Hotter Topics in Feline Medicine - Challenging Cases for Advanced Practitioners

Mini Series

Session 1: Dyspnoea and coughing

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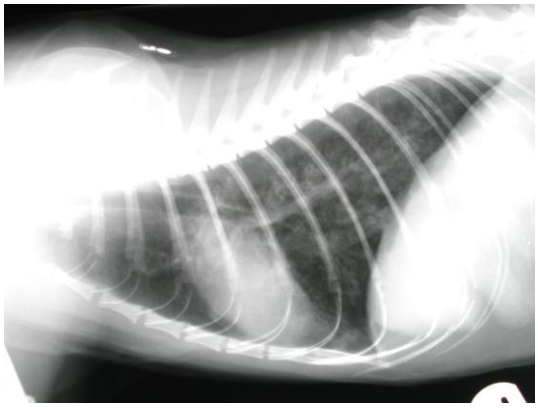

DYSPNOEA IN CATS

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Dyspnoea is a clinical sign that is seen relatively commonly in cats. It describes difficulty in breathing. This can result from a decreased ventilatory capacity, or an increased ventilatory demand. Dyspnoea can therefore result from respiratory or non-respiratory causes.

- Non-Respiratory causes (Figure 1)
- Upper respiratory tract (URT) disease (Figure 2)
- Lower respiratory tract (LRT) disease (Figure 3)
- Pleural space disease (Figure 4)

Dyspnoea is often associated with **coughing,** and as a clinical sign coughing is more easily recognized by owners than dyspnoea. Many cats are presented to veterinary practice because they have a chronic cough. While these cases can be very complex and/or protracted, undertaking their investigation and treatment is often highly rewarding.

The first step of the investigation is to determine whether or not the cat is actually coughing. Careful questioning of the owner should rule out retching, gagging, or vomiting (particularly of fur balls). However, some cats will occasionally retch or vomit following a forceful bout of coughing, so the presence of a terminal retch should not be misinterpreted as evidence of gastrointestinal (GI) disease.

Why do cats cough?
Coughing results from the stimulation of cough receptors that are located within the larynx, trachea, and bronchial tree. In cats, coughing is usually a sign of disease affecting the LRT, particularly the larger airways. It can also be associated with URT disease, but is rarely associated with disease of the lung parenchyma, heart or pleural space.

In cats, most coughing is caused by irritation or inflammation of the trachea or bronchial tree. This can result from the presence of foreign material, inhaled liquids or gases, be caused with infectious agents, allergic or hypersensitivity reactions or, occasionally, with neoplastic processes. Since there are no cough receptors in the peripheral lung tissue, disease affecting just the periphery of the lungs will not cause coughing, that is, until it extends into the upper airways.

Cats, unlike dogs, rarely cough in association with heart disease, or with disease affecting the mediastinum. This may result from a number of different factors, including the finding that the trachea and main-stem bronchi in the cat appear to resist compression that results in coughing much more commonly in dogs.

Coughing associated with URT disease usually results from inflammation of the larynx. It can also occur where disease within the nose results in mucopurulent material from the caudal nasopharynx dripping down and irritating the larynx (termed 'post-nasal drip').

LOCALISATION OF THE CAUSE OF DYSPNOEA

The first step in diagnosing the cause of dyspnoea is to determine if it is due to non-respiratory causes, URT disease, LRT disease or disease affecting the pleural space. This differentiation should be possible by taking a detailed history and performing a thorough physical examination (Table 1). It is necessary to determine whether the dyspnoea is inspiratory or expiratory, or whether the cat is only tachypnoeic. **Inspiratory dyspnoea** is usually associated with URT disease (when it is causing airway obstruction), disease of the alveolar space or pleural disease (when it is preventing full lung expansion). The presence of other clinical findings may help to direct the clinician to the particular area of concern. For instance, URT disease is typically accompanied by sneezing, nasal discharge, wheezing, snoring, snorting, facial deformity, obstructed nares, or dysphagia, while laryngeal disease may cause a change in the cat's voice. When coughing is also present the dyspnoea is most likely to be of respiratory origin. **Expiratory dyspnoea** (i.e. difficulty breathing out) is usually a sign of LRT (i.e. airway) disease. **Tachypnoea** (rapid breathing) or orthopnoea (dyspnoea when recumbent) do not help in localising the cause of the dyspnoea. It is important to remember that many non-respiratory cause of dyspnoea will often present mainly with tachypnoea (e.g. hyperthyroidism, metabolic acidosis, abdominal enlargement, hyperthermia, fear, stress, pain).

The respiratory rate and pattern should be further assessed to determine whether the dyspnoea is restrictive or obstructive. Restrictive diseases prevent the lungs from expanding properly, and therefore lead to rapid, short, shallow breaths. Causes of **restrictive respiratory patterns** include pulmonary parenchymal diseases and diseases of the pleural space. **Obstructive respiratory patterns** arise from narrowing of the airways, leading to slower, deeper breathing patterns. The most common causes of airway narrowing are chronic bronchopulmonary diseases, such as feline asthma, but an obstructive respiratory pattern is also seen in animals with laryngeal paralysis.

Table 1. Localisation of the cause of dyspnoea

Cause	Nature of dyspnoea	Sneezing/nasal discharge	Cough
Non-respiratory	Tachypnoea	No	No
URT	Inspiratory	Yes or No	Yes or No
LRT	Expiratory	No	Yes or No
Pleural disease	Inspiratory	No	Very rarely

URT – upper respiratory tract disease, LRT – lower respiratory tract disease

UPPER RESPIRATORY TRACT DISEASE

ACUTE URT DISEASE - CAT 'FLU'

Aetiology

Cat 'flu' is the common name used to describe infectious acute URT disease. It is frequently seen in unvaccinated cats and kittens, particularly when they are kept in large groups, either in private homes, or rescue centres. While the disease can be caused by a number of different organisms, over 80% of cases are caused by infection with either feline calicivirus (FCV), feline herpes virus (FHV-1, previously called feline rhinotracheitis virus), or both. Other organisms may also be involved, including feline coronavirus (FCoV), reovirus, *Influenza A* virus (rarely), mixed bacteria; *Bordetella bronchiseptica, Pasturella multocida* and *Mycoplasma species, Chlamydophila felis* (formerly *Chlamydia psittaci*) and, rarely, *Streptococcus equi* subspecies *zooepidemicus*. Many cases of cat 'flu' involve infection with a number of different organisms. Environmental factors, such as poor ventilation, high humidity, and over-crowding may exacerbate the problem.

Factors involved in cat 'flu':

- Feline herpes virus (FHV-1)
- Feline calicivirus (FCV)
- Feline coronavirus (FCoV)
- Reovirus
- *Bordetella bronchiseptica*
- *Pasturella multocida*
- *Mycoplasma species*
- *Chlamydophila felis*
- *(Streptococcus equi* subspecies *zooepidemicus)*
- (Rarely; *Influenza A virus* – either from humans or birds)
- Poor ventilation, high humidity, dusty environment, over-crowding.

FHV-1 is a labile DNA virus of a single serotype and consistent pathogenicity that is readily destroyed outside the host. The most important source of this virus is clinical cases. However, most cats recovered from FHV-1 infection become long-term latent carriers, and can shed virus intermittently, typically in response to stress, concurrent disease or following the use of corticosteroids.

FCV is an RNA virus with variable virulence and pathogenicity that is more resistant within the environment and to disinfection. Clinical cases are also the most important source of the virus. However, asymptomatic carriers are common as most cats shed FCV for at least a month following infection, ~50% are still shedding by 75 days, and ~25% of recovered cats may become long-term viral carriers (sometimes for months or years) and may either shed virus continually or excrete virus intermittently, again usually under the influence of stress, concurrent disease or following the use of corticosteroids.

B. bronchiseptica is a Gram-negative coccobacillus that can act as a respiratory pathogen in a number of species, including pigs, dogs (where it is one of the causes of kennel cough), cats and humans (particularly when immuno-compromised). It can cross-species and has potential zoonotic risk. Affected cats may remain persistently infected and shed bacteria.

C. felis has a special predilection for the conjunctiva and, in the UK up to 30% of cats with conjunctivitis are infected with this pathogen. It is an obligate intracellular bacterium with Gram-negative characteristics. While some strains of Chlamydia may be zoonosic, *C. felis* is not generally believed to be. Affected cats may remain persistently infected and shed bacteria long-term.

Pathogenesis

Most of the organisms that typically cause cat 'flu are transmitted by aerosol and/or direct contact of eyes, noses and mouths. FHV-1 replicates in the epithelial cells of the nasal epithelial cells, tonsils, conjunctiva, and trachea. It causes local necrosis of mucosa and leads to a serous and subsequently mucopurulent discharge. Infiltration of the mucosa with neutrophils commonly occurs, as does secondary bacterial infection. FCV targets similar cells but more often causes oral ulceration and ulceration of the external nares. Ulceration may involve the tongue, hard palate, soft palate and pharynx. These ulcers form from vesicles which burst due to tissue necrosis and cellular infiltration with neutrophils. An acute synovitis can occur occasionally (resulting in limping syndrome**)** as can an alveolitis (leading to interstitial pneumonia). Recently, highly pathogenic strains of FCV has arisen (in USA and UK), where they causes very severe disease, including jaundice, subcutaneous oedema and vasculitis, and a very high level of mortality (see below).

Clinical signs

Clinical signs of cat 'flu are most frequently observed in young cats although any age group can be affected. The incubation period is around 6 days. Morbidity is high while mortality should be low with appropriate treatment. Clinical disease may be more serious in some pure bred cats.

Sneezing is typically the first clinical sign observed. This is followed by a serous ocular and nasal discharge which rapidly becomes mucopurluent due to secondary bacterial infection. Affected cats are usually depressed and pyrexic. Conjunctivitis can cause the eyelids to become 'sticky' leading to closure, or keratitis and corneal ulceration. The nose may block leading to a total loss of olfaction and mouth breathing. Ulceration of the oral cavity leads to salivation and loss of appetite. Coughing and dyspnoea are seen less commonly, and tend to be associated with FHV-1 and *B. bronchiseptica*. While none of the infections cause specific clinical signs *C. felis* is particularly associated with conjunctivitis, which may initially be unilateral, FHV-1 tends to cause more severe disease than FCV, with more prominent conjunctivitis, perfuse nasal discharge, and obvious coughing, and FCV (except for the newly recognised severe strains) tends to be associated with milder clinical signs, and oral ulceration. Oral ulceration can also be seen with FHV-1, and both VS-FCV and FHV-1 can result in skin ulceration, either on the

face or limbs. Abortions may result from generalised disease and debility, or be caused by the organisms themselves (FHV-1 and *C. felis).*

The severity of infection may be associated with several factors, including the age, breed and vaccine status of the cat, which organisms are present and how virulent they are, the nutritional status and health status of the cat, and the presence of FeLV and FIV. Clinical signs should resolve within 2-3 weeks. However, chronic disease, often called chronic rhinitis or 'snufflers', can occur and may continue for months or years. Chronic disease may be linked to immuno-suppression associated with FIV and FeLV.

Clinical signs of cat 'flu':

- Sneezing
- Conjunctivitis
- Ocular and nasal discharge – initially serous progressing to mucopurulent
- Ulceration of the tongue and mouth
- Excessive salivation
- Inappetence
- Depression
- Fever
- Coughing
- Limping syndrome (FCV – due to acute viraemia and localization of the virus and/or immune complexes in the joints: affected cats typically also show lethargy and pyrexia)
- Jaundice, swollen face, collapse and death (new highly pathogenic strains of FCV that causes vasculitis – see later section VS-FCV)

Diagnosis

- A presumptive diagnosis is usually made on the presence of typical *clinical signs* and a *history of possible exposure* to causal organisms. While different organisms tend to produce characteristic clinical signs in the laboratory situation, in mixed natural infections it is not usually possible to determine which organisms are involved from clinical signs alone. That said, FHV-1 tends to cause more severe disease than FCV, with more prominent conjunctivitis, perfuse nasal discharge, and obvious coughing. FCV tends to be associated with milder clinical signs, and oral ulceration. *C. felis* is usually associated with conjunctivitis, which may initially be unilateral. B. bronchiseptica may cause coughing, and is generally seen when kittens are kept in over-crowded conditions.
- Nasal or oropharyngeal swabs can be taken for isolation and culture or PCR (in the case of FHV-1, *C. felis* and *Mycoplasma*). Care should be taken when interpreting the results since FHV-1 is shed only intermittently, and FCV shedding may result from infection with either pathogenic or non-pathogenic field strains of virus, or vaccine virus. Bacteriology is generally of little value unless the diagnostic laboratory is instructed to look for specific agents e.g. *B. bronchiseptica*, *Mycoplasma* spp., or *C. felis*. It is advisable to speak to the laboratory prior to collecting the samples since specific transport media may be required.

- There are now good multiplex PCR tests e.g. the extended feline respiratory pathogens assay from CTDS which tests for FCV, FHV-1, *C. felis, Mycoplasma felis, Mycoplasma gateae, and Aelurostrongylus abstrusus.*
- Serology can be used to determine whether or not a cat has been previously exposed to FCV or FHV-1. However, it is of limited value since most cats have usually been vaccinated. A rising titre against *C. felis* may be detected in unvaccinated cats.
- *C. felis* may be detected as intranuclear inclusion bodies in Giemsa-stained conjunctival smears around 7 days post infection.
- A famcyclovir treatment trial is a good way of 'testing' for FHV-1 (see below).

Treatment

Treatment usually involves symptomatic therapies and good nursing care.

