granulomatous” in nature but that is incorrect! Macrophages are the normal cell to be seen on a good BAL.

Cultures from the lower airways are helpful in establishing a specific diagnosis and selecting an appropriate antibiotic based on sensitivity results. Gram stains help in interpreting culture results and provide early insight into correct antibiotic selection. Contamination resulting from the mixing of upper respiratory tract secretions with lower airway samples must obviously be avoided. (finding squamous epithelium and/or the large Simonsiella sp. bacterium are indicative of oral cavity contamination). It has been reported that quantitated BAL cultures are important in the differentiation of airway colonization from actual infection. Mycoplasma cultures are possible using specialized transport media (e.g., Amies media) and overnight shipment to selected laboratories. Check with your lab but normally they will prefer 2-3ml of fluid in a sterile tube vs, a swab in media for these cultures. Microbiological results must always be interpreted in light of the cytology obtained from the same site.

**Electrocardiography (ECG) an Echocardiography (Echo):** One of the major differential diagnoses for the coughing dog (not cat) is primary heart disease. Chamber enlargement due to volume overload may be associated with pulmonary edema and coughing. LAE has been reported to induce coughing directly by direct compression of the left principal bronchus but recent published articles question that assumption. Enlargement of other chambers, e.g. the RA and RV, have been associated with chronic lower respiratory tract diseases and the development of cor pulmonale.

**Thoracotomy** – if other diagnostics have failed to establish a firm diagnosis exploratory surgery should be considered, pulmonary fibrosis for instance requires a tissue sample to confirm this diagnosis. Thoracoscopy is beginning to be used to obtain lung biopsies for histopathologic confirmation of a variety of lung problems.

**Examples of lower airway problems that may lead to respiratory distress include:**

**Tracheal collapse** – Tracheobronchial malacia, of which tracheal collapse is the classical and obvious example, is brought on by small airway disease leading to the previously described histochemical changes in the cartilage which allows collapse to occur as increased intrathoracic pressures are generated to during exhalation. The medical treatment of these cases is very similar to the treatment for CB. Diet is critical and these animals must be prevented from becoming obese. Collapse may involve the lobar and segmental bronchi, the intrathoracic or less commonly cases only the extrathoracic trachea.

Selected cases of tracheal collapse may benefit from surgery; careful examination of the airways (bronchoscopy) is needed to select these cases. The placement of external plastic ring supports has been used with good success in selected cases, specifically those proven (based on scoping) to only involve the cervical trachea are candidates for this surgery. This procedure in the hands of an experienced surgeon is an excellent treatment option.

Recently intraluminal tracheal stents have been reported in tracheal collapse cases but should be only considered in very severe cases and can lead to potential complications (granulation tissue formation). Stents can be placed under fluoroscopic, radiographic and bronchoscopic guidance. Case selection and tracheal measurements are critical, owner education is
mandatory as they must understand the limitations and potential complications of what is basically a salvage procedure.

A new study showed that functional (bile acids) as well as biochemical (ALT and ALP) changes would improve following successful surgical treatment of tracheal collapse cases. Severe dental disease should be treated aggressively to minimize the possibility of secondary bacterial showering of the lower airways in these and in CB patients.

**Pulmonary fibrosis** - West Highland White Terriers have been noted to develop a progressive disorder characterized by chronic coughing, tachypnea and crackles. The location of the pulmonary infiltrates as well as the location of audible crackles seems to be more caudodorsal than in other bronchitis cases. Fibrosis is thought to be present in these cases but detailed clinical and pathologic studies of the condition are lacking. High resolution CT or preferably lung biopsy is needed to confirm this diagnosis. Treatment is palliative and similar as for CB cases.

**Neoplasia** – We encounter primary and metastatic tumors on a regular basis. Three view chest radiographs are indicated in order to fully evaluate all lung fields for involvement. Diagnosis is based on cytology or histopathology from a tissue biopsy. Abdominal ultrasound is indicated to ensure that there are no distant primary sites before surgery is considered. Surgical intervention for suspected primary lung tumors is recommended as early in the disease process as possible. The median survival time for primary lung tumors varies significantly based on whether the hilar lymph node is involved or not – always have a hilar node biopsied as part of the surgery!

**Foreign body** – On occasion an owner will witness and know that a foreign body (FB) was aspirated; usually it is the ensuing pneumonia that alerts us to this possibility. The animal’s use (i.e. a hunting dog that runs in fields) is an important part of the history and can alert the veterinarian to this possibility. Diagnosis is based on finding the FB, on bronchoscopy or at the time of surgery (lung lobectomy). Treatment for the ensuing bacterial pneumonia is important following removal. Bronchiectasis may develop secondary to the FB being in the bronchus and even if it can be removed a lobectomy may be required to finally resolve the pneumonia.
Is there any information that says one particular protocol is better than another or that one particular drug really works?? Which antibiotic is best? Am I at risk in using fluoroquinolones in young pneumonic dogs in my practice? How long do I treat for? Are bronchodilators effective? Should I use steroids? What about aerosol therapy – should I be using inhalers? Are there newer drug delivery systems and equipment that I should consider?

