Feline Respiratory Disease
Lower Respiratory Tract Disease

Martha Cannon
BA VetMB DSAM(fel) MRCVS
RCVS Specialist in Feline Medicine

www.vet-eCPD.com
www.centralcpd.co.uk
Feline Chronic Bronchial Disease

Chronic inflammation of the lower airways (chronic bronchial disease) is a common cause of coughing, wheezing and acute expiratory dyspnoea in cats. Affected cats have inflammation of the bronchial mucosa, increased bronchial mucus production and narrowing of the lower airways. Clinical signs may be intermittent or persistent and most cases respond well to corticosteroids.

Chronic Bronchitis vs Feline Asthma

Studies of the cytological content of bronchoalveolar lavage (BAL) samples from affected cats have suggested that there are two distinct sub-groups and this has lead to a suggestion that there may be at least two different disease processes that may produce the same clinical characteristics:

- **Chronic Bronchitis**: the majority of cases have a predominantly neutrophilic bronchoalveolar inflammation, although bacterial involvement appears to be rare.
- **Feline bronchial asthma**: proposed to be an allergic airway reaction to inhaled allergens and characterised by a primarily eosinophilic or mixed inflammatory cell content of the bronchial mucus.

In humans asthma appears to be a type 1 hypersensitivity reaction to inhaled allergens, and it is characterised by reversible airway narrowing due to airway hyper-reactivity; increased mucus production and smooth muscle hypertrophy secondary to lower airway inflammation. The majority of cats with chronic lower airway do not meet these criteria, but they are found in a small proportion of cats with naturally occurring chronic bronchial disease and can also be induced experimentally to produce a feline model of allergic asthma.

At present there are no widely accepted, standardised criteria that can be used to distinguish chronic bronchitis from feline asthma and consequently confusion exists in the literature as to how to define the two conditions, or indeed whether it is appropriate to attempt to do so.

Clinical Presentation

Chronic bronchial disease (CBD) can occur at any age but is most commonly seen in young to middle-aged adult cats. It affects cats of all breeds but Siamese and Oriental cats appear to be over-represented.

Clinical signs include chronic cough, lethargy, exercise intolerance, exercise induced open mouth breathing, audible expiratory wheeze, tachypnoea, dyspnoea, and acute respiratory distress. These signs may be acute or chronic and non-progressive. The cough is typically harsh and associated with active abdominal effort, often leading owners to report that the cat has a fur ball, or a foreign body stuck in the throat. Coughing can be intermittent or may be relatively constant and may be exacerbated by airway irritants such as cigarette smoke, house dust or pollen.

Some affected cats develop acute bronchoconstriction causing severe respiratory distress, tachypnoea, cyanosis or collapse, not always associated with a previous history of cough or laboured respiration.

Physical Examination

Most affected cats present with tachypnoea, with or without a prolonged expiratory phase or an expiratory / abdominal push. The presence of increased expiratory effort is an indication of lower airway narrowing or obstruction. Cats with chronic airway disease may display a barrel-chested appearance and decreased thoracic compressibility because of over-inflation and emphysema.

Cough is a common feature of feline bronchial disease, and detection of a cough in the cat that presents with respiratory distress or tachypnoea is a major clue to the presence of underlying inflammatory airway disease. Affected cats show variable degrees of tracheal sensitivity following palpation and increased tracheal noise on tracheal auscultation.

Thoracic auscultation reveals harsh lung sounds, inspiratory crackles, or expiratory wheezes in around 66% of cats; however, the absence of such sounds does not rule out inflammatory airway disease.

Emergency Treatment
Pleural Effusion in Cats

Diagnostic tests should be kept to a minimum initially in cats presenting with signs of acute bronchoconstriction such as cyanosis, tachypnoea, and open-mouth or abdominal breathing. Stabilisation can be achieved by providing an oxygen-enriched environment and using parenteral administration of a β2 agonist such as terbutaline. This is an effective bronchodilator in cats with airway disease that have reversible airway constriction. It is a relatively safe drug with few cardiac side effects and can be administered subcutaneously, intramuscularly or intravenously at 0.015 mg/kg. It is rapid in onset, and an additional dose can be administered after 30 minutes if required.