- *Antibiotics* – ideally, where specific organisms are detected, antibiotics should be selected by culture and sensitivity. If not, a safe broad-spectrum antibiotic, that is active against bacteria commonly found in the feline oropharynx, should be given for 2-3 weeks. e.g amoxycillin-clavulanic acid or a cephalosporin. Since affected cats typically find swallowing painful it is often better to use syrups or parenteral administration (where available) rather than tablets or capsules. Where *B. bronchiseptica, Mycoplasma spp.,* or *C. felis* have been detected give doxycycline 10mg/kg/day, or oxytetracycline at 20mg/kg q8h, plus an ophthalmic tetracycline ointment. Oral tetracycline should not be used in kittens as it will discolour the teeth. ALL of the cats in the unit should be treated at the same time, and the treatment should be continued for two weeks AFTER clinical signs have resolved. Oral doxycycline should always be followed by a syringe of water to ensure the medication has passed down into the stomach and so reduce the risk of oesophageal stricture formation. Alternative antibiotics include fluroquinolones and azithromycin (5-10 mg/kg PO q24h for 3 days, then twice weekly – which can be a good choice for kittens as it comes as a syrup. Although Pfizer have said that they do not recommend the aliquoting Zithromax powder prior to suspension they have said that because of the way it is made it would be possible to do so. So ... 5g of Zithromax with 2.5ml water will make 2.5ml of a 40mg/ml suspension. But it definitely cannot be kept for longer than 5 days once reconstituted.
- *Nutritional and fluid support* – this usually entails giving intravenous fluids and often the placing of a feeding tube. Care should be taken when placing naso-oesophageal tubes as the cat's nasal turbinates are already inflamed. Oesophageal feeding tubes are therefore preferred. Cats should be encouraged to eat by use of warmed tempting food. Use of appetite stimulants is controversial; the author's preferences are cyproheptadine (Periactin) @ 0.1-0.5mg/kg PO q8-12 hours; or possibly mirtazapine @ 1/8 of a 15mg tablet PO q3 days. Diazepam is no longer used because of its association with fatal idiosyncratic hepatic necrosis.
- *Supportive nursing care* – it is important to keep the cat's eyes and nose clean, and its coat groomed.
- *Multivitamins* – anorexia can result in a lack of certain vitamins, especially B_{12}. This can in turn exacerbate anorexia. Supplementation can be beneficial, e.g. B_{12} @ 125-250 ug/cat q7days SC.

- *Ocular anti-inflammatory drugs* – for use when ocular signs cause significant pain and/or inflammation. However, they can slow the healing of corneal ulcers. Ocufen (flubiprofen) 0.3 mg/ml apply 2-3x daily; Ketoralac 5 mg/ml solution, apply 2-3x daily; (£2-3/drop as single use vials in the UK).
- *Mucolytics* – mucolytics may help to ease respiratory tract congestion; e.g. bromhexine (Bisolvon) @ 3mg/cat IM q24 hours, or 1mg/kg PO q24 hours.
- *Nebulised air* – the use of steam or nebulised air can help to clear the airways. Where necessary, bronchodilators can be added to the air current.
- *Decongestants* – intranasal oxymetazoline (Afrazine) may give temporary relieve to nasal congestion @ 1 drop/nostril q12 hours for 48 hours maximum.
- *Antivirals* – cat 'flu' is usually caused by FCV or FHV-1, and specific antiviral therapy is being used more commonly. Where FHV-1 infection is present, *famcyclovir* can be given at 40 mg/kg PO q8-12h for 1-3 weeks (Malik et al, JFMS 2009, 11(1):40-48). Prof D Maggs (pers comm) states that a treatment trial with famciclovir is unequivocally the best diagnostic test for ocular FHV-1. When he sees treatment failure at 40mg/kg q12h, he increases to q 8 hour, with good results. Oral L-lysine may potentially be beneficial @ 200 mg q12-24h, PO with food, although new data on this looks less promising.
- *Topical antivirals* – while studies have shown that these may help to reduce FHV-1 viral shedding and clinical signs (trifluridine >> idoxuridine > vidarabine >> acyclovir), their use is often limited by their availability, cost, need for frequent administration, and ability to cause local irritation. Suggested treatment: trifluorothymidine 1% eye drops given q1-2h for 24h then 6x daily for 3 weeks may improve ocular condition. Recently, cidofovir has gained favour, being non-irritant and only needing to be given q12h: 0.5% solution q12h, but is expensive and needs reformulation.
- *Interferon* – while many non-specific immune stimulants are currently available, few have proven efficacy and safety. Perhaps most studies have been performed with recombinant feline interferon ω (Virbagen Omega, Virbac), which can act as an antiviral at high doses and a non-specific immune stimulant at lower doses. However, the most effective dose has yet to be determined; suggested doses range $1x10^3$-$5x10^6$ M IU/cat IV, SQ or PO q24h, for 5 days or more; a practical dose is $5x10^4$ IU PO or SQ q24h). (Minimum purchase 2x10 M IU vials (~ £125). Dilute 1 vial in 100 of saline, aliquot into 10ml volumes, freeze for up to a year. Defrost as required, dilute if required, keep refrigerated for up to 2 weeks). Alternately, recombinant human interferon alpha (hrIFNα) can be obtained as 3, 5 or 10M IU, which can then be diluted in one litre of saline, aliquoted into 1ml volumes, and frozen for up to a year. It can then be defrosted as required, diluted to the appropriate concentration, and kept refrigerated for up to 2 weeks. It is usually given @ 1-30 IU, PO, q24h. Given parenterally at high doses it will cause toxicity and induce antibody production.
- Topical ωIFN – IFN diluted in saline IFN has been shown to be safe (up to 1 M IU/ml), and has a dose-dependent anti-FHV-1 effect at >100 IU; suggested dosage is 10 M IU + 20 ml normal saline → 1 drop per eye 5x daily for 7-10 days, then 2x daily for another 3 weeks.
- Do NOT use corticosteroids, especially systemically.

Prevention and control

To reduce respiratory disease within a group of cats it is necessary to address infectious and non-infectious causes. This may require instigating a suitable vaccination and/or isolation programme, treating with suitable antibacterial agents, improving ventilation, and reducing over-crowding.

- Introduce a suitable vaccination program (see below)
- Decrease stocking density
- Increase air flow
- Ensure good sneeze barriers are present between separate groups of cats
- Improve overall hygiene, and use suitable disinfectant (ideally 1:32 bleach as some stains of FCV may not be killed as easily as the FCV-F9 vaccine strain that tends to be used as a standard and virus may therefore persist in the environment for several days to several weeks on dried surfaces, or longer in colder damp conditions)
- Have individual cats give birth and then wean their kittens in isolation
- Have a suitable quarantine facility and quarantine all incoming cats for 3 weeks
- Stop breeding – kittens are most susceptible to infection
- In colonies known to be free of infection should use inactivated vaccines only, and only introduce cats that have been tested to be free of infection

Vaccination

Vaccines against *FCV* and *FHV-1* include attenuated live and inactivated vaccines given SC, and in the US, attenuated live intranasal vaccines. Initial vaccination should start at 8-9 weeks of age with a second vaccination at 12 weeks, and possible a third vaccination at 16 weeks (in kittens with persistent maternally derived immunity [MDA]). While boosting is often given annually new guidelines suggests that after the booster at 1 year, boosting more frequently than once every 3 years is not always needed. Where available, intranasal vaccines are particularly useful when a rapid onset of protection is required, and a single dose may be sufficient to overcome MDA and induce immunity so these vaccines can be particularly useful in kittens during a 'flu outbreak.

While these vaccines are generally effective there are a number of concerns, particularly with FCV vaccines:

- Vaccination fails to produce a sterilizing immunity so it can only protect against the development of clinical signs of disease, not against infection itself. This is why there has been little change in the overall prevalence of FCV infection since the introduction of vaccination: 10-40%, depending on the nature and size of the population sampled, with large groups of random-source cats living in colonies and shelters usually having a higher chance of being infected.
- There are concerns over the relative risks and merits of live verses inactivated vaccines. For example, live vaccines may lead to clinical signs of disease following vaccination (particularly if a vaccine designed for parenteral administration becomes aerosolised or deposited on the cat's coat and is then licked off and enters the cat via the oro-nasal route). In addition, live vaccine virus can persist within a colony of cats, gaining the potential to mutate and so become pathogenic. While it was previously believed that live vaccines tended to generate superior immune responses to those seen with inactivated vaccines, with modern advances in vaccine development this is

no longer necessarily the case, as has been shown with Merial Purevax, which can give fast effective immunity within one week of vaccination. However, inactivated vaccines are more likely to require the incorporation of an adjuvant, and the potential role of these substances in the development of injection-site sarcomas is still of concern.

- Since field strains of FCV mutate and develop over time (particularly in response to immune pressure resulting from vaccination), there is concern about the ability of traditional vaccines, for example FCVF9 and FCV255, to protect against current field strains. Recent studies looking at the *in vitro* neutralisation of field strains of FCV by antisera raised against FCV vaccine strains have produced variable results. For example, in 1 study FCVF9 was shown to neutralise 87.5% of UK field isolates compared to 75% with FCV255. However, in a separate study, FCVF9 and FCV255 neutralised only 20 and 21% or 37 and 56%, respectively, while the newer vaccine strains FCVG1 or FCV431 neutralised 29 and 70% or 67 and 87%, of field strains respectively. A third study found FCVF9 to neutralise 25%; FCV255 24%; FCVG1 81%; FCV431 85%. While a fourth found FCV255 to neutralise only 23%, but when it was combined with FCVDD1 this increased to 70%. Unfortunately, it is very difficult to directly compare the results from the different studies. This is because they used different experimental protocols and different field strains (with variable percentages of ill cats included, and strains from different countries). That said, while the older vaccines are still to some extent broadly cross-reactive, it is better to develop vaccines with broader heterologous protection, for example, by incorporation a number of different FCV strains.

Vaccines against *C. felis* include attenuated live and inactivated vaccines given SC. Initial vaccination should start at 8-9 weeks of age with a second vaccination at 12 weeks and boosting should be annually. Mild signs of infection may occur post vaccination when using live vaccines. Pregnant queens should not be vaccinated. Vaccination is usually only considered when a unit has an identified *C. felis* problem.

The vaccine against *B. bronchiseptica* is live attenuated, and given intranasally. Initial vaccination should start at 8-9 weeks of age with a second vaccination at 12 weeks and boosting should be at least annually. Mild signs of infection may occur post vaccination. Pregnant queens should not be vaccinated. Vaccination is usually only considered when a unit has an identified *B. bronchiseptica* problem.

Virulent Systemic - FCV Disease (VS-FCV)

Cases of severe systemic haemorrhagic-fever disease due to particularly pathogenic strains of FCV were first seen in the US in 1998, and similar cases have been seen in the UK since 2003, and in France, Italy and Germany. Clinical signs become apparent within 1-5 days of infection and affected cats show a range of clinical signs, including upper respiratory disease (oculo-nasal discharge, oral ulcers), pneumonia, peripheral oedema and skin sloughing (typically affecting the head and limbs) which is due to peripheral vasculitis, and systemic vasculitis with disseminated intravascular coagulation that can result in multiple organ failure and death (see below). The mortality can be >50% even in previously healthy, vaccinated cats, with adult cats suffering significantly higher

morbidity and mortality than kittens (which may only show more classical signs of 'flu). The duration of disease from first signs to death is typically from 4-9 days, but occasional cases have been more protracted.

Clinical signs of VS-FCV:

- Anorexia, lethargy, depression
- Pyrexia (can be >105^{o}F/40.6^{o}C) (~80%)
- Subcutaneous oedema and ulcerative dermatitis – particularly on the nose, lips, pinnae, around the eyes, and distal limbs and fluid may ooze from the affected areas (>50%)
- Mouth ulcers (~50%)
- Nasal discharge (~30%)
- Severe respiratory distress: pulmonary oedema and/or pleural effusion* (~20%)
- Ocular discharge (~10%)
- Jaundice* (~10%)
- Gastrointestinal signs: vomiting, diarrhoea
- Signs of coagulopathy: petechiae, ecchymosis
- Sudden death

* These signs are associated with a poor prognosis.

Laboratory investigation may reveal changes in serum biochemistry (moderate hypoproteinaemia, and increases in total bilirubin and creatinine kinase), a mild neutrophilia and lymphopenia, non-regenerative anaemia, and severe coagulopathy. Necropsy typically confirms the external changes and may reveal severe pancreatitis with saponification of the peripancreatic fat, necrotizing or interstitial bronchopneumonia, and/or hepatocellular, lymphoid and splenic necrosis.

Potential **differential diagnoses** include pancreatitis/vasculitis/sepicaemia, e.g. causes by Salmonella, *Streptococcus equi* subspecies *zooepidemicus, Influenza A* virus, *E. coli*, and potentially *Mycoplasma* species or Toxoplasmosis.

Diagnosis of VS-FCV may be suspected when a number of in-contact cats show clinical signs as described above, and are found to be positive for FCV by virus isolation (typically from pharyngeal swabs). However, there is currently no way of confirming the diagnosis as all outbreaks have been caused by viral strains of differing sequences so a genetic test has not been developed. Finding that the cat is shedding FCV may help in the diagnosis but it is always possible that the cat is ill because of another reason (e.g. severe pancreatitis), but is concurrently shedding either a normal field or vaccine strain of FCV. Immunohistochemistry to detect the presence of FCV within tissue biopsies can be helpful in indicting the presence of the virus within the pathological lesions.

Most outbreaks have involved the introduction of a cat from a rescue centre immediately prior to the disease spreading rapidly within the veterinary practice, shelter or private home. It has therefore been suggested that crowded, high-stress environments, such as found in shelters, may contain high levels of viral biodiversity (i.e. many different FCV strains which can lead to sequential re-infection, rare persistently FCV-infected cats

[which enable progressive evolution of FCV within an individual cat], and even cats infected with more than one FCV strain [which raise the possibility of viral recombination]). This, plus high levels on non-neutralising immunity, may select for highly contagious and virulent viral strains. Under these conditions viral variants that are capable of replicating faster and to higher titres will be more likely to be transmitted and positively selected for. Once selected, these strains can then spread rapidly. Cats growing up in these environments and kittens born to infected mothers within these environments will tend to have matched immune responses so can suppress viral replication and at most develop only minimal clinical signs. However, when these viruses gain assess to populations that have not been previously exposed to them (e.g. veterinary practice or another home) this can result in an outbreak of VS-FCV. VS-FCV is believed to result from increased viral pathogenicity and altered cell tropism (invasion of epithelium and endothelium), and altered host cytokine response. This results in systemic vascular compromise, multi-organ failure, haemorrhage, shock and death.

The infection can be easily spread by cat handlers and fomites (oro-nasal secretions, skin-ooze from areas of ulceration, faeces and urine) and infection may still manage to spread despite the introduction of strict isolation and barrier nursing. Asymptomatic and recovered carrier animals also exist. Somewhat inexplicably, all outbreaks have so far been self-limiting, have typically involved <100 cats, and resolved within 2 months.

