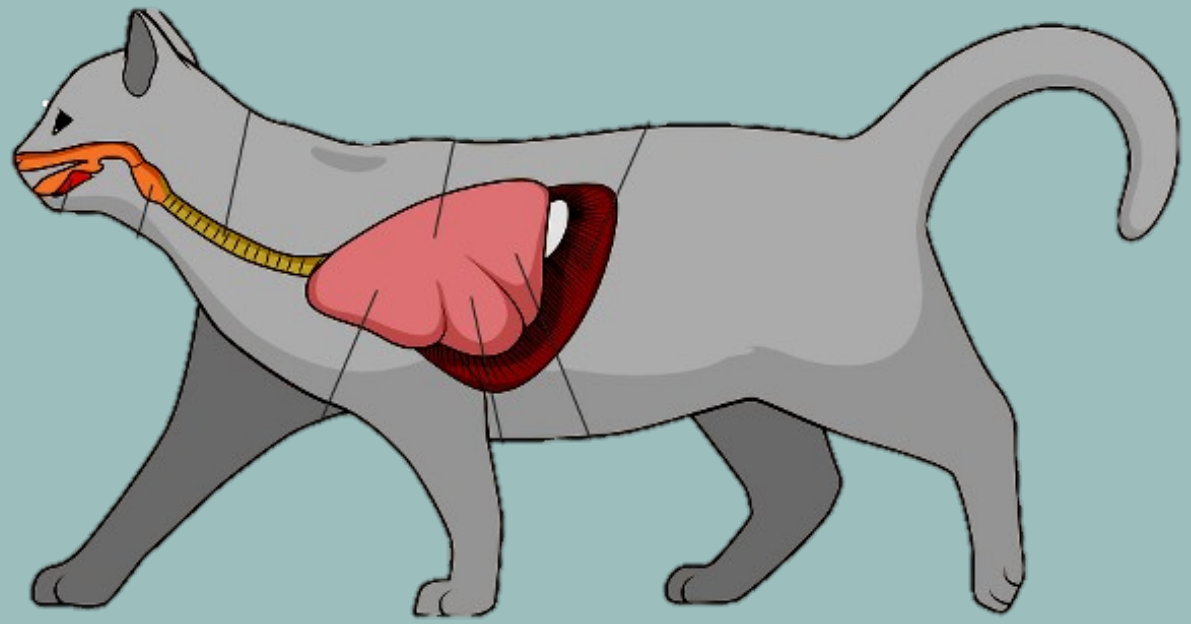