Butorphanol (0.3 – 0.5 mg/kg i/m or s/c) will reduce anxiety without lowering blood pressure or affecting cardiovascular function and may allow the cat to cope better with handling for emergency treatment.

Respiratory rate and effort should then be monitored visually in the first hour of observation to determine a therapeutic response. If the cat does not respond to terbutaline, use of a short-acting corticosteroid (dexamethasone: 0.25 – 0.5 mg/kg i/m or i/v; inhaled fluticasone) often results in rapid alleviation of clinical signs caused by inflammatory airway disease. While systemic use of corticosteroid affects further diagnostic testing it may be required to stabilise the cat.

If the cat fails to respond to these measures, causes for respiratory distress other than chronic bronchial disease should be investigated. Pulmonary oedema is the most likely remaining differential diagnosis in the cat presenting with acute cough and dyspnoea and it differentiating chronic bronchial disease from cardiogenic pulmonary oedema can be challenging in the emergency situation. Trial treatment with frusemide may be appropriate. An in house SNAP test will soon be available to assess feline pro-BNP. While the test has significant limitations as a screening test in healthy cats, it should prove useful in distinguishing most cats with congestive heart failure from those with non-cardiac disease, especially when used in conjunction with other physical, ultrasound and radiographic findings

Further Investigations

Chronic bronchial disease is the most common cause of chronic or intermittent coughing in cats. Other differential diagnoses include:

- Parasitic infections:
  - Round worms can cause transient coughing due to visceral larva migrans – more common in kittens than in adult cats.
  - Lungworm - *Aelurostrongylus abstrusus*, present in some geographic regions of the UK. Most infections are self-limiting and sub-clinical, but can cause coughing and in rare cases severe respiratory distress and pneumothorax or pyothorax. Clinical disease is more likely in kittens or immunosuppressed adult cats. If infection is documented or suspected as a cause for airway inflammation treatment is with fenbendazole (50mg/kg p/o q 24 hrs for 3 days), or single applications of imidacloprid/moxidectin (Advocate), or emodepside/praziquantel (Profender – effective against *Aelurostrongylus abstrusus*, but not against *Eucoleus aerophilus*).
  - Heartworm – *Dirofilaria immitis*, rare in cats and not present in the UK, but may be of concern in cats imported from elsewhere
    - Fur balls – owners will frequently describe the action of attempting to clear a fur ball as a “cough”
    - Bronchopneumonia – see later
    - Pulmonary oedema – see later
    - Pulmonary neoplasia – see later

Thoracic Radiography

Well positioned, inflated thoracic radiographs are an important part of the investigation of the coughing cat. To get good diagnostic films will usually require sedation or anaesthesia and the latter may be preferred as it ensures control of the airway and allows the lungs to be gently inflated, providing the most diagnostic information from the films.

Radiographic findings are highly variable: the classic indicators of lower airway disease are:

- Lung hyperinflation, leading to flattening of the diaphragm and increased space between the caudal edge of the cardiac shadow and the diaphragm
- Peribronchial infiltrates – appearing as “doughnuts” or “tram-lines”. Changes may be severe and generalised, but may be subtle or even absent.
Pleural Effusion in Cats

- Lobar collapse – usually involving the right middle lung lobe
- Some cats develop a mild interstitial pattern, or focal alveolar infiltrates due to mucous plugging of large airways causing secondary atelectasis.

Radiographic changes are therefore highly variable; they may be non-specific, subtle or even absent in some cases. Thoracic radiographs are nevertheless important for ruling out other causes of cough.

**Bronchoscopy**

If bronchoscopy is available it can be a useful adjunct to other diagnostic investigations.

A small endoscope (preferably 2.5 to 3.8 mm outer diameter) is required – the smaller the insertion tube the easier it is to manipulate within the airways of cats. The cat is anaesthetised with intravenous agents (e.g. alfaxan, propofol) and oxygen supplementation is supplied through an oxygen cannula (e.g. a cut down canine urethral catheter) passed down the trachea. The endoscope is passed into the trachea and all large airways are examined.

Abnormalities that may be seen include hyperaemia, oedema, mucus accumulation and reduction in airway diameter.