Traditional FCV vaccinations (containing FCVF9 or FCV255) offer little protection against VS-FCV (although very recently vaccinated cats may be slightly less likely to become ill). However, a recent study revealed that Merial Purevax (containing FCVG1 and FCV431) protected against VS-FCV strains from Europe, and there have been 2 vaccines generated against VS-FCV strains by Fort Dodge in the US. One of these (FCV2280) offered no protection against European VS-FCV isolates, which underlines the problem of strain variation between the different VS-FCV strains meaning that protection against other VS-FCV strains cannot be assumed. The other vaccine (FCVDD1) has been combined with their classical FCV vaccine (FCV255) and in a recent publication this bivalent vaccine gave protection against European and US VS-FCV strains (at the time of writing this is not currently available in Europe).

All suspicious cases should be handled with strict hygiene and quarantine precautions, ideally treated away from the veterinary practice (to reduce the risk of nosocomial infection), and kept in isolation until they have been shown to have stopped shedding virus (which may take a few weeks). To prevent the infection spreading it is important to trace all in-contact cats and to quarantine all potential suspects.

Treatment: While nothing has been published a pragmatic approach would consist of high dose interferon (to suppress viral replication [and suppress the excessive immune response which can be so damaging] ωIFN 0.5-2.5x10^6 M IU/kg IV q24h, for 3 days), plus IV fluids, covering antibiotics, analgesia (ideally methadone and maropitant – which is a good visceral analgesic), supportive care and, if needed, systemic corticosteroids.

CHRONIC URT DISEASE

CAUSES

- *Chronic post-viral rhinitis / idiopathic chronic rhinitis:*

The majority of cases of chronic URT disease are defined as *chronic post-viral rhinitis/sinusitis.* The initial viral infection causes damage to the nasal mucosa, which allows secondary infection with oro-pharyngeal bacteria, and hence the establishment of chronic osteomyelitis of the turbinate bones. However, since it is usually not possible to detect FHV-1 or FCV at this late stage of disease, the condition should perhaps more correctly be termed *chronic idiopathic rhinitis.* Bacteria commonly cultured from these cases include *Pasturella,* and in the case of rhinosinusitis, *Pseudomonas.*

- *Chronic bacterial rhinitis:*

Occasional cases have been seen associated with *Pseudomonas, Mycoplasma, B. bronchiseptica,* or *Mycobacteria species.*

- *Fungal rhinitis:*

Cryptococcus neoformans infection is seen world wide; however it is rare in the UK. Infection with *Aspergillus* spp. is seen even less commonly. Saprophytic fungi (e.g. *Pseudoallescheria boydii, Alternaria spp.*) have caused occasional cases of fungal rhinitis. These are typically associated with plant material that has become lodged in the nasopharynx.

- *Allergic rhinitis:*

Allergic rhinitis has occasionally been diagnosed in cats, and may be more common than we appreciate. Typical allergens include cat-litter dust, certain aerosol sprays, and cigarette smoke. In some cases, allergic rhinitis may occur concurrently with 'feline asthma'.

- *Nasopharyngeal polyps:*

These inflammatory polyps are usually associated with chronic inflammation of the middle ear, from where they are believed to originate. While they are usually seen in young cats, they can be seen in cats of all ages. Nasopharyngeal polyps usually cause obstructive URT disease. When they extend into the caudal nasopharynx they may also cause dysphagia or gagging. When they extend from the middle ear into the outer ear they may cause ear pain, otitis externa and otorrhoea.

- *Nasonasal polyps:*

Nasonasal polyps originate within the nasal chambers. They arise secondary to chronic inflammation. Since their mucosa is very friable they may be associated with epistaxis.

- *Nasopharyngeal stenosis:*

This is seen when an inflammatory membrane develops across the caudal nasopharynx. It usually arises secondary to chronic inflammation.

- *Neoplasia:*

The most common tumours of the nasal cavity are lymphoma (LSA) and adenocarcinoma. Other tumours that may be seen in this location include undifferentiated carcinoma, squamous cell carcinoma (SCC), fibrosarcoma, and chondrosarcoma. Tumours may arise secondary to chronic inflammation. The author has seen nasal LSA develop in cats that have had chronic idiopathic (lymphocytic/plasmacytic) rhinitis. One cat, which had chronic idiopathic rhinitis, later developed nasonasal polyps, then undifferentiated carcinoma.

- *Foreign body:*

Intranasal foreign bodies typically consist of plant material, and usually enter via the nasopharynx. Fungal spores associated with the plant material may occasionally lead to a secondary fungal rhinitis. Removal of the foreign body, and any associated fungal cast, usually results in a good recovery.

- *Trauma:*

Trauma is usually caused by road traffic accidents or cat fights. Road traffic accidents may cause hard palate separation, the generation of oro-nasal fistulae, or damage to the maxillary bones. Cat fights occasionally result in the loss of teeth within the opponent's nose, or maxillary bone fractures. This type of damage may in turn lead to infected sequestra.

- *Dental disease:*

Severe peridontal disease or tooth fracture can result in the generation of an oronasal fistula.

- *Congenital defects:*

Cleft palate, defects of the external nares or nasal septum can all result in chronic URT disease.

- *Laryngeal - Paralysis / Trauma / Oedema / Polyp / Granulomata / Neoplasia:*

Laryngeal disease is seen far less frequently than rhinitis. Paralysis is seen most commonly secondary to neck trauma. While tumours of the larynx are uncommon, they are usually of similar types to those seen in the nose or pharynx, with SCC and LSA being seen most often.

DIAGNOSIS

Diagnosis of URT disease, as with all diagnostic investigations, relies on a combination of knowing the signalment of the patient (i.e. its age, sex and breed), gaining a complete medical history, performing a thorough physical examination, and then undertaking selected further investigations.

The *signalment* can be of help since congenital detects will usually cause clinical signs within a few days of birth. However, cat 'flu' is seen most frequently in older kittens, and

neoplasia is seen most typically in old cats. While the breed rarely has a bearing on URT disease, the author has seen nasonasal polyps most frequently in Oriental breeds of cat.

From the *history* it is important to determine;

- what type of environment the cat lives in
- what other animals it lives with
- where it has previously lived
- whether or not it has been vaccinated, and if so, with what and when
- whether there is any history of previous illness, facial trauma, dental disease or ear infections
- at what age signs of URT developed
- what was the pattern of onset of clinical signs
- were other animals from the same household affected
- did the cat ever have cat 'flu' (remember - chronic post-viral rhinitis is the most common cause of chronic URT disease)
- how has the disease progressed
- have the clinical signs ever responded to previous treatments
- is there a history of dysphagia or dysphonia?

Physical examination;
The main signs of URT disease are sneezing, nasal discharge and difficulty in breathing. The exact nature of the discharge, whether both sides of the nose are affected, and the presence of other clinical signs are dependent on the nature of the underlying disease, and on the presence of any other illness the cat may have.

Particular points to look out for include:

- The presence of *nasal discharge,* and whether it is bilateral or unilateral. Some diseases tend to show unilateral signs (e.g. foreign bodies, or neoplasia), while others more often cause bilateral signs (e.g. chronic post-viral rhinitis). While the nature of discharge can be helpful (e.g. haemorrhage is seen commonly with neoplasia, fungal infections and nasonasal polyps), it can be misleading (e.g. haemorrhage can occasionally be seen with foreign bodies, or severe chronic post-viral rhinitis).

- The *character of breathing,* and whether or not the breathing is noisy when the cat breathes through its mouth, may help to localise disease to the nasal area or the larynx. Generally, disease in the URT causes inspiratory dyspnoea. The breathing is more stertorous (snoring) when disease is in the nose, but more stridorous (high pitched and harsh) when disease affects the larynx. Both nostrils should be checked for deformity, obvious obstruction and presence of airflow. Dysphonia may be associated with laryngeal disease.

- *Facial examination* may reveal a lack of symmetry or facially swelling (most typically associated with neoplasia or fungal infections). Facial pain and resentment of facial examination is common among cats with URT obstruction, especially those with intranasal foreign bodies, or polyps. In Siamese cats the facial hair overlying the inflamed nasal chambers may become de-pigmented.

- *Ocular examination* should involve assessment of the periocular area, the anterior and posterior chambers, and the retina. Examination may reveal a serous ocular discharge resulting from tear duct damage associated with previous URT viral disease, or occasionally associated with cancer within the nose. Previous FCV, FHV-1 or *C. felis* infections can result in chronic conjunctivitis, which in the case of FHV-1 infection may also result in keratitis. Retinal lesions may be seen associated with intranasal neoplasia or fungal rhinitis.

- *Aural examination* may reveal evidence of painful or infected ears associated with inflammatory polyps.

- *General body condition and body weight.* Cats with URT obstruction often have a poor appetite and so experience a degree of weight loss. Marked weight loss is more suggestive of neoplasia, fungal disease or severe systemic disease.

- Cats with chronic URT disease frequently have mild to moderate submandibular *lymphadenopathy*. If submandibular lymphadenopathy is marked, or if lymph nodes elsewhere in the body are also affected, neoplasia, mycobacteriosis or fungal infections are most likely to be the cause.

- Kidneys should be assessed for size and shape since nasal LSA may be associated with renal LSA.

Since different diseases can present very similarly it is important not to over-interpret the presence of a particular clinical sign. A few general rules usually hold true, e.g. facial deformity with associated pain, especially if accompanied by a unilateral nasal haemorrhage or marked lymphadenopathy, is usually suggestive of nasal neoplasia or fungal infection. However, a lack of these findings does not rule out these diagnoses, and some cases of nasal LSA cause bilateral nasal obstruction and little nasal discharge of any kind. Also, although post-viral rhinitis usually presents with chronic bilateral purulent discharge, it can also present with unilateral discharge, sometimes blood tinged and occasionally with frank haemorrhage.

Further investigations:

Assessment of *serum biochemistry, haematology, and FeLV/FIV status* will help to gain an overall picture of the cat's health.

Attempts to make a diagnosis from *nasal swabs* taken from a conscious cat are rarely successful (unless *C. neoformans* is detected). If *C. neoformans* is detected its presence should be confirmed by culture and/or serology. Bacteria detected in this manner usually represent only secondary contaminants.

The detection of FHV-1 or FCV by *oro-pharyngeal swab and viral culture or PCR* is rarely helpful. Vaccinated cats and cats that have been previously infected with FCV may

also be shedding virus. Since FHV-1 is shed only intermittently, failure of its detection does not negate against it playing a significant role in disease.

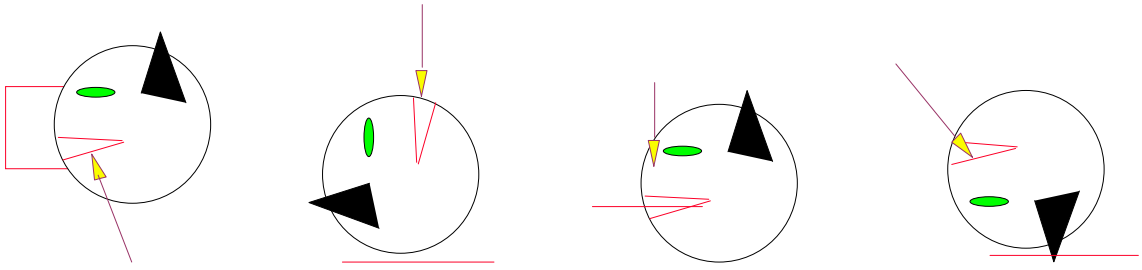
It is usually only by performing a detailed examination of the URT (for which the cat has to be anaesthetised), taking radiographs (CT or MRI investigation*), and collecting samples for microbiological and histopathological examination, that a definitive diagnosis may be made. These procedures are performed under general anaesthesia; anaesthesia is induced, the mouth and larynx are examined as the cat is intubated, radiographs are taken, and then the nasopharynx and nasal chambers are examined. The investigations can be performed under the same anaesthetic. Radiographs, or any advanced imaging, should be taken before the introduction of flushing solutions, an endoscope, or biopsy instruments since these procedures may result in haemorrhage that will alter the radiographic appearance.

*Where it is available advanced imaging can be very useful in the investigation of URT disease. Because CT enables detailed visualisation of boney detail as well as soft tissue structures it is often of more use than MRI.

Radiographic investigations:

To prevent head movement radiographic investigations should be performed with the cat under general anaesthetic. When taking the radiographs it is advisable to remove the endotracheal tube to prevent it obscuring essential details.
The investigation should include:

- Whole skull radiographs (lateral and VD views) – to assess the overall structure of the skull, the frontal sinuses, the size and content of the pharynx, etc.
- Intraoral view – to assess the nasal chambers and the maxillary dental arcade.
- Open mouth view – to assess the tympanic bullae.
- Lateral oblique views – to look for the presence of dental disease and to highlight the tympanic bulla.



Lateral oblique view *Open mouth view* *Intraoral views*

Radiographs should be assessed for the presence of dental disease, evidence of middle ear infection, obstruction of the nasopharynx by soft tissue, soft tissue density within the

frontal sinuses, loss of integrity of the nasal septum, and loss of turbinate detail. Whether the loss of turbinate detail is unilateral or bilateral, and its position within the nasal chambers may help to localise the disease. The loss of turbinate detail may be due to an overall loss of turbinate bone, or an overlying increase in soft tissue. While the nature of the change should be assessed, it is rarely specific. An overall loss of turbinate bone may be seen with chronic destructive post-viral rhinitis, neoplasia, reaction to a foreign body, or fungal rhinitis. An overlying increase in soft tissue may be seen with chronic post-viral rhinitis, neoplasia, nasonasal polyps and allergic rhinitis.

Physical examination

• *Teeth, hard palate, soft palate, oro-pharynx and tonsils:*

This examination is performed under general anaesthesia, preferably with a gently cuffed endotracheal tube in place. The teeth, hard and soft palates, oro-pharynx and tonsils are examined visually and digitally for signs of disease.