No doubt those therapeutic choices can be difficult and confusing. However, establishing a specific diagnosis will make your treatment selection much easier. There are three general goals of respiratory therapeutics that I will talk about: 1) controlling secretions, 2) maintaining alveolar ventilation and 3) normalizing pulmonary (excessive) reflexes.

**Control of secretions:** Secretions may be controlled by either decreasing their production (the best choice) or increasing/facilitating the removal of excess, accumulated secretions.

Methods of decreasing secretion production: Antibiotics and corticosteroids - culture and cytology are the main methods in determining when each is indicated. Bacterial cultures from the upper airways (nasal cavity) are rarely helpful as infections there are secondary; cultures from the lower airways must be obtained from the lower airways, tonsillar swabs are not indicative of flora in the lower airways. It is important to remember that significant bacterial growth is **not** normally associated with chronic bronchitis in dogs or in cats.

**Drugs -**

**Antibiotics:** Use bactericidal antibiotics that have a good spectrum of activity. A Gram stain is helpful in determining which class of antibiotics might be more useful, although each case should have its own sensitivity if possible (especially if you observe Gm negative organisms). For upper airway diseases antibiotics with a good Gm positive spectrum are best. Most pathogens in the lower airways (~85+ %) are Gram negative (e.g. *Bordetella, E. coli, Klebsiella, Pseudomonas spp.* etc.). Cephalosporins, potentiated sulfas, amoxicillin/clavulanate or amoxicillin and especially the fluoroquinolones are good choices for lower airway infections.

The route of administration is a concern for lower airway diseases. If the infection is thought to be tracheobronchial (intra-luminal) then there should be concern about antibiotic penetration into the lumen of the airways (i.e. does the antibiotic actually penetrate into bronchial secretions). Aerosolized antibiotics are helpful in selected cases of canine infectious tracheobronchitis (specifically those due to *Bordetella* infections), but are not appropriate as the sole therapy for pneumonic cases.

**Corticosteroids:** These drugs constitute an important treatment option for allergic diseases as well as in chronic bronchial disease to decrease inflammation and cellular infiltration. I tell owners that chronic bronchitis will never be completely cured, but hopefully the coughing can be controlled and the animal made comfortable. A 70-80% reduction in the animal's cough is a very good response IMHO. I indicate to owners that the cough reflex is a protective reflex and that 100% cough suppression is not desirable.
Oral short acting steroids (prednisone/prednisolone) are preferred for ease of dosage adjustments which is important in chronic conditions. Inhaled steroids are being used more frequently although recent reports suggest that there indeed is systemic absorption from this form of therapy (likely from swallowed drug).

**Antifungals:** With the availability of new oral antifungals (itraconazole, fluconazole, voriconazole), effective antifungal therapy can be accomplished for most infections (e.g. cryptococcosis). Topical treatment (enilconazole, clotrimazole) is preferred for nasal aspergillosis in dogs but only after the gross fungal plaques have been removed (debrided) from the affected nasal cavity and sinus (endoscopically or surgically).

**Non-specific methods of controlling secretions.** Non-specific means of removing secretions including methods designed to "loosen" secretions (e.g. bland aerosol therapy and expectorants) and those which are designed to improve the rate of their clearance from the tracheobronchial tree (e.g. encouraging activity, cough facilitation and chest physiotherapy) should be used. Agents which “dry up” secretions may be tried when other means have failed (often chronic, bilateral mucoid nasal discharge cases).

**Aerosol therapy:** The goals of this form of therapy are designed either to loosen secretions (always in conjunction with physiotherapy) or more recently to deliver drugs into the lower airways. Efficacy is uncertain (there is minimal published veterinary research on this). Antibiotics should not be aerosolized unless it is directly via a facemask and then are indicated only for airway infections. Be sure that systemic hydration is adequate before resorting to aerosol therapy. Some pre-formulated human medications are usable (metered dose inhalers containing steroids or bronchodilators are available); aerosolized drug solutions can also be generated using either an Ultrasonic or jet nebulizer; they produce particles of between 0.5-3 micra in size which are best for deposition in the lower respiratory tract. Again, direct face mask delivery is the only acceptable method. The newer discus formulations are not appropriate for use as they require an active (oral) inspiratory effort and breath hold maneuver to be effective.