**NB:** Bronchoscopy can induce severe bronchospasm in cats with chronic airway disease. Pre-treatment with a bronchodilator such as terbutaline may reduce this risk (0.015 mg/kg i/m or s/c given 2 to 4 hours prior to induction of anaesthesia). Should bronchospasm occur manual ventilation will be required until the bronchospasm relaxes and atropine may help to relieve the smooth muscle constriction.

**Bronchoalveolar Lavage**

Collection of airway samples for cytology and bacterial culture is an important part of the investigation of lower airway disease in the cat. Collection of good samples can be achieved safely and inexpensively without the aid of a bronchoscope:

- Pre-treat the cat with terbutaline- 0.015 mg/kg i/m or s/c, 2 to 4 hours prior GA
- Anaesthetise the cat and use an uncuffed ET tube and inhalation anaesthetic to induce stable anaesthesia, and to allow thoracic radiography and any other investigations that may be required.
- Position the cat in lateral recumbency then re-intubate with a sterile, uncuffed ET tube of the widest diameter that can comfortably be passed into the trachea
- Ensure i/v access is maintained, and use aliquots of alfaxan or propofol to maintain an adequate plane of anaesthesia.
- Pass a sterile 6 or 8 French catheter through the ET tube and advance the catheter until it lodges within the distal airway. Infuse 5 – 10 mls of warmed sterile saline then immediately re-aspirate as much fluid as possible back into the catheter and syringe.
  - Coupage of the chest during the lavage procedure may improve the yield of mucus retrieved
  - Typically approx 40-50% of the volume instilled is retrieved, much of which will remain in the catheter – maintain negative pressure on the catheter as it is removed to prevent loss of this portion of the sample
  - The presence of foam on the meniscus of the sample indicates the presence of surfactant and confirms an alveolar sample
- Repeat the process with a fresh supply of saline.
- Administer 100% oxygen through the ET tube for 5-10 minutes following the procedure.

**Sample Handling:**

Depending on the volume of material retrieved: pool the samples and divide it between:

- A plain sterile collection tube to be submitted for bacterial culture
- An EDTA tube to submit for cytology
- A plain eppendorf for in-house cytology:
  - Centrifuge immediately or place on ice for later analysis
  - After centrifugation make an air-dried smear from a sample of the pellet
  - Stain with diff-quick or Wright’s stain
  - Examine under the microscope and count at least 200 cells per slide to determine the differential cell count

**Cytology**
Pleural Effusion in Cats

Cats with idiopathic lower respiratory tract inflammation can have primarily neutrophilic or eosinophilic cytology. The significance of the primary cellular infiltrate currently is unknown, and it appears that more cats have primary neutrophilic inflammation than eosinophilic inflammation.

**Bacteriology**

Culture for aerobic bacteria and culture or PCR testing for *Mycoplasma* should be performed in cats with cough or tachypnoea but the results should be interpreted with care:

- Light growth of bacteria from the lower airways of cats with and without bronchial disease is common, occurring in approximately 75% of healthy or bronchitic cats. True infection typically is associated with systemic signs of illness, degenerative or septic airway cytology, and a positive response to antimicrobial therapy.
- The role of *Mycoplasma* spp infection in respiratory disease is controversial. It has been isolated from cats with various types of lower respiratory disease, but not from healthy cats. *Mycoplasma* infection may worsen airway hyper-reactivity even if it is not a primary cause of lower airway disease.

**Treatment**

Situations that might provoke bronchoconstriction should be avoided, particularly in cats that develop acute attacks of severe respiratory distress. Cigarette smoke, dusty cat litters, aerosol sprays, polluted environments, stressful situations, and upper respiratory virus infection (e.g. herpes virus, calicivirus) can trigger clinical signs in susceptible cats.

Current treatment involves a combination of anti-inflammatory agents and broncho-dilators. Approximately one half to two thirds of cats require lifelong medication.

**Corticosteroids** are effective in emergency therapy and in chronic management of this disease. They reduce inflammation by controlling inflammatory mediators and by decreasing migration of inflammatory cells into the airway. The duration and dose of corticosteroid therapy depends on the degree and chronicity of clinical signs, the severity of the pulmonary infiltrate, and the severity of inflammation on cytology.