• *The nasopharynx:*

The caudal nasopharynx is then examined using a dental mirror and a bright light, or a retroflexed bronchoscope. If the soft palate needs to be drawn forward to improve visualisation this should be done by placing 'stay sutures' though its caudal margin, or using atraumatic tissues forceps (not Alice tissue forceps). Any unusual findings should be biopsied.

• *The rostral nasal chambers:*

Prior to investigating the nasal chambers it is important to pack the caudal oro-pharynx with surgical swabs. This is done because even minor trauma to the nasal mucosa can result in significant haemorrhage. It is important to prevent this blood from entering the trachea. For this reason it is also advisable to use a gently cuffed endotracheal tube. While the rostral nasal chambers can be assessed using an auroscope fitted with a small cone, this approach generally affords very poor visualisation. Where available, a narrow rigid rhinoscope/arthroscope is more suitable, and in large cats may even permit biopsies to be collected with endoscope guidance. When using either a rhinoscope or taking blind biopsies it is important that the instrument is measured against the animal's face, and marked with a tape tag at the distance from the tip of the nose to the medial canthus of the eye on the same side. This prevents iatrogenic damage to the brain when the instrument is introduced into the nose.

Sample collection:

Samples for cytological and microbiological examination can be collected by a number of methods. Pros and cons exist for each of the methods.

• *Direct swabs:*

While direct nasal or pharyngeal swabs are non-invasive they rarely yield useful information (see earlier section in "further investigations").

• *Direct aspirates/flushes:*
Flushing sterile saline through the nasal chambers may help to clear away mucus and debris, and the resultant flush can be used for analysis. Unfortunately, analysis of this fluid is likely to detect only surface contaminants.

• *Traumatic flush:*
A traumatic flush entails scarification of the intranasal mucosa at the same time as flushing the nose with saline. While the cellular yield is increased using this technique, the cellular detail is generally poor and the risk of haemorrhage considerable.

• *Forced flush:*
A forced flush is performed after firmly packing the caudal pharynx, then forcing approximately 10ml of saline up one nostril while holding the other nostril shut. This technique can be used to dislodge foreign bodies, inspissated pus, necrotic debris, and occasionally, tumours or polyps. The solid tissue collects on the pharyngeal swabs. The procedure should be performed carefully, as excessive force may flush material through the cribriform place if it has already been damaged by local pathology.

• *Pinch biopsies:*
Pinch biopsies are most easily collected using endoscopic biopsy grabs. Only in very large cats can the biopsies be endoscopically guided. Blind biopsies are usually adequate, provided that 2-3 samples are collected from each side of the nose.

• *Nasal core biopsy:*
Nasal core biopsies can be collected by cutting down a 16 gauge over-the-needle IV catheter, and using it like an 'apple corer' to collect a nasal biopsy.

• *Surgery:*
The most representative and diagnostic biopsies will be gained during surgical exploration of the nose.

Haemorrhage:
While many methods of sample collection have been devised it is important to remember that the larger the biopsy sample, the better the chance of an accurate diagnosis, but the greater the risk of haemorrhage. Since nasal investigations frequently result in bleeding it is strongly recommended that patients have their clotting times checked prior to beginning the procedure. If intra-operative haemorrhage does occur the intranasal instillation of ice-cold saline or adrenaline may help, along with packing of the pharynx and closing the nostrils.

Submission and non-specific findings:
Samples should be submitted for cytology/histopathology (where appropriate staining for fungi and/or mycobacteria), aerobic and anaerobic culture and a non-fixed sample can be sent for *Mycoplasma* PCR. Unfortunately, the collection of suitable samples does not always lead to a definitive diagnosis. Since most cases of chronic URT disease result from chronic post-viral damage, many of the tests will give negative or non-specific

results, at best confirming the presence of chronic-active inflammation. A diagnosis of chronic post-viral rhinitis is usually a diagnosis of exclusion.

TREATMENT

When undertaking the treatment of a cat with chronic URT disease it is helpful (where possible) to differentiate between the possible underlying causes (see diagnosis). This allows for the correct treatment to be given and a prognosis to be considered. However, since most cases of chronic URT disease result from chronic post-viral damage, it is important to remember that the likelihood for full recovery is poor.

Where a specific disease is diagnosed, specific treatment should be given:

- *Nasopharyngeal polyps* can be removed by gentle traction, pulling the polyp towards the oro-pharynx. To reduce the risk of recurrence inflammatory material can also be removed from the middle ear. This is usually achieved via an ipsilateral ventral bulla osteotomy.

- *Nasonasal polyps* can be surgically resected, as can the inflammatory membrane of *nasopharyngeal stenosis* (a condition which can also be resolved by balloon dilation)

- *Foreign bodies* can be removed. Local infection can be reduced by curettage. Following foreign body removal, especially where local damage is extensive, a long course of antibiotics is recommended (e.g. 6-8 weeks).

Fungal rhinitis should be treated with antifungal drugs (e.g. itraconazole, fluconazole, ketoconazole, and/or amphotericin B, and these drugs may need to be given for 2-18 months depending on the severity of disease).

- *Laryngeal paralysis* can be ameliorated by performing a unilateral 'laryngeal tie-back'. Any underlying cause should be determined and corrected.

- *Post-viral rhinitis/idiopathic rhinitis* is rarely curable. The emphasis is on management not cure. Many of the therapeutic options discussed in the section on treatment of cat 'flu' also apply here (see earlier section).

- *Antibiotics* – While antibiotics rarely result in a cure, their strategic or long-term use can reduce the severity of clinical signs, and so improve the cat's quality of life. A good response is sometimes gained using a long course of antibiotics (6-8 weeks), starting immediately following intranasal investigations. Recently findings suggest that a long course of doxycyclin or azithromycin may be particularly good choices. Chronic antibiotic usage can predispose to *Pseudomonas* overgrowth - these cases can be very difficult to treat. Ideally you would hospitalise and give iv fluids plus one of the aminoglycosides plus nebulize with gentamycin twice daily. Consider using tobramycin as it has more activity against than gentamycin or amikacin against *Pseudomonas* but is more toxic than these drugs: 5-8 mg/kg iv, im or sc q24h for <5 days.

- *Anti-inflammatory agents* – While safety is an issue, recent studies have suggested that meloxicam may be a particularly good choice.
- *Famcyclovir* – where chronic FHV-1 is involved famcyclovir may be useful when given at 62.5-125 mg/cat PO q8-24h for 1-3 weeks (Malik et al, JFMS 2009, 11(1):40-48).
- *Inhaled corticosteroids* – These can help in the general reduction of inflammation, and can be particularly useful in cases of allergic rhinitis (for more information see the section on Treatment of Chronic Bronchopulmonary Disease).
- *Leukotriene receptor antagonists:* e.g. *Zafirlukast* or *Montelukast.* No published trials on the use of this type of drug in cats with chronic URT disease have been published. While it has been suggested that they may help in some cases see section on Treatment of Chronic Bronchopulmonary Disease before considering their use.
- *Therapeutic flush* – A therapeutic flush entails adding an antibiotic, antiseptic or other therapeutic agent (e.g. IFN) to the intranasal flush. This may have beneficial effects when performed at the end of a nasal investigation.
- *Nasal curettage* – While this procedure results in a degree of improvement in some cases, other cases benefit little. Also, the procedure is not without risk, and can be very painful. This procedure should not be undertaken lightly, and post-operative analgesics are essential.
- *Frontal sinus ablation, trephination and irrigation* – These procedures may be considered where inflammation has extended into the frontal sinuses. Response to these procedures is not always favourable and post-operatively the cat's can be in considerable pain. Analgesics are essential.

LRT DISEASE and THORACIC CAVITY DISEASE

CAUSES OF LRT DISEASE (Figure 3)

In cats, the most common cause of chronic coughing is chronic bronchopulmonary disease. Because of this, it may, on occasion, be tempting to make a presumptive diagnosis, rather than undertaking a full investigation. However, this is not to be recommended as many of the other differential diagnoses carry very different treatment options and/or prognoses. In addition, different types of chronic bronchopulmonary disease may respond better to slightly differing treatment approaches and are frequently complicated by secondary infections.

1. Chronic bronchopulmonary disease:

This describes a commonly occurring yet poorly understood group of conditions that affect the airways and alveolar space. It includes 'feline asthma', chronic bronchitis, chronic broncho-pneumonia, chronic obstructive pulmonary disease (COPD), emphysema and idiopathic pulmonary fibrosis. By definition, asthma is characterized by airway hyper-responsiveness and reversible bronchoconstriction, while chronic bronchitis (or COPD) is characterized by airway inflammation and excessive mucus production, and leads to irreversible narrowing of the airways. However, given current diagnostic facilities the distinction between the two disease entities is at best difficult, and often completely arbitrary. Somewhat incorrectly, the term 'feline asthma' tends to be used for those cases that are found to have a strong component of airway hypersensitivity,

combined with an increased number of eosinophils on bronchoalveolar lavage (see later). In most cases, the exact aetiopathogenesis of the different conditions remains unclear.

The main clinical signs are coughing, wheezing, dyspnoea and respiratory distress. Clinical signs may be episodic, intermittent or persistent, and arise because of:

- Tracheobronchial inflammation and irritation
- Excessive airway secretion
- Bronchoconstriction

Disease is seen most frequently in young to middle aged cats (2-8 years of age), with Siamese, Burmese and other Oriental breeds being over-represented. Historically, the cats may have previously experienced cat 'flu', have initially shown a degree of seasonality to their disease, or had their clinical signs exacerbated by airway irritants (smoke, temperature changes, aerosols, dusty cat-litter, or sleeping on their owners bed – sometimes defined as being 'worse at night'). Coughing may conclude with a terminal retch to clear mucus from the pharynx, which is then swallowed.

In cats with episodic signs clinical examination is often unrewarding. However, while many asthmatic cats appear normal, thoracic auscultation frequently reveals that the respiratory pattern has a prolonged expiratory phase. During an episode of coughing or in cats with more protracted disease, increased lung sounds may be heard on auscultation (typically wheezes and, in more severe cases, crackles). In severe cases the chest may be barrel-shaped, and a 'heave line' may be evident. Percussion may reveal hyperinflation of the chest (with resonance extending to the 12^{th} rib), and air-trapping can result in reduced thoracic compressibility. Palpation of the cervical trachea may trigger a severe bout of coughing, and coughing can be sufficiently severe to cause spontaneous fractures of the caudal ribs (dorso-caudally).

2. Pneumonia:

This can be caused by various infectious agents (viruses [feline herpes virus FHV-1, feline calicivirus FCV, cow pox virus – from voles, rarely *Influenza A virus* – either from infected humans or eating infected birds], bacteria [*Pasteurella multocida, Bordetella bronchiseptica, Mycoplasma* spp *(e.g. M. felis, M. gateae,* and *M. feliminutum),* extra-intestinal pathogenic *Escherichia coli* (ExPEC), beta haemolytic *Streptococcus* spp. {a common cause of pneumonia in US and Swiss studies – being seen most commonly in kittens of <12 weeks of age], *Neisseria* spp. (EF4), *Salmonella* spp., *Mycobacterium bovis, M. microti*, rarely *Streptococcus equi* subspecies *zooepidemicus* – from horses], parasites [*Toxoplasma gondii,* lungworm e.g. *Aelurostrongylus abstrusus and Capillaria aerophilus,* heart worm e.g. *Dirofilaria immitis*]), or inhaled or circulating toxins or irritants (lipid or food aspiration, smoke inhalation, uraemia, pancreatitis, sepsis, or potassium bromide administration for seizures [which can lead to eosinophilic peri-bronchial infiltrates).

Bacterial pneumonia is seen most frequently in immunocompromised individuals, or in individuals with compromised lung function. Bacterial bronchopneumonia usually presents with a cough, tachypnoea, dyspnoea, nasal discharge, fever and depression.

Auscultation may reveal increased lung sounds, crackles, wheezes, and silent areas (due to pulmonary consolidation, infiltration, neoplasia or bullus formation). Primary bacterial pneumonia, with mixed and pure cultures of *B. bronchiseptica* or PCR positive *Mycoplasma* spp. may be found in kittens of 5-10 weeks of age that have come from environments where husbandry is poor. *B. bronchiseptica* can also be spread from dogs. Pneumonia due to ExPEc or *Streptococcus* spp. can result in systemic spread, meningitis, joint and/or kidney infection, endocarditis and disseminated intravascular dissemination.

Primary bronchopneumonia may also result from infection with members of the tubercle group (typically *Mycobacterium microti* and *M. bovis*, both believed to be most commonly caught from voles and mice). These infections are seen quite regularly in the UK and Ireland. Clinical signs are rather insidious in onset, dyspnoea is usually more obvious than coughing, and cutaneous lesions are usually present.

Bacterial pneumonia can also arise secondary to other disorders. These include chronic bronchopulmonary disease, the long-term presence of a foreign body, or previous damage from inhalation or aspiration. With chronic bronchopulmonary disease secondary infection occurs most typically with *Mycoplasma spp., P. multocida*, or *B. bronchiseptica*, and in these cats the signs of pneumonia are often quite subtle, usually presenting as an exacerbation of an already chronic condition.

Parasitic pneumonia: Aelurostrongylus abstrusus is probably the most common lungworm of cats, although *Eucoleus aerophilus* (previously *Capillaria aerophila)* infection may also occur. While *A. abstrusus* may be present in up to 20% of free-roaming cats, it rarely causes clinical signs of disease. Clinical signs are more prevalent in immunosuppressed cats, but can also be found in found fit and even pedigree cats. Cats are infected by eating infected slugs or snails (the intermediate host), or infected rodents, lizards or birds (the transport hosts). Affected cats may present with a chronic cough, with associated crackles and wheezes, occasionally with concurrent pleural fluid. Perhaps the most important consideration of *A. abstrusus* infection is its differentiation from chronic bronchopulmonary disease, particularly 'feline asthma'. Since both conditions can result in an eosinophil-rich bronchoalveolar lavage fluid (see later) it is advisable to treat all coughing cats with a therapeutic course of fenbendazole or other appropriate wormer (see later), prior to undertaking further investigations.

Heart worm (e.g. *Dirofilaria immitis*) is endemic in warm and tropical regions, including Southern Europe, the USA and Canada. Affected cats may present with clinical signs typical of chronic bronchial disease, vomiting, or may present with acute, often fatal, severe dyspnoea associated with pulmonary thromboembolism.