**Expectorants:** In principle an excellent idea, but a poor idea in reality.

**Decongestants** - Designed to dry up secretions, I use them rarely, usually when a specific diagnosis was not obtained, the discharge persists and is a problem for the owner. Alpha agonists (pseudophed 0.1-0.4mg/kg BID-TID, PO) may help.

Some nasal conditions result in structural abnormalities (nasal polyps, nasopharyngeal webbing) leading to airflow obstruction and must be treated surgically. Destructive rhinitis in cats following chronic viral disease may be associated with significant retained secretions and benefit from simple saline administration (aerosol or nose spray) or when severe and recurring actual physical debridement (rhinoscopically).

Non-specific airway inflammation (irritation) is one problem which I have encountered which seems to be very difficult to resolve. It is typically characterized by sneezing and a bilateral, slightly opaque to
whitish nasal discharge. Diagnostics to document an underlying problem are indicated as outlined but frequently unrewarding; biopsies show the non-specific lymphoplasmacytic rhinitis we have all grown to hate. Anti-inflammatory therapy (steroids or NSAIDs such as piroxicam) and doxycycline may be used, at least on a trial basis. A change in dog’s environment may also help.

**Maintenance of alveolar ventilation:** Adequate alveolar ventilation is the principal requirement for normal blood gases, tissue oxygenation and acid-base balance. Arterial blood gas analysis is required to quantify these abnormalities. Animals with disease of the lung parenchyma often manage to maintain alveolar ventilation and eliminate carbon dioxide, but do so at an increased cost (work of breathing). Measurement of the DA-aO2 (difference in partial pressure of oxygen between the alveolus and the arterial blood) is a sensitive way to detect abnormalities in the overall efficiency of gas exchange in the lungs. The work of breathing is always of concern in respiratory cases – muscle fatigue is a problem in chronic cases. Theophylline has been shown to be a positive ionotrope to the diaphragm (in dogs a 25% increase in diaphragmatic contractility has been reported with plasma theophylline in the “normal” rage) and could be reasonably considered in many cases of chronic respiratory distress.

Many of these chronic respiratory diseases result in clinical hypoxemia. We have used home oxygen administration to help treat these cases, especially in those confirmed to be hypoxic or have pulmonary hypertension. Small to medium sized dogs (or cats?) can spend their night time hours (at minimum) in these semi closed containers (cages) so as to relieve any hypoxic pulmonary vasoconstriction during those hours (33% of the day isn’t bad for “cardiac relief!”). Concerns for excessive CO2 build-up (manifested as hyperventilation) or excess humidity build-up have not been encountered.

Using a rented oxygen concentrator I have measured the FIO2 in a homemade cage at 52% after 2 dogs had been in it overnight – with no increase in respiratory rate, temperature or humidity. Flow rates of up to 5 lpm are possible with these units.

**Normalization of reflexes:** Excessive reflexes, which are of concern, include sneezing and reverse sneezing, coughing and airway narrowing reflexes (laryngospasm and bronchospasm). These reflexes are a part of the normal pulmonary defenses and should not be suppressed unless they are excessive and/or debilitating – instead do the diagnostics to find the cause!

Coughing is the sudden, violent and often loud ejection of air from the lungs. It is a normal protective reflex, not commonly observed in healthy animals, but necessary in the diseased animal. During a cough, the intrapleural pressure rises dramatically and as a result the intrathoracic airways are compressed. High velocity air is expelled through a narrowed airway and this serves to dislodge irritant materials. Cough is most effective at removing materials from the intrathoracic larger airways, but is not effective in clearing the bronchioles. Coughing is an essential clearance mechanism in lung disease and should not be suppressed unless the cough is dry (non-productive) or physically tiring to the animal, and an attempt has been made to treat a specific cause.
Antitussives – Cough suppression, when indicated, should be doses at the recommended starting dose and then increased to obtain the desired effect if coughing persists. Classes of these drugs include:

- Peripherally acting antitussives include mucosal anesthetics, mucolytics, demulcents, and perhaps bronchodilators.
- Centrally acting antitussives include both the narcotic and the non-narcotic drugs such as morphine, codeine, hydrocodine, butorphanol and dextromethorphan.

Anti-inflammatories – airway inflammation is of concern in many respiratory distress diseases including chronic bronchitis and “feline asthma”. Systemic corticosteroids are commonly recommended (e.g. prednisolone in cats), typically starting out at 0.5-1.0mg/kg PO BID and tapering to an EOD schedule when possible. I prefer to use oral prednisolone and educate the owners as to how and when to adjust their pet’s requirements (based on the frequency of coughing). Long acting, repositol steroids (e.g. DepoMedrol) are effective but should be avoided if possible due to the inability to manage fluctuating steroid requirements and potential adverse side effects including diabetes mellitus or heart failure in cats.