For long term treatment several routes of administration are possible, the choice will depend on the severity of the disease and the compliance of the owner and the cat:

- Prednisolone 1 mg/kg PO twice daily for 5 to 10 days, then if a good response is achieved gradually taper the dose to the minimum effective dose over a period of 2 – 3 months.
  - Recurrent episodes of coughing or respiratory distress requires a return to the original dose.
  - Monitoring is required for common side effects such as weight gain and diabetes mellitus

- Inhaled fluticasone propionate (Flixotide) via face mask and spacer chamber (e.g. Aerokat). 110-250 µg twice daily
  - It can take a little time to acclimatise a cat to the regular use of a face mask. In the interim standard doses of oral steroids can be used for the first few weeks, tapering downward once effective inhaled therapy is underway.
  - Side effects noted in human medicine include adrenal suppression with long-term and high-dose use, thinning of the skin, perioral dermatitis and oral infection (particularly with candidiasis). These complications appear to be rare in veterinary patients.
  - Inhaled medications are significantly more expensive than oral or injectable alternatives and this may prove to be prohibitive for some owners especially for cats on life-long treatment

- Depot injections of methylprednisolone acetate (10 to 20 mg IM every 2 to 8 weeks) may be adequate in some cases and may be required in cats that are non-compliant with tablets or inhaled medication. However this is the least ideal route as it provides only sporadic control of airway inflammation.

**Bronchodilators:** Airway narrowing and smooth muscle hypertrophy can contribute significantly to the clinical signs or wheezing, increased respiratory effort, cough and lethargy. Bronchodilators reduce airway resistance and can be helpful in both the emergency treatment and the long term management of chronic airway disease. Concurrent use of a bronchodilator may reduce the dose of corticosteroid required to control the clinical signs and in mild cases bronchodilators alone may control the signs.
Pleural Effusion in Cats

However caution is required when using bronchodilators as sole therapy - in humans sudden deaths have been reported where bronchodilators have been used alone, increasing airway patency allows inflammatory mucus to be inhaled deeper into the bronchial tree causing obstruction of lower airways. Concurrent use of anti-inflammatory agents should reduce this risk.

- **Terbutaline** (Bricanyl) can be administered orally at a dose of 0.1-0.2 mg/kg twice daily
  - Generally very well tolerated, but potential adverse effects include tachycardia, CNS stimulation, tremors and hypokalaemia.
  - Use with caution in cats with heart disease, hyperthyroidism, hypertension, diabetes or seizure disorders.
- **Theophylline** (Corvental-D) 6-8 mg/kg p/o twice daily.
  - Potential adverse effects include tachyysrhythmias, increased gastric acid secretion and CNS stimulation. Increased risk of toxicity if administered with cimetidine or enrofloxacin and increased risk of seizures when administered with ketamine.
- **Salbutamol/Albuterol** (Ventolin) can be administered via the inhaled route, dose 90 µg when needed. Useful as an emergency treatment during an acute episode, or for long term control of mild cases with intermittent signs (clinical signs occurring up to twice a week) where only intermittent use is required.
  - Chronic daily use of salbutamol has been associated with increased severity of airway inflammation in feline experimental models.
  - If using both inhaled bronchodilators and corticosteroids, administer the bronchodilator first, followed by the corticosteroid 5 – 10 minutes later.

**Antibiotics** should be prescribed based on culture and sensitivity and cytology results because airway infection may contribute to bronchial inflammation and hyper-responsiveness. If infection with *Mycoplasma spp* is documented a clinical trial of doxycycline (5 to 10 mg/kg PO q12 – 24 hrs) can be used.

**Other Treatment Options**

Alternative anti-inflammatory drugs may be beneficial in some cats:

- **Cyproheptadine** (Periactin, 2 mg per cat, once or twice daily). In an experimental model of feline asthma, cyproheptadine, a serotonin-receptor blocker, attenuated airway constriction of isolated bronchial strips in vitro. Serotonin levels have not been measured in naturally occurring feline bronchial disease but some cats appear to benefit from cyproheptadine.
- **Cyclosporine** (Atopica; Novartis): an inhibitor of T lymphocyte activation, attenuates bronchoconstriction and airway remodelling in asthmatic human patients and in a feline model of airway hyperreactivity. Other agents are more suitable for first-line therapy of feline bronchial disease; but cyclosporine could be considered for cases that are nonresponsive to standard therapy.