3. Neoplasia:

Pulmonary neoplasia may be primary or metastatic. While primary neoplasia is rare in cats it can include adenoma, bronchoalveolar adenocarcinoma, and bronchial gland carcinoma. Affected cats are usually older (average age 10-14 years), with clinical signs consisting of coughing, wheezing and/or dyspnoea, depending on the location and extent of the tumour. Interestingly, lameness may be seen in ~25% of cats with malignant lung

tumours because some of these tumours may metastasise to the digits. Since metastatic lung tumours are seen more typically within the lung parenchyma, rather than the bronchial tree, they rarely result in coughing.

4. Foreign bodies:
Foreign bodies within the trachea or bronchial tree will initially cause acute coughing. However, if the foreign body is not removed chronic coughing and dyspnoea can result. This is often accompanied by halitosis as secondary infection develops.

5. Pulmonary oedema:
In cats, most cases of pulmonary oedema result from congestive heart failure. Occasional cases of non-cardiogenic pulmonary oedema may result from severe pancreatitis, uraemia, shock, sepsis, near-strangling, near-drowning, electrocution, smoke-inhalation, or cranial trauma. The history and other clinical findings are likely to indicate the cause of the disease. Uncomplicated pulmonary oedema, because it is located within the lung parenchyma, rarely causes coughing.

6. Pulmonary contusion (trauma):
Blunt trauma to the chest (road traffic accidents, 'high-rise' falls) can result in pulmonary contusion, haemorrhage, oedema, atelectasis, and gas-filled cyst formation. Other injuries may include fractures of ribs, sternebrae, mandible or fore-limbs, pneumothorax or pneumomediastinum. Pulmonary contusions rarely cause coughing unless the trauma results in tracheal damage or significant haemorrhage within the bronchi.

7. *Pulmonary thromboembolus*
This is not seen commonly in cats, although it may be under-recognised. It should be considered in any cat with significant acute-onset dyspnoea with minimal radiographic changes.

8. *Pulmonary hypertension*
This may occur secondary to a number of different diseases, including cardiac and chronic respiratory tract diseases (e.g. idiopathic pulmonary fibrosis), and may results in dyspnoea and eventually, cyanosis. Echocardiography is the most practical way of making this diagnosis.

CAUSES OF THORACIC CAVITY DISEASE (Figure 4, Table 2)

- *Thoracic effusions:*

Fluid may accumulate within the chest cavity for many reasons (Table 2).

Hydrothorax describes the accumulation of a serous to serosanguineous fluid within the thoracic cavity. It may result from hypoproteinaemia, congestive heart failure, intrathoracic neoplasia, obstruction of lymphatic drainage, diaphragmatic or pericardial hernia, lung-lobe torsion, pancreatitis, or feline infectious peritonitis (FIP).

Haemothorax describes the accumulation of blood or heavily blood-stained fluid within the thoracic cavity. It may result from organ or major blood vessel rupture which may be

associated with trauma, neoplasia or thrombosis, an oesophageal perforation, or lung-lobe torsion, or a bleeding disorder (such as warfarin poisoning, or thrombocytopenia).

Chylothorax describes the accumulation of a milky fluid within the thoracic cavity. It may be associated with congestive heart failure, intrathoracic neoplasia, ruptured lymphatic drainage, or obstruction of lymphatic drainage.

Pyothorax describes the accumulation of pus within the thoracic cavity. Bacterial infection may be associated with oesophageal perforation, a penetrating wound, a migrating foreign body, extension of infection from elsewhere, or haematogenous spread.

- *Pneumothorax / Pneumomediastinum:*

Pneumothorax usually results from air leaking from ruptured lung parenchyma. It may result from trauma associated with a road traffic accident, a dog-bite to the chest, or iatrogenic damage occurring during thoracic disease investigation. The air accumulates around the lungs, preventing their full expansion. A pneumomediastinum may result from air leaking from a tear in the pharynx, trachea, or chest wall. Air accumulated in the mediastinum generally affects lung expansion less severely than a pneumothorax.

- *Ruptured diaphragm:*

This usually results from a road traffic accident. Since the abdominal organs do not always migrate into the chest cavity immediately, some cats may present weeks to months after the traumatic incident. It is usually the small intestines, stomach and/or liver that enter the chest cavity. When the stomach becomes trapped and bloated, or the liver becomes strangulated and effusive, the presentation can be very severe and acute.

- *Pericardioperitoneal hernia:*

A pericardioperitoneal hernia is a congenital defect resulting from failure of closure of the pericardial sac and incomplete formation of the diaphragm. While the defect is present from birth it does not always result in clinical disease. Cats of any age can therefore present with dyspnoea and/or regurgitation resulting from intestines having passed into the pericardial sac. The condition is seen most frequently in Persian cats, British Shorthaired cats, and cats having descended from these breeds, with grey cats being over-represented.

- *Mediastinal disease:*

Disease in the mediastinum is usually associated with neoplasia, infection, or trauma. In cats, mediastinal disease is most commonly neoplastic; anterior mediastinal LSA (thymic LSA), thymoma, or extension of a tumour from elsewhere in the chest cavity. Infections are rarely located primarily within the mediastinum, they usually spread from the pleural cavity, or are associated with more generalised infection (e.g. pyothorax, or FIP).

- *Compromise of the chest wall:*

This may be seen in very young Burmese or Bengal kittens which develop ‘flat chest disease’, in kittens of any breed that are born with severe sternal deformities, or be associated with rib fractures in cats of any age.

DIAGNOSIS OF LRT DISEASE and THORACIC CAVITY DISEASE

In practice, the differentiation of LRT disease and thoracic cavity disease is not always obvious. However, it is essential to determine which is present since the investigation and treatment are very different.

Signalment and history

Cats with respiratory compromise are often difficult to handle. Stressful handling can result in respiratory decompensation, hysteria and death. This is because while normal cats use less than 5% of their oxygen intake to supply their muscles of respiration, dyspnoeic cats can be using over 50% of their inhaled oxygen for the same function, leaving no room for further compensation. Severely affected cats often benefit from being placed in an oxygen-enriched environment (oxygen box or tent) prior to being handed for the physical examination. In all cases, it is important to collect as much background detail as possible, prior to undertaking the physical examination, as this may give an indication of most likely differential diagnoses. Interestingly, ~40% of cats with ultimately fatal infectious pneumonia lack clinical signs referable to the respiratory tract, particularly a cough. Clinical signs more typically consist on lethargy and anorexia.

The *signalment* of the patient can be of help: While cats of any age, breed or gender may develop a chronic cough; kittens from an unhygienic and crowded environment are more likely to develop bacterial pneumonia; cats with clinically significant lung worm infections are typically young adult males that hunt and eat their prey; Siamese and Burmese middle-aged cats are over-represented in cats with chronic bronchopulmonary disease; and primary lung tumours are seen mainly in older cats. Very young Burmese or Bengal kittens may be seen with 'flat chest disease', Siamese cats of under 2 years of age appear to be predisposed to the development of FeLV-negative thymic lymphoma, young pedigree cats from multi-cat households are most likely to develop FIP, and young Persian or British Shorthaired cats are more likely to be presented with a pericardioperitoneal hernia.

From the *history* it is important to determine;

- what type of environment the cat lives in (or has previously lived in)
- whether or not it is allowed outside, and whether or not it hunts
- whether or not there is any history of previous illness, or trauma
- at what age did the clinical signs begin
- what was the pattern of onset of the clinical signs
- how have the clinical signs progressed
- have the clinical signs ever responded to previous treatments
- what other animals it lives with
- have any other animals from the same household been affected

This will help to determine what potential pathogens and/or irritants the cat may have been exposed to. It is very helpful to know whether or not the disease was acute in onset, or slowly progressive. Foreign bodies initially cause acute disease. A cough that starts

seasonally may be suggestive of 'feline asthma' or lungworm infection. 'Asthmatic' cats may cough more at night when sleeping on their owner's bed, or at the end of a bout of play, and their clinical signs may be exacerbated by their owner's smoking. Cats that go outside, hunt, or eat snails are more likely to become infected with *A. abstrusus* (lungworm). A history of a road traffic accident may suggest a ruptured diaphragm, pneumothorax, or haemothorax.

Physical examination
The physical examination should always be carried out gently and thoroughly. However, in very dyspnoeic cats it may need to be interspersed with periods of time in an oxygen chamber. Particular points to look for include:

- The *character of the breathing:* Generally, LRT disease is associated with expiratory dyspnoea. Severely 'asthmatic' cats may have a much exaggerated expiratory effort. Disease affecting the URT, alveoli or pleural cavity usually results in inspiratory dyspnoea. An increased abdominal effort is seen in many dyspnoeic cats. Orthopnoea (dyspnoea when recumbent), tachypnoea (rapid breathing), or open-mouthed breathing are generally associated marked respiratory compromise, as is paradoxical abdominal movement (where the thorax and abdomen move in opposite directions). However, it is important to remember that dyspnoea may result from non-respiratory as well as respiratory causes (e.g. cardiovascular disease [anaemia, congestive heart failure, hypotension or polycythaemia], abdominal enlargement [ascites, organomegaly, pregnancy], hyperthermia, metabolic acidosis [e.g. diabetic ketoacidosis], fear, anxiety, severe pain, or respiratory muscle weakness.

  The *respiratory rate and pattern*: Diseases which give rise to *restrictive respiratory patterns* prevent the lungs from expanding properly, and therefore lead to rapid, short, shallow breaths, e.g. pulmonary parenchymal diseases and diseases of the pleural space. *Obstructive respiratory patterns* arise from narrowing of the airways, leading to slower, deeper respiration, e.g. chronic bronchopulmonary diseases, such as feline asthma, or with laryngeal paralysis.

- The *presence and character of a cough:* A cough may be seen in LRT disease when the larger airways are affected. A dry harsh cough is found most commonly associated with tracheal or bronchial irritation, while a productive moist cough is usually associated with bronchopneumonia. The nature of a cough in a cat with obvious URT disease may help to determine the underlying cause. If the cough is dry and harsh it is most likely to result from 'post-nasal drip', where muco-pus from the caudal nasopharynx drips down and irritates the larynx and trachea. When the cough is productive and moist it is more likely to be associated with a secondary bronchopneumonia.

- The presence of *tracheal sensitivity* confirms inflammation of the upper airways.

- Assessment of the *mucous membranes* can help to assess the level of general peripheral perfusion, determine whether or not the animal is cyanotic (an indication

of severe respiratory dysfunction*), assess the patient's level of hydration, and see whether or not the patient is septic (injected dirty-red membranes). The presence of petechial haemorrhages may suggest a clotting disorder. *Unfortunately, since >5g/dl of deoxyhaemoglobin is needed in the blood before it can be detected by the human eye as cyanosis, many 'cyanotic' anaemic cats (PCV <15%) will simply appear as pale.

- *Thoracic palpation* should be used to check for the presence of trauma (bruises, pain, fractured ribs), or congenital defects ('flat-chested' kittens, or kittens with sternal deformities). Thoracic palpation will also help to localise the position of the apex beat of the heart, and detect whether or not a cardiac thrill is present. In severely 'asthmatic' cats the exaggerated expiratory effort may lead to a barrel-chested appearance, and enhanced musculature (a 'heave line').

- *Thoracic compression* will be reduced in cases of extensive pleural fluid accumulation or when an intrathoracic mass is present. It may also be reduced in COPD (or severe 'asthma') as a result of air trapping within the pulmonary parenchyma. Reduced anteriour thoracic compression is seen most commonly in cases of thymic lymphoma (LSA). (Interestingly, we now recognise that Siamese and Oriental cats of less than two years of age appear to be predisposed to FeLV-negative thymic or anterior mediastinal LSA). However, it is important to recognize what is normal, e.g. young kittens have very compressible chests, while old cats have reduced compressibility because of mineralization of their costochondral cartilages.

- *Thoracic percussion* can help to detect the presence of fluid or soft tissue masses within the chest (a reduction in resonance, typically ventrally), or unusual gas accumulations (an increase in resonance, typically dorsally). It can also be used to determine the extent of the thoracic cavity, and this is often increased in cats with COPD because of air trapping. Thoracic percussion is a particularly useful procedure in cats, since so many of them purr which makes auscultation less useful. However, it does require some practice to perfect and care should be taken when performing percussion on cats with severe respiratory compromise as it can exacerbate clinical signs and/or cause pain.

- *Thoracic auscultation* can be used to detect the presence of wheezes and crackles, harsh or dull lung sounds, an increase or decrease in respiratory noise, to detect the extent of the respiratory field, and as part of the cardiac examination. Wheezes are high pitched musical sounds or squeaks which result from air moving through narrowed airways, and are most commonly heard in cats with broncho-constriction as is common in asthma. Crackles are most commonly heard at the end of inspiration and usually represent air bubbling through fluid, therefore signifying the presence of fluid within the alveoli. Harsh crackles can result from the opening and closing of small airways in cats with bronchial disease. Harsh lung sounds are pronounced bronchovesicular sounds that can signify turbulent flow within the airways. Respiratory noise may be increased in LRT disease, referred for the URT, or amplified due to the presence of air in the pleural space. To determine which is the

case it is necessary to auscultate over the trachea to determine how much of the sound is referred. Percussion may help to differentiate LRT disease from a pneumothorax. A decrease in respiratory noise may be associated with fluid or soft tissue within the pleural space. It is worth noting that hearing apparently normal lung sounds in a dyspnoeic or tachypnoeic cat is not normal; it indicates that something is masking the sound.

- *Physical examination of cardiac function*; this includes an assessment of the heart rate and rhythm and intensity of beat, capillary refill time, mucous membrane colour, quality of peripheral pulses, position of the apex beat, presence of a cardiac thrill, presence of jugular distension, a jugular pulse and/or positive hepatojugular reflex (hepatic-jugular reflux), or presence of pulse deficits, and cardiac auscultation. The presence of a cardiac thrill, jugular distension, a jugular pulse, a positive hepatojugular reflex, or abnormalities detected on cardiac auscultation warrants a more detailed cardiac examination (see below). *It is worth noting that while cardiac disease in cats can lead to either LRT disease (pulmonary oedema), or thoracic cavity disease (pleural fluid), unlike the situation in dogs, it very rarely causes coughing.*

Examination of the Cardiovascular System: Meticulous examination of the cardiovascular system is necessary to aid in the differentiation between respiratory and cardiac causes of dyspnoea. However, it should be emphasized that there can be severe cardiac disease without abnormalities on cardiac auscultation; furthermore, primary respiratory disease can be accompanied by cardiac abnormalities.