Airway narrowing: Both laryngospasm and bronchospasm occur in response to irritation of the epithelial receptors. Normally laryngospasm is not a clinical problem unless there is actual laryngeal manipulation or when chronic irritation leads to edema. Topical anesthetics, corticosteroids and “TLC” are the treatments/preventions.

Bronchodilators are commonly used in the treatment of canine and feline airway disease and potential bronchospasm. Pulmonary function testing is used in human medicine to determine the indication for the use of these agents. The indications I employ for using bronchodilators in dogs and cats are quite subjective, but include historical (chronic cough, wheezing), and physical findings (expiratory effort/abdominal push, crackles, increased tracheal sensitivity) as well as radiographic findings (bronchial pattern, diaphragmatic flattening). Beneficial effects of these drugs include bronchodilation, increased mucociliary clearance, improvement in diaphragmatic contractility, decreased pulmonary artery pressure, increased CNS sensitivity to PaCO₂ and stabilization of mast cells (depending on drug) to name a few.

There are three types of bronchodilators that are available in human and veterinary medicine:

Anticholinergics - these have unwarranted side effects that preclude long-term use. Newer anticholinergics, developed for use in human medicine, are available as self-actuated aerosol inhalers (requiring a coordinated inspiratory effort to activate).

Beta-adrenergic agonists - terbutaline (0.625 mg/cat Q12; 1.25-5 mg/dog Q8-12; and albuterol, 25-50 mcg/kg Q8 in dogs) have been recommended in treating chronic obstructive airway disease. Injectable terbutaline (0.01 mg/kg IV/SQ) is used for severe bronchoconstriction (e.g. “status asthmaticus”). Albuterol inhalers are useful in many crisis situations but should racemic albuterol mixtures should not be routinely used as Dr. Reino at Missouri has shown this to actually lead to airway inflammation in cats (also reported in people).

Methylxanthines. This family of drugs has been used in veterinary medicine for over 80 years, and includes theophylline, caffeine and theobromine. Numerous theophylline (all human) products have
been evaluated in dogs and cats; however only a few have shown suitable pharmacokinetics to be used on a routine clinical basis. Theo-Dur and Slo-bid were 2 such products that were available in the US for human use but unfortunately were discontinued in 2001. Use of other extended release theophylline products is an option but with use caution as to potential side effects as we do not know how these behave or should be dosed in small animals (plasma levels can be checked if interested).

Newer therapies for the treatment of feline tracheobronchial disease have included serotonin (found to be a mediator of feline airway constriction) receptor inhibition (e.g. cyproheptadine) and the use of cyclosporine in refractory cases (as another method for suppressing airway inflammation) have been shown beneficial based on Dr. Padrid’s experimental model of feline asthma. Unfortunately there are as yet no clinical reports of their successful use in clinical cases.

Many human asthmatics are now treated with new drug therapies such as leukotriene receptor blockers, or inhibitors of the enzyme 5-lipoxygenase (the enzyme responsible for the formation of leukotrienes themselves). These “human” drugs include Zileuton (Zyflo) an inhibitor of 5-lipoxygenase, montelukast (Singular) and zafirlukast (Accolate), both leukotriene receptor blockers. Clinical efficacy in people has been demonstrated in a number of large clinical trials. There has been a lot of electronic (internet) press for using these agents in feline airway disease but (based on 2 separate scientific studies) this class of drugs has not been shown to be effective in cats to date.

Recently, there has been considerable discussion about the use of metered dose inhalers (MDIs). Although there are many testimonial cases (mine included!) that attest to the efficacy and success of inhaled steroids and bronchodilators, no detailed peer-reviewed articles have been published to my knowledge. The major point with MDIs is the delivery system. In human medicine considerable time and training is provided patients to ensure the correct delivery of these aerosols. In veterinary medicine we must rely on spacers (as is needed in infants and children) to hold the aerosolized medications while the animal breathes it in.

A facemask must be used and we are just learning how to effectively do this. Aerocat, Aerodawg and other numerous pediatric units are available that may work as well (e.g. the Panda mask and chamber fits cats nicely).

Attention to the animal’s environment is an important part of good respiratory therapy. Looking for potential airway irritants can be time consuming but when found very rewarding. Some of the possible triggers of airway irritation that I ask owners about include: smokers in the house, dusty and/or scented cat litter, use of room fresheners or deodorizers, frequency of filter changes on air conditioners and forced air furnaces, recent house changes (moving, remodeling) etc.

RESPIRATORY CASE DISCUSSIONS
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