**Drugs to Avoid:**

Feline airways are rich in sympathetic innervation, and β2-adrenergic activation is important in providing bronchodilation. Therefore β-blockers such as propanolol (a nonspecific beta blocker) and atenolol (primarily a β1-blocker) should be avoided if bronchial disease is suspected.

Atropine is a potent bronchodilator and can be used in the management of acute bronchospasm but should not be used chronically because it thickens bronchial secretions and encourages mucous plugging of airways.

Chronic daily use of inhaled salbutamol has been associated with increased severity of airway inflammation in feline experimental models.
Other Causes of Chronic Cough

Chronic bronchial disease / asthma is the most common cause of chronic coughing in cats. Other potential causes include:

- Pulmonary oedema: most affected cats suffer tachypnoea and dyspnoea but not cough, however some individuals will present with a cough, which is frusemide responsive
  - In cats pulmonary oedema is often patchy and diffuse with highly variable radiographic appearance
  - Cardiogenic pulmonary oedema is the most common cause, but other causes such as recent seizure activity, electric shock, anaphylaxis etc are possible
- Bronchopneumonia: Acute inflammatory exudate initially fills alveolar spaces radiating from the bronchioles causing areas of consolidation oriented around terminal bronchioles, in cats, it most commonly occurs in cranioventral lung lobes.
  - Most commonly bacterial (e.g Mycobacterium spp), mycoplasma or aspiration in origin.
  - Treatment includes broad-spectrum antimicrobials such as amoxicillin/clavulanate or clindamycin and supportive therapy.
- Pulmonary neoplasia: most cats with pulmonary neoplasia, whether primary or metastatic, show few if any clinical signs until disease is advanced. Coughing is more likely if the site and size of the mass causes physical obstruction to the trachea or major bronchi.
- Idiopathic Pulmonary Fibrosis: A chronic disease that frequently presents with an apparent acute onset. Most common in middle-aged and older cats.
  - Causes severe multifocal interstitial fibrosis with foci of fibroblast/myofibroblasts, alveolar epithelial metaplasia, interstitial smooth muscle metaplasia/hyperplasia, but no inflammatory response.
  - Produces an inspiratory dyspnoea, or a mixed inspiratory and expiratory dyspnoea.
  - There are no consistent hematologic or biochemical abnormalities, and radiographic changes are highly variable, but predominantly interstitial.
  - Bronchoalveolar lavage, and/or fine needle aspirate are acellular because there is no significant inflammatory component. They may help rule out other causes of lung disease but it should be noted that cats with idiopathic pulmonary fibrosis may not tolerate BAL and in some cases it can precipitate acute and fatal decompensation.
  - Confirmation of diagnosis requires histopathology (usually at post-mortem).
  - There is no effective treatment: corticosteroids and bronchodilators are often used but with doubtful effect.
  - Average reported survival time is 5-6 months.
Pleural Effusion in Cats

Pleural effusion is a common cause of severe dyspnoea in cats, which often presents as an emergency with an apparently acute onset despite the effusion having built up over a period of days or even weeks to months.

Acutely dyspnoeic cats must be handled with extreme care to avoid potentially fatal stress-induced decompensation of the compromised cat.

Minimal handling, cage rest, warmth and oxygen support are essential components of the initial investigation and treatment of any dyspnoeic cat.

If the cat is significantly stressed by its environment and disease consider using butorphanol (0.3 – 0.5 mg/kg i/m or s/c). This will reduce anxiety without lowering blood pressure or affecting cardiovascular function and may allow the cat to cope better with handling for emergency treatment.

Identifying Pleural Effusion

A good clinical history and physical examination should provide strong indicators as to whether a dyspnoeic cat has pleural effusion and can be achieved with minimal handling/restraint

• Clinical History: Most cats with pleural effusion will have chronic disease so there are likely to be some indications of previous changes in the clinical history, even if the owner has not been sufficiently concerned to seek veterinary help.
  o Some causes of pleural fluid are genuinely acute in onset – e.g. haemothorax due to trauma or rodenticide poisoning
• Respiratory Pattern: Pleural space disease causes dyspnoea with increased inspiratory effort.
• Thoracic Auscultation: Muffled lung sounds ventrally, muffled heart sounds
  o May be associated with heart murmur or gallop rhythm if cardiogenic
• Other physical findings: Ventral dullness on thoracic percussion, poor thoracic compressibility on gentle compression of the cranial thorax.