The heart rate and rhythm should be evaluated. The position of the heart may be shifted if there is collapse of lung lobes, or if there is fluid or soft tissue within the thoracic cavity. It can therefore be useful to note whether or not the heart is in its usual position, or if the apex beat is shifted. The intensity of the heart sounds should be assessed. The heart sounds may be diminished in obese animals, but can also be decreased with emphysema, pleural or pericardial disease, or when left ventricular contractility and cardiac output are decreased. In contrast the heart sounds are increased in thin or fit animals, or in hyperdynamic states (such as anaemia, pyrexia or hyperthyroidism). Bradycardia is a very worrying finding as it typically results from either primary or secondary myocardial failure (the latter may be seen with sepsis, pancreatitis, FIP, neoplasia, etc.). Extra heart sounds may be auditable (gallop sounds). These occur due to intensification of either the third or forth heart sound (or both). Gallop sounds often indicate advanced myocardial disease or heart failure. Rapid ventricular filling generates the third heart sound, the intensity is determined by the speed at which early ventricular filling occurs. An accentuated third heart sound is commonly associated with restrictive myocardial disease, or diastolic ventricular overfilling. The forth heart sound is produced by atrial systole, and is therefore attenuated in conditions in which there is impaired ventricular relaxation, such a hypertension, hypertrophic cardiomyopathy (HCM) or hyperthyroidism. If both the third and forth heart sounds are audible, a summation gallop may be audible.

The presence and character of any murmurs should be noted. Thorough auscultation of the heart should include auscultation along the sternum because in many cats murmurs are often heard at this site. If a murmur is auscultated, the point of maximum intensity should be localised, as this may help to determine from where the murmur is arising (while this is useful in the dog, it is rarely of much use in the cats due to the close proximity of the valves in this species). The timing (systolic, diastolic, or both) and intensity of the murmur should be ascertained and a note made as to whether or not the murmur is dynamic (altering with alterations in heart rate) or static. Diastolic murmurs are rare in the cat and are most commonly associated with congenital defects (stenosis of the atrioventricular valves). Continuous murmurs are also rare in the cat; again these are typically associated with congenital abnormalities (PDA or multiple congenital abnormalities). Systolic murmurs are frequently identified. When a dynamic systolic murmur is auscultated this is frequently the result of ventricular outflow obstruction (which may be of either the left or right atrium). Unfortunately, in such cases the grade of the murmur will vary with heart rate and is therefore, not a good representation of the extent of disease.

The rhythm of the heart should be assessed. Sinus arrhythmia is not a normal finding in the cat (at least not in the clinical situation). The presence of sinus arrhythmia is suggestive of increased vagal tone, and is most common with URT obstruction, although it can also be identified with cervical disease or trauma, and is not uncommon in abdominal diseases such as gastritis or pancreatic pathology. In addition the character and nature of the peripheral pulses should be noted. If a cardiac arrhythmia is evident, the presence or absence of any pulse deficits can help to determine the cause of the arrhythmia (for example there are often multiple pulse deficits in a cat with atrial fibrillation due to the variation in ventricular filling). If the peripheral pulses are small and weak, it is likely that the cat has a reduced stroke volume, increased peripheral resistance and narrow pulse pressure (the difference between the systolic and diastolic components). Common causes of this type of pulse include left ventricular failure and hypovolaemic shock.

- *Regurgitation* may be present when disease within the thoracic cavity impedes the transit of food through the oesophagus (e.g. with mediastinal LSA). When regurgitation and coughing are seen together mixed disease is usually present, e.g. megaoesophagus resulting from mediastinal disease, with secondary aspiration pneumonia and coughing. Mediastinal disease on its own rarely causes coughing.

- *General body condition and body weight.* Cats With significant amounts of pleural fluid often have hepatic retropulsion, which can be felt as usually normal sized lived extending beyond the costal arch. Severely dyspnoeic cats often have a poor appetite and so experience a degree of weight loss. Marked weight loss is more suggestive of neoplasia, or severe systemic disease, such as congestive heart failure.

- *General physical examination:* Many intrathoracic diseases have systemic involvement. *Ocular examination* may suggest the presence of uveitis or retinitis in cases of FIP, or signs of hypertension associated with myocardial hypertrophy.

Detection of goitre may be helpful as hyperthyroid cats may develop myocardial hypertrophy. *Examination of the abdomen* may reveal a lack of contents in cases of diaphragmatic rupture or pericardioperitoneal hernia. Ascites may be present in cases of FIP, congestive heart failure, hypoproteinaemia or generalised neoplasia. Generalised or regional *lymphadenopathy* is seen most frequently in cases of neoplasia or mycobacterial infection.

FURTHER INVESTIGATIONS

Prior to undertaking further investigations, or even completing a full physical examination, it may be necessary to stabilize the patient. This can be done most simply by placing the cat in an oxygen-enriched environment (oxygen box, tent, or mask). In cases suffering from thoracic cavity disease, draining the pleural space of fluid or air may be a life-saving procedure that should be performed at this point in the investigation (see section under collection of samples).

While assessment of *serum biochemistry, haematology, and FeLV/FIV status* will help to gain an overall picture of the cat's health, they rarely lead to a definitive diagnosis. For this, radiography, and the collection of samples for cytological, histopathological, and microbiological examination, are usually required.

Serum biochemistry may on occasion be of help, suggesting a diagnosis of FIP (raised globulins and bilirubin). *Haematology* may support a diagnosis of pyothorax or pneumonia (a raised neutrophil count with a left shift, and possibly the presence of toxic changes within the neutrophils). Lymphopenia may be associated with FeLV or FIV infections, or with FIP, or indicate severe disease. Eosinophilia may be associated with 'feline asthma' or lungworm infection, or be unrelated to the thoracic disease (e.g. concomitant flea infestation). While many texts will suggest that most mediastinal LSA are FeLV positive, many clinicians do not now find this to be the case. That said, the FeLV and FIV status should be assessed as an aid to determining prognosis. Any cat found to have HCM should have its serum total T4 assessed.

Lungworm larvae *(A. abstrusus)* can be detected by *faecal examination* using Baermann floatation. Or, where available, PCR on Baermann sediment, faeces, pharyngeal swabs or BAL fluid. Alternatively, it may be more convenient to perform a therapeutic trial, using fenbendazole @ 50mg/kg/day PO for ~10 days.

Where there is a suggestion of cardiac dysfunction a more detailed *cardiac examination* should be performed. This may include ECG, thoracic radiographs, assessment of blood pressure, and echocardiography.

The CTDS mt62 Extended PCR Panel for Respiratory Pathogens can quantitatively detect: FCV, FHV-1, *Chlamydia felis*, *B. bronchiseptica*, *Mycoplasma felis* and *M. gateae*, and *A. abstrusus* – this can be run on pharyngeal swabs or BAL fluid.

Radiographic investigations:
Ideally, the investigation should include good quality dorsoventral (DV – good for cardiac detail), ventrodorsal (VD – good for pulmonary detail), and lateral views. A general anaesthetic may be helpful as it allows control of respiration, enabling radiographs to be taken at the end of inspiration. It also allows the patient to have an increased oxygen supply. If facilities are available a standing lateral radiograph can be very useful in assessing cats with pleural effusions.

Radiographs should be assessed for the integrity of the thoracic skeleton, presence of pleural or mediastinal fluid, masses or gas shadows, lung density and position, heart size and position, the presence of masses within the lung-fields, and the integrity of the diaphragm. Abdominal radiographs may be needed to assess the position of the abdominal organs, the size of the liver, and the presence of ascitic fluid.

Care should be taken when assessing thoracic radiographs since on some occasions they may show no changes, despite the presence of severe disease. This is often true of chronic bronchopulmonary disease, or pulmonary thrombosis. To assess these cases further radiography may need to be repeated at a later date. Where fluid is present radiography should be repeated after thoracocentesis.

Radiography of cats with chronic bronchopulmonary disease usually reveals a prominent bronchial pattern, with or without interstitial changes, and/or patchy alveolar infiltrates. The right middle lobe may occasionally be collapsed, presumably due to occlusion of the bronchi with mucus and debris. The lungs may appear over-inflated due to air-trapping, with flattening of the diaphragm and peripheral emphysema. In very severe cases rib fractures may be evident (typically caudal ribs, close to the spine).

Ultrasound examinations:
Ultrasound examination can be useful at detecting masses located within the thoracic fluid. It can also be used to provide guidance for fine needle aspiration (FNA) or True-Cut needle biopsy of thoracic masses, and in the assessment of cardiac function (echocardiography).

Bronchoscopy:
Where available, a small bronchoscope may enable the clinician to view the trachea and main-stem bronchi. It can be used to look for the presence of tracheal inflammation, narrowing, oedema, collapse, foreign bodies, granuloma, neoplasia, or helminths. Where the correct tools are also available foreign bodies can be removed and bronchoalveolar lavage can be directed to particular lung lobes. Cases of chronic bronchopulmonary disease may reveal erythema of the tracheal and bronchial mucosa, and/or the presence of excessive mucus/mucopurulent material within the airway.

Collection of samples:
By this stage of the investigation it should be obvious whether samples need to be collected from the LRT or the pleural space. Samples can be collected using one of a number of different methods:

Tracheal wash
Bronchio-alveolar lavage (BAL)
Bronchial mucosal biopsy
Transthoracic FNA of a soft tissue mass
Ultrasound guided True-Cut needle biopsy of a soft tissue mass
Thoracocentesis

- *Tracheal washes* can rarely be performed in conscious cats, and the technique can only sample the upper respiratory tree. The author finds this procedure stressful and unrewarding.

- *Bronchoalveolar lavage (BAL).* This technique is much more rewarding. The cat is lightly anaesthetised, and placed in sternal or lateral recumbency. Lateral recumbancy may be used when disease is predominantly one-sided, and the diseased side placed is ventrally. Where a human paediatric bronchoscope is available an endoscopically-guided BAL can be collected. When performing the technique without endoscopic guidance a narrow sterile catheter is measured against the cat's chest and marked at a level ~2/3 of the way down the chest. A canine urinary catheter or an endoscopic catheter may be used. (Note: the narrower the catheter the further down the respiratory tree it is likely to be able to reach, and the more successful the BAL is likely to be). The catheter is then introduced through the sterile endotracheal tube and advanced gently until it can be advanced no further (approximately to the level at which it was pre-marked) (catheters can sometimes get 'caught' at the tracheal bification, in which case gentle repositioning may be required). Warmed sterile saline is then flushed down the catheter (~3-10ml/cat). Very little of this first flush can usually be re-aspirated. A second and third flush/aspiration cycle are then performed. The cat's chest can be coupáged (clapped) between each flush as this helps to release cells into the saline. The second flush is generally used for microbiological culture, while the third flush is assessed cytologically. The third flush usually has the best harvest of alveolar cells. Fluid that is aspirated back should be slightly cloudy (cellular) and frothy (denoting the presence of surfactant). After performing a BAL the cat should be given oxygen enrichment for a few minutes prior to being allowed to recover from the anaesthetic. Since BAL can occasionally stimulate bronchoconstriction it is sensible to pre-medicate with a bronchodilator (e.g. terbutaline 0.01 mg/kg SQ) and in severe cases have a second emergency dose ready for use (0.01 mg/kg IV). In severe cases it may be sensible to pre-treat with terbutaline for up to 24h (0.01 mg/kg SQ q4-12h).

  There is considerable debate as to what constitutes a BAL as opposed to a tracheo-bronchial lavage. Some authors state that much higher volumes of saline are required to perform a BAL (up to 50 ml/cat!). However, the author finds this unnecessary. It is relatively easy to determine whether or not the samples contain material from the alveoli: Fluid recovered from the alveoli contains mostly alveolar macrophages, while fluid from the bronchial tree tends to contain mostly epithelial cells.

  From cats, normal BAL fluid contains: 150-450 nucleated cells/µl

60-90% macrophages
2-30% eosinophils*

Cats with bacterial bronchopneumonia usually have elevated numbers of neutrophils (which may be seen to contain engulfed bacteria), while chronic bronchopulmonary disease usually results in increased neutrophils, macrophages, hyperplastic epithelial cells, and/or excessive amounts of mucus. Cats with allergic lung disease ('feline asthma') may have raised numbers of eosinophils, mast cells, neutrophils and macrophages.
*Occasionally, normal healthy cats can have up to 85% eosinophils in BAL fluid.

- *Bronchial mucosal biopsy* can be performed with or without endoscopic guidance. It is usually achieved using endoscopic biopsy grabs. The procedure should not be undertaken without prior training as the generation of a full-thickness perforation may lead to pneumothorax and/or pyothorax. The collection of bronchial cells using an endoscopic brush is considerably less traumatic.

- *Transthoracic FNA of a soft tissue mass* can be performed with or without ultrasound guidance. When collecting FNA samples from masses in close association with the heart or major vessels, or collecting samples by *True-Cut needle biopsy*, ultrasound guidance is recommended. In both cases it is strongly advised that the patient be anaesthetized. The skin overlying the area of interest must be aseptically prepared.

- *Thoracocentesis of pleural fluid* can be easily achieved in practice. It can be used diagnostically and therapeutically. The cat is usually placed in sternal recumbency. Quiet cats generally need no sedation. Providing that the pleural fluid is not pocketed, it is usually possible to drain both sides of the chest via a unilateral approach. A reasonable area of the chest wall should be clipped and aseptically prepared. Unless the fluid is confined to just the left-side of the chest, a right-sided approach is usually made. While local anaesthetic is sometimes recommended, it is not often necessary. When used, it is generally instilled into the skin, subcutis and musculature of the 7^{th} - 8^{th} intercostal space. The location of the area is generally determined by the location and nature of the substance to be drained. Where fluid is suspected the needle is inserted 2/3 of the way down the chest wall. When a pneumothorax is suspected the needle is inserted 2/3 of the way up the chest wall. Generally, a 19-21 G needle, or butterfly-needle, is adequate. This should be attached to a 3-way tap and a 10ml syringe. The needle should be advanced while maintaining negative pressure since this alerts the clinician to the moment of entry into the pleural space. Using this technique, and including an extension set to help to reduce needle-tip movement, the risk of iatrogenic lung damage is reduced. Alternatively, an over-the-needle intravenous catheter can be used.

Treatment of samples:
BAL fluid should be assessed by culture and cytology. Pleural fluid can be assessed by these methods and a number of others, depending on its appearance.

- *Culture:* This requires a sterile container. All of the air should be removed from the container if anaerobic culture is to be performed. Ideally, all fluids should be assessed for aerobic and anaerobic bacteria, fungi and yeasts. It is very important to contact the diagnostic laboratory prior to collecting and sending the samples as special transport media may be required. Since most laboratories do not routinely look for *Mycoplasma spp.* or *B. bronchiseptica* it is important to ask them to do so as we now recognize that they are much more common infectious agents than previously thought; up to 20-25% of cats with chronic bronchopulmonary disease are found to have a *Mycoplasma spp.* infection.

- *PCR:* The CTDS mt62 Extended PCR Panel for Respiratory Pathogens can quantitatively detect: FCV, FHV-1, *Chlamydia felis*, *B. bronchiseptica*, *Mycoplasma felis* and *M. gateae*, and *A. abstrusus.*

- *Cytology*: Heparin or EDTA tubes are used for cytology. They should be processed promptly before cellular detail is lost. Where samples are to be sent away for assessment 4-6 slides should be prepared at the time of collection as preferred by the cytologist (air dried, spray fixed or fixed in alcohol). If few cells are present, the sample can be spun (200 rpm for 2-4 minutes), then smears can be made with the cell pellet. For in-house assessment Gram stain and 'Diff-Quick' are suitable stains. Cell counts can be performed on EDTA anti-coagulated samples.

- *Biochemistry*: This requires a plain tube. Fluids can be assessed for total protein level, albumin:globulin ratio (A:G), and the presence of triglycerides, cholesterol, or lactate dehydrogenase (LDH).

- *Haemorrhage:* By comparing the PCV of the fluid to that of a venous sample it is possible to determine the extent of intra-thoracic haemorrhage. Generally, if the PCV of the fluid is <5%, haemorrhage is mild, while >10% indicates significant haemorrhage.

Care should be taken when interpreting fluid collected from long-standing cases, particularly those that have been sampled previously. Inflammation can arise secondary to thoracocentesis, such that the nature of the fluid may change with time.

Differentiation of pleural fluids:
Combined with the tests detailed above, pleural fluid samples are visually assessed for colour and turbidity. From these investigations it should be possible to determine whether the fluid is a transudate, modified transudate, or exudate, whether it is septic or sterile, and whether or not there are any neoplastic cells present (Table 3). This will shorten the list of possible differential diagnoses (Table 2), and indicate which way further diagnostic investigations should be planned.

Further investigations:
- *Transudates:* Further investigation should determine the cause of any hypoproteinaemia (serum biochemistry, urinalysis), or assess cardiac function.

- *Modified transudates or exudates:*

Where neutrophils predominate;

- In *pyothorax* the fluid is an exudate. It can have a variable appearance, is often malodorous, and has a very high cell count, with degenerate neutrophils and bacteria. Haematology may reveal a neutrophilia, with a left shift. The cat should be assessed for signs of pyrexia, anorexia, etc.

- In *FIP* the exudate generally has a cell count of <10000 x 10^6/l, which consists of non-degenerate neutrophils and macrophages. The fluid is usually clear, straw coloured and viscous, with a total protein level of >35g/l, >50% of which is globulins. The A:G of the effusion is frequently < 0.4. The diagnosis may be consolidated by changes in the haematology, serum biochemistry, serology, and clinical signs (ascites, ocular changes).

- *Intra-thoracic neoplasia* may result in a modified transudate or an exudate. Most of the cells are usually non-degenerate neutrophils and macrophages, ± neoplastic cells. The total protein level, and A:G may be variable. Repeat radiography following thoracic drainage may be helpful in visualizing the mass. The mass can then be assessed by FNA.

Where neutrophils do not predominate;

- *Intra-thoracic neoplasia* may occasionally result in a modified transudate or an exudate where neoplastic cells predominate e.g. LSA.

- In *haemothorax* red blood cells predominate. The PCV and total protein are usually >25% of peripheral blood values.

- *Diaphragmatic hernia* usually result in a modified transude or exudate, with variable total protein levels and cytology.

- *Cardiac failure* usually results in a modified transude with total protein levels of <50g/l. The LDH is typically < 200U/l (compared to higher values with inflammatory fluids as see with neoplasia, FIP, pancreatitis, or pyothorax). Cytology reveals mainly macrophages and mesothelial cells.

TREATMENT OF LRT DISEASE or THORACIC DISEASE

With LRT disease the treatment will generally depend on the specific diagnosis. Pleural effusion can, at least initially, be empirically treated by thoracocentesis. While this can usually be achieved using the method described previously, occasional cases will require the placement of a thoracic drain (see later).

1. Management of bronchopulmonary disease:

The treatment of chronic bronchopulmonary disease aims at the control clinical signs rather than to achieve a cure. Therapy should be tailored to each individual case. The aims are to:

- Alter life-style
- Reverse bronchoconstriction: (β-adrenergic agonists, theophylline)
- Reduce inflammation: (corticosteroids, antibiotics, anti-serotonergics, and perhaps leukotriene receptor antagonists)

Alter life-style:

A marked improvement in the cat's well being can often be achieved by reducing its exposure to airway irritants (smoke, cat-litter, aerosol, dusty environments, sudden changes in temperature), preventing its access to drugs that can cause bronchoconstriction (β-blockers, aspirin), avoiding stressful events and, for obese cats, instigating a weight loss program.

Medical therapy:

In all cases altering the life-style is usually beneficial (see above). The first line of medical therapy is to treat any infection and give a bronchodilator. It is only if this does not work, or when the disease is more severe, that corticosteroids are added. While oral medication has previously been the main-stay of treatment, inhaled medications are now being used more widely, particularly in more complicated cases. Their major advantage is their general lack of systemic side effects. That said, it is important to remember that few medications (oral or inhaled) have been scientifically trialed in cats, and even fewer have undergone long-term studies.

Inhaled medication (approximate prices):

While the successful use of an inhaler, drug-chamber and small face mask does take a little practice by the owner and the patient, many cats do very well on inhaled medications. It is best to have the owner introduce the mask to the cat at home, rather than in the clinic, as this leads to more rapid acceptance. Introducing the mask and chamber in a non-threatening, stepwise manner is best, and the application of a small amount of the cat's favorite food to the inside of the mask may help in its acceptance. Only once the mask has been accepted should the drug be added. The AeroKat Chamber (~£75; see later for details) has been specifically designed for cats and is the preferred choice. While the Babyhaler or Paediatric Volumatic chambers from Allen & Hanburys can also be considered, they usually require higher doses of medication. (These chambers are cheaper; ~£20, but the higher drug dosages soon accumulate costs).

Suggested treatment regimens:

Mild cases: *Salbutamol* (100 micrograms (μg) metered dose inhaler [MDI] ~£9), give one dose (one puff), as needed. Bronchodilators should not be used on their own (i.e. without corticosteroids) other than in very mild cases which only require occasional medication.

Moderate cases: i.e. clinical signs are occurring on a daily basis.

Salbutamol, 1-2 doses, 2-4 times daily. As an alternative to many repeated doses of salbutamol, *Salmeterol* may provide more prolonged bronchodilation; 25 μg MDI (£40): 1-2 doses, twice daily. When using salmeterol the cat may occasionally need additional doses of salbutamol, in which case it should be given on an 'as needed' basis – up to 4 times daily.

Inhaled corticosteroids:

- *Fluticasone* has been used most frequently in cats. It is expensive, 50-250 μg MDI (~£30-120): 1-2 doses, twice daily. Many cases may be controlled with 50 μg MDI 1-2 doses, twice daily.
- *Budesonide*, like fluticasone is minimally absorbed from the lungs. Dose as for fluticasone.
- *Beclomethasone* may be considered as an alternative. 100 or 200 μg MDI (~£15): 1-2 doses, twice daily.
- *Qvar* is a form of *beclomethasone* that is currently under investigation as its smaller particle size may allow for using lower doses. 50 μg MDI (£12): 2 doses, 2-3 times daily.

It can be beneficial to use a combined inhaler as this reduces the overall number of 'puffs' the cat receives, e.g. 'Seretide' which contains 25 μg of salmeterol, plus either 50, 125 or 250 μg of fluticasone (depending on the formulation: give 1-2 puffs twice daily; most cats need only 50-125μg of fluticasone) (~£60-120). ***This provides optimal treatment for most cases, typically using Seretide 125 which contains 25 μg of salmeterol, plus 125 μg of fluticasone: give 1-2 puffs twice daily.***

The doses listed are only suggestions, and it is best to try to use as low a dose as is effective. Where more than one dose is required put one dose into the Chamber then place the mask on the cat's face for 5-10 seconds. Then repeat this for the second dose. Always give bronchodilators before corticosteroids (unless they are being given in a combined form) so that the airways are as open as possible to absorb the drugs.

Severe cases: Treat as for moderate cases (i.e. Salbutamol [1-2 doses, 2-4 times daily] or *Salmeterol* [25 μg MDI: 1-2 doses, twice daily] + inhaled steroids [1-2 doses, twice daily]). However, since inhaled steroids may take 1-2 weeks to achieve maximal effect oral steroids are also required. These can usually be reduced or discontinued once the disease is under better control, typically over 2-4 weeks. (i.e. 5mg prednisolone twice daily for 1 week, then 5mg prednisolone once daily for 1 week, then 5mg prednisolone every other day for 1 week, then stop).

Oral medication:

Where oral medication is to be used the author usually starts with a two-week trial of long-acting theophylline. If this fails to achieve sufficient control of the clinical signs, prednisolone is usually added. Where one bronchodilator (e.g. long-acting theophylline) fails to give a positive response, a different class of bronchodilator (e.g. salbutamol, or terbutaline) may be used instead. (Some authors prefer to use salbutamol or terbutaline as their first choice of treatment). Where prednisolone cannot be given (recurrent infections, intolerance, diabetes mellitus), and inhaled medication will not be tolerated, the author then tries an anti-serotonergic agent, or occasionally a leukotriene receptor antagonist.

Over-weight cats that prove hard to diet may benefit from a reduced corticosteroid dose, which may be compensated for by the inclusion of inhaled medication.

Reverse bronchoconstriction:

- **Beta $_2$ adrenergic agonists:**
  Salbutamol (Albuterol, 'Ventolin'), single dose MDI, give as required, effective within 5-10 minutes. (i.e. it is more rapidly acting when given by inhalation than PO, SQ or IM) (see above for treatment regimens). Use of high doses can result in tachycardia and muscle twitching.

  Salmeterol ('Serevent', or combined with fluticasone [see above] in 'Seretide'), is a long-term bronchodilator that takes up to 1-2 hours to take effect but lasts ~8-12 hours (see above for treatment regimens). Use of high doses can result in tachycardia and muscle twitching.

  Terbutaline ('Bricanyl') 0.625-1.25 mg PO q12h
  As with all of these drugs, this drug is not licensed for use in cats. However, it has been used frequently with few problems reported. Side effects include GI upset, weakness, tachycardia and hypotension. Care should be taken when used concurrently with corticosteroids. It is perhaps less useful than Salbutamol when either are given orally.

- **Theophylline:** *Slow release theophylline* ('Corvental-D') 20-25mg/kg PO q24h.
  Theophylline is a weak bronchodilator that also improves mucociliary transport, stabilizes mast cells, and increases the strength of respiratory muscle contractions. It has a narrow therapeutic window, with toxicity resulting in GI upset, hyperactivity, seizures, and cardiac arrhythmia. Efficacy is very dependent on formulation; Corvental-D and Theo-Dur are recommended.

- In severe or refractory cases theophylline and terbutaline may be given together as their actions can be synergistic, and they may have some anti-inflammatory actions.

- **Propentofylline** (Vivitonin) 5mg/kg PO q12h.
  This is another methyxanthine derivative, with bronchodilating effects comparable to theophylline, but a better therapeutic index. Also has anti-inflammatory effects (adenosine-potentiation), and is an antioxidant.

Reduce inflammation:

- **Corticosteroids:**
  Fluticasone propionate ('Flixitide'), *Beclomethasone bipropionate* ('Becotide','Qvar') and *Budesonide* ('Pulmicort') are available as inhaled medications. They have virtually no systemic effects (especially fluticasone and budesonide). In cats they can occasionally cause airway irritation. (See above for treatment regimens).

  Prednisolone 1-2 mg/kg PO q12h, then taper off slowly.

Corticosteroids are very effective at reducing airway inflammation, and in prolonged dosing may reduce airway hyper-responsiveness. Short-term high-dose therapy should be avoided as a rebound hyper-responsiveness may result.

- **Anti-serotonergics:** *Cyproheptadine* ('Periactin') 0.1-1.0mg/kg PO q8-24h
  Given that feline mast cells release high concentrations of serotonin, a number of clinicians have been using anti-serotonergic drugs to treat refractory cases of 'feline asthma'. While cyproheptadine has been used successfully to control a number of difficult cases, it has a considerable appetite stimulatory effect that can be unhelpful. It can also cause drowsiness and inco-ordination. This drug is not licensed for veterinary use.

- **Leukotriene receptor antagonists:** *Zafirlukast* ('Accolate') 0.5-1.0 mg/kg PO q12-24h; *Montelukast* ('Singulair') 0.25-0.5 mg/kg PO q24h. In humans, a number of other anti-inflammatory drugs have come into use, including these leukotriene receptor antagonists. However, although the author has found Zafirlukast to be useful in occasional cases of feline asthma, experimental data suggests these drugs are unlikely to give major benefits in cats. In addition, the unexplained sudden death of one of the research cats may suggest this group of drugs should be avoided. They often need to be given for four weeks before their full effect is seen. These drugs are not licensed for veterinary use.