Further Investigations

Where the history and physical examination provide strong indications of pleural effusion proceed to thoracocentesis once the cat is stable – this will provide samples for essential further diagnostic investigations but will also relieve the immediate life-threatening respiratory compromise.

If the history and physical examination findings are equivocal use diagnostic imaging to confirm the diagnosis, but proceed with caution in the acutely dyspnoeic cat:

• NEVER restrain a dyspnoeic cat in lateral recumbency for radiography or ultrasonography
• If ultrasound is available, allow the cat to rest comfortably in sternal recumbency and provide oxygen. Do not clip the coat; apply surgical spirit and ultrasound gel to the lateral thoracic wall at or just below the level of the costo-chondral junctions and apply the ultrasound probe to establish whether fluid is present. Do not attempt a full examination of the heart and thorax. If fluid is present, proceed to thoracocentesis.
• If ultrasound is not available consider whether it is safe to take a conscious dorso-ventral thoracic radiograph, Use minimal restraint. Do not aim for perfect positioning, take what you can get – it will be adequate to identify pleural effusion if it is present in moderate to large volume.
  o Set up the x-ray generator and cassette, pre-set the required exposures and collimate the beam. Position all required markers on the cassette.
  o Gently encourage the cat to adopt a comfortable sterna-ral recumbent position and GENTLY restrain with sand bags if necessary and if tolerated.
  o Consider using a narrow upright cardboard box, open at one end and with a “viewing hole” in the other end. Some cats will take the opportunity to crawl into the box for safety, and the
box will maintain the cat in a roughly sternal position under the primary beam allowing a
“rough and ready” radiograph to be taken.
Common Causes of Pleural Effusion:
In cats the most common causes of pleural effusion are:

- Congestive heart failure
- Feline Infectious Peritonitis (FIP)
- Pyothorax
- Chylothorax – most commonly due to congestive heart failure, but can be secondary to neoplasia, or may be idiopathic.
- Intra-thoracic neoplasia: lymphoma, mesothelioma

Less common causes of pleural fluid / effusion include:

- Acute pancreatitis - may cause pleural and/or abdominal effusions as a consequence of the release of systemic inflammatory mediators (Systemic Inflammatory Response Syndrome).
- Diaphragmatic hernia and secondary lung lobe torsion
- Haemothorax due to coagulopathy, trauma or a bleeding neoplasm.
- Severe hypoalbuminaemia, most commonly secondary to nephrotic syndrome

Investigation of Pleural Effusion:
As listed above the differential diagnosis list for a cat presenting with severe dyspnoea due to pleural effusion is relatively short. The clinical history and physical examination will help to rank these differentials and allow a logical approach to emergency treatment and stabilisation.

Collection and analysis of a sample of effusion will then provide further information as well as relieving the immediate respiratory compromise. Samples of fluid should be collected into EDTA, heparin and plain tubes to allow the full range of tests that might become relevant:

Classification of Pleural Effusion in Cats

<table>
<thead>
<tr>
<th>Classification</th>
<th>Total Protein (g/l)</th>
<th>Total Nucleated Cell Count ($10^9$/L)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transudate</td>
<td>&lt;25</td>
<td>&lt; 1,000</td>
<td>Rare in cats. Rule out hypoalbuminaemia, congestive heart failure, fluid overload</td>
</tr>
<tr>
<td>Modified Transudate</td>
<td>25 - 35</td>
<td>500-10,000</td>
<td>Least specific. Differentials ranked according to clinical criteria and gross characteristics of fluid</td>
</tr>
<tr>
<td>Exudate</td>
<td>&gt;30</td>
<td>&gt; 5,000</td>
<td>May be sub-classified as septic, non-septic, chylous, neoplastic. Rule out FIP, infection, neoplasia</td>
</tr>
<tr>
<td>Chylous Effusion</td>
<td>May have total protein and cell counts of a modified transudate or an exudate. Defined as effusion with a triglyceride content of &gt; 1.12 mmol/L</td>
<td></td>
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