- **Antibiotics:** Cats with chronic bronchopulmonary disease are very susceptible to opportunistic airway infections. Whenever infection is found it should be treated. Ideally, selection of antibiotics should be made on culture and sensitivity. However, empirical choices include doxycycline, penicillins, and fluoroquinolones. Treatment for 4-6 weeks is often required. Recommended treatment for mycoplasmosis is doxycycline 5mg/kg PO q12h.

- **Mucolytics:** *Bromhexine* ('Bisolvon') 3mg/cat IM/day, or 1mg/kg PO/day.
  While the author has rarely found mucolytics to be beneficial, some authors recommend them to help ease respiratory tract congestion.

Acute decompensation:
This requires very prompt intervention. It is important to keep restraint to a minimum, and increase the oxygen concentration of the air the cat is breathing (oxygen tent or box).
Rapidly acting drugs include;
Methylprednisolone Na succinate@ 50-100mg/cat SQ, IM, IV
Dexamethasone @ 0.2-2.2 mg/kg SQ, IM, IV
Terbutaline @ 0.01 mg/kg SC, IM, IV q4h (is also absorbed very rapidly PO).
Unfortunately, supply has recently become unreliable.
Aminophylline @ 5 mg/kg IV q8-12 hours (is also absorbed very rapidly PO).
This is painful when given IM or SC.

Some drugs can be administered via an inhaler or in nebulised air. Unfortunately, administration via nebulised air can result in their therapeutic concentrations taking a

longer time to be reached. However, some drugs are more effective than others when given by this route e.g. Salbutamol (two doses every 30 minutes for up to 2-4 hours) and/or Fluticasone (see above) can have beneficial effects, particularly in cats that have previously been diagnosed as asthmatic.

In severe respiratory distress;

Adrenalin	@ 0.1ml of a 1:1000 solution SC, IM, IV or via ET tube
Atropine	@ 0.015 mg/kg IV, 0.04 mg/kg SC – will block vagal bronchoconstriction and reduced bronchial secretions, but increases heart rate and can cause cardiac arrhythmia.

Unfortunately, very severe cases may be too unstable to allow a physical examination to be conducted. In these cases, it may be impossible to tell whether the cat is asthmatic, bronchoconstricted or in congestive heart failure - it is therefore not inappropriate to give a single IM injection of short-acting steroid (e.g. dexamethasone), a bronchodilator (e.g. terbutaline) and frusemide [i.e. "lasi-dexa-butaline!"].

2. Bacterial bronchopneumonia:

Treatment of bacterial bronchopneumonia usually includes a protracted course of antibiotics. Ideally, antibiotics should be selected by culture and sensitivity. Long-term treatment is often necessary, 1-4 weeks beyond clinical and radiographic resolution e.g. 4-8 weeks. Useful broad-spectrum antibiotics include amoxycillin, cephalosporins, doxycycline, trimethoprim-sulpha, and aminoglycosides. Combinations of drugs may be required to give 4-quadrent cover against unknown infectious agents; e.g. amoxicillin/clavulinate (10 mg/kg IV q8-12h; 12-25 mg/kg PO q8-12h) and marbofloxacin (2 mg/kg PO [slow IV] q24h). Although this combination is unlicenced, it can be given IV in critical patients. Where consolidation is severe consider marbofloxacin plus clindamycin or azithromycin as these all have good penetration into congested lung. Where *B. bronchiseptica* or *Mycoplasma spp.* have been detected give doxycycline, a fluroquinolones or azithromycin (this is concentrated in the lungs 200x that of the plasma so is a good choice for suitable respiratory infections). *B. bronchiseptica* and *Mycoplasma spp.* are surface dwelling infections so they may respond to nebulised gentamicin (25mg in 3-5ml saline/nebulisation). *B. bronchiseptica* from cats is generally not very sensitive to amoxicillin-clavulinate. If Toxoplasmosis is a possible differential give clindamycin (10 mg/kg IV, PO q12h) or azithromycin. Oxygen enriched environment, fluid therapy, airway humidification, bronchodilators, and daily coupáge may also be helpful. N-Acetyl cystine (NAC – 200-500mg PO or IV q12h) may help in severely inflamed lungs to remove excessive mucous and cellular debris.

3. Lungworm infection:

In mild cases supportive therapy may be sufficient. In more severe cases intervention may be needed. Treatment consists of something to kill the worms e.g. Fenbendazole @ 20-50mg/kg/day PO for 10-21 days, Broadline® (eprinomectin; Merial) or Profender® (Emodepside; Bayer) – the spot-on treatments should be repeated after 30 days. In addition to this it is advisable to give bronchodilators (see above), antibiotic cover to prevent secondary infection of the damaged lung tissue, and an anti-inflammatory dose of

glucocorticoid to reduce the inflammation that tends to arise as the cat's immune system removes the dead and dying worms. Potential alternatives to fenbendazole are Advocate (moxidectin/imidacoloprid spot-on; Bayer) which has a registered claim for treatment of *A. abstrusus* in the UK, as is Broadline. Other potential treatments include ivermectin (0.4 mg/kg SQ), abamectin (0.3 mg/kg SQ, repeated 2 weeks later), or topical emodopside/praziquental or selamectin (6mg/kg). Levamasole (25-30 mg/kg divided into 8 hourly doses and given on alternate days for 5 treatments) should be given with care as it can be toxic to cats (and tastes very bitter).

4. Thoracic drainage:

In cases of pyothorax, complete removal of the pleural fluid may only be achieved using a thoracic drain. This is achieved by placing an in-dwelling chest drain. While any soft sterile catheter of a suitable size can be used, a purpose-designed pediatric chest drain is ideal. If the catheter has only a single opening, a number of other holes can be cut along its length. Care should be taken not to make these too large, since this risks the catheter becoming kinked. The cat generally needs to be given a general anaesthetic, or sedated and locally anaesthetized. The chest is clipped and surgically prepared. A skin incision is usually made at the 8th intercostal space. The chest drain tube is then advanced though a bluntly-dissected subcutaneous tunnel using a haemostat, pushed into the chest cavity at the 6-7th intercostal space, then advanced further towards thoracic inlet. If the catheter is to remain in place it can be secured to a tape tag with a single stitch, and then sutured to the patient, usually using a secure 'Chinese finger-trap' suture. The catheter should be secured under a sterile dressing, and an Elizabethan collar fitted. The chest is lavaged daily with warm, sterile, lactated Ringers solution (10-20ml/kg). This is performed until the fluid withdrawn looks like a modified transudate. The addition of 1500 units of heparin per 100 ml of lavage solution may help reduce fibrosis, but the instillation of antibiotics has not been shown to be beneficial. The tube is removed when <2-3 ml/kg/day of effusion can be aspirated. Systemic antibiotics typically need to be given for 4-6 weeks.

Figure 1. Non - respiratory causes of dyspnoea

- Cardiovascular disease
  - Anaemia (can hide cyanosis)
  - Heart failure (output failure)
  - Hypotension (shock)
  - Polycythaemia
- Abdominal enlargement (ascites, organomegaly, pregnancy)
- Hyperthermia
- Metabolic acidosis
- Fear / anxiety / severe pain
- Respiratory muscle weakness

Figure 2. Upper respiratory tract causes of dyspnoea

Nose and pharynx

- Infectious
  - Viral: Feline herpes virus (FHV-1)
    Feline calicivirus (FCV)
    Rarely Feline Coronavirus (FCoV), *Influenza A virus*
  - Bacterial: Secondary invasion by bacteria from the oropharynx
    Bordetella bronchiseptica, *Mycoplasm* spp., Mycobacterial infections, *Streptococcus equi* subspecies *zooepidemicus*
  - Fungal: *Cryptococcus neoformans, Aspergillus spp.*
    Opportunistic saprophytes
- Inflammatory:
  - Post-viral rhinitis / chronic idiopathic rhinitis
  - Allergic rhinitis
  - Nasopharyngeal or nasonasal polyps
  - Nasopharyngeal stenosis
- Neoplasia
- Foreign body / Trauma / Dental disease
- Congenital defects

Larynx

- Paralysis / Trauma / Oedema / Polyps / Granulomata / Neoplasia

Trachea

- Infection:
  - Viral - FHV-1 / FCV
  - Bacterial - *Bordetella bronchiseptica* (‘Kennel Cough’)
  - Invasion by bacteria from the oropharynx
  - Parasitic - *Aelurostrongylus abstrusus* (Lungworm)
- Foreign body / Trauma

Figure 3. Lower respiratory tract causes of dyspnoea

- **Chronic broncho-pulmonary disease:** 'Feline asthma', chronic bronchitis, chronic broncho-pneumonia, chronic obstructive pulmonary disease (COPD), emphysema and idiopathic pulmonary fibrosis.
- **Pneumonia:**
  Infectious agents
  Viruses - feline herpes virus (FHV-1), feline calicivirus (FCV), cow pox virus, Rarely Feline Coronavirus (FCoV), *Influenza A virus*
  Bacteria - *Pasteurella multocida, Bordetella bronchiseptica, Mycoplasma spp., Escherichia coli, Mycobacterium bovis, M. microti, Streptococcus equi* subspecies *zooepidemicus*
  Parasites - *Toxoplasma gondii,* lungworm e.g. *Aelurostrongylus abstrusus, Eucoleus aerophilus* (previously *Capillaria aerophilia),* heart worm e.g. *Dirofilaria immitis*
  Inhaled or circulating toxins or irritants - lipid or food aspiration, smoke inhalation, uraemia, pancreatitis, sepsis, or potassium bromide
- Neoplasia
- Foreign bodies
- Pulmonary oedema: Congestive heart failure or non-cardiogenic pulmonary oedema (severe uraemia, pancreatitis, shock, sepsis, near-strangling, near-drowning, electrocution, smoke-inhalation, or cranial trauma).
- Pulmonary contusion (trauma)
- Pulmonary thromboembolus
- Pulmonary hypertension

Figure 4. Thoracic cavity causes of dyspnoea

- Thoracic effusions
  - Pyothorax
  - Haemothorax
  - Hydrothorax
  - Chylothorax
- Pneumothorax
- Ruptured diaphragm
- Pericardioperitoneal hernia
- Mediastinal disease
- Neoplasia
- Pneumomediastinum

Table 2. Intrathoracic causes of dyspnoea

Soft tissue density	- Cardiomegally - Enlargement of mediastinal and/or bronchial lymph nodes due to neoplasia or inflammation - Enlargement of lung lobes due of neoplasia, inflammation or torsion - Increased density of lung parenchyma due to congestion, inflammation, neoplasia, haemorrhage, fibrosis, etc. - Displacement of abdominal organs into the thoracic cavity (ruptured diaphragm) or peritoneal sac (pericardio-peritoneal hernia) - Obesity – Pickwickian Syndrome - (excess fat in and around the thoracic cavity)
Gas accumulation (pneumomediastinum or pneumothorax)	- Traumatic penetration of the thoracic wall - Rupture or tear of the pharynx, trachea or lungs - Gas-forming bacterial infection - Extension from pneumoperitoneum
Fluid accumulation (pleural fluid)	
Transudate*	- Hypoproteinaemia; glomerular disease intestinal malabsorption or protein loss severe chronic liver disease - Neoplasia - Obstruction of lymphatic drainage / lymphangectasia
Modified transudate	- Congestive heart failure - Neoplasia; obstruction of blood vessels and/or lymphatics - Lung-lobe torsion
Serosanguineous or non-purulent exudate	- Feline infectious peritonitis (FIP) - Diaphragmatic or pericardial hernia, pancreatitis - Neoplasia
Purulent exudate	- Extension of infection from elsewhere - Oesophageal perforation - Penetrating wound or migrating foreign body - Haematogenous spread
Haemorrhagic effusion	- Organ or major blood vessel rupture; associated with trauma or secondary to ruptured neoplasm - Oesophageal perforation - Bleeding disorder; warfarin poisoning, thrombocytopenia - Lung-lobe torsion - Thrombosis
Chyle	- Congestive heart failure - Ruptured or obstructed lymphatic drainage/lymphangectasia - Neoplasia

* When present for any length of time, a transudate will become modified. This is particularly true of transudates that develop slowly, such as those associated with congestive heart failure. Modified transudates are therefore more common than un-modified ones.

Table 3. Differentiation of pleural fluids

	TRANSUDATE	MODIFIED TRANSUDATE	EXUDATES	CHYLOUS EFFUSION
Clarity	Clear	Clear - cloudy	Variable	Cloudy*
Colour	Colourless to pale yellow	Yellow or pink	Variable	White to pale pink
Cell types	Predominantly mesothelial cells	Macrophages, mesothelial ± PMN ± neoplastic cells	PMN , ± macrophages, ± neoplastic cells	Predominantly small lymphocytes
Cell count $x10^6/l$	<1000	< 5000	> 5000	Variable
Protein content	< 20 g/l	20-30 g/l	>30 g/l	20-30 g/l
Specific gravity	< 1.015	1.010-1.030	> 1.018	1.010-1.030

This table is meant only as a guide. Many effusions will not fit neatly in a particular group. PMN = neutrophils.
Triglyceride levels will be increased if the fluid is chylous, but not if it is pseudochylous. Can also be differentiated from a pseudochylous effusion by performing an ether-clearance test. The addition of ether or chloroform will usually cause clearing of a chylous fluid but not a pseudochylous one. Pseudochylous effusions are rare, but may be seen with neoplasia, or occasionally infection.

AeroKat Spacers can be obtained from:

USA: Martin Foley, Vice President, Advanced Product Design,
Trudell Medical International, 725 Third Street,
London, Ontario,
Canada N5V 5G4
Phone: +1 519 455 7060 ext 2203 Fax: +1 519 455 6478
Email: MFoley@trudellmed.com www.aerokat.com

UK: Jon Slattery, Managing Director, BreathEazy Ltd
154 Worcester Road
Malvern
Worcestershire WR14 1AA, United Kingdom
Tel: +44 845 680 8975 Fax: +44 845 680 8976
E-Mail: JSlattery@Breatheazy.co.uk Web: www.breatheazy.co.uk

AeroKat is stocked by VSS Co Ltd, NVS, Centaur and Dunlops

Other helpful sites for owners and vets are:
www.felineasthma.co.uk
www.fritzthebrave.com
http://www.felineasthma.org
http://groups.yahoo.com/groups/felineasthma/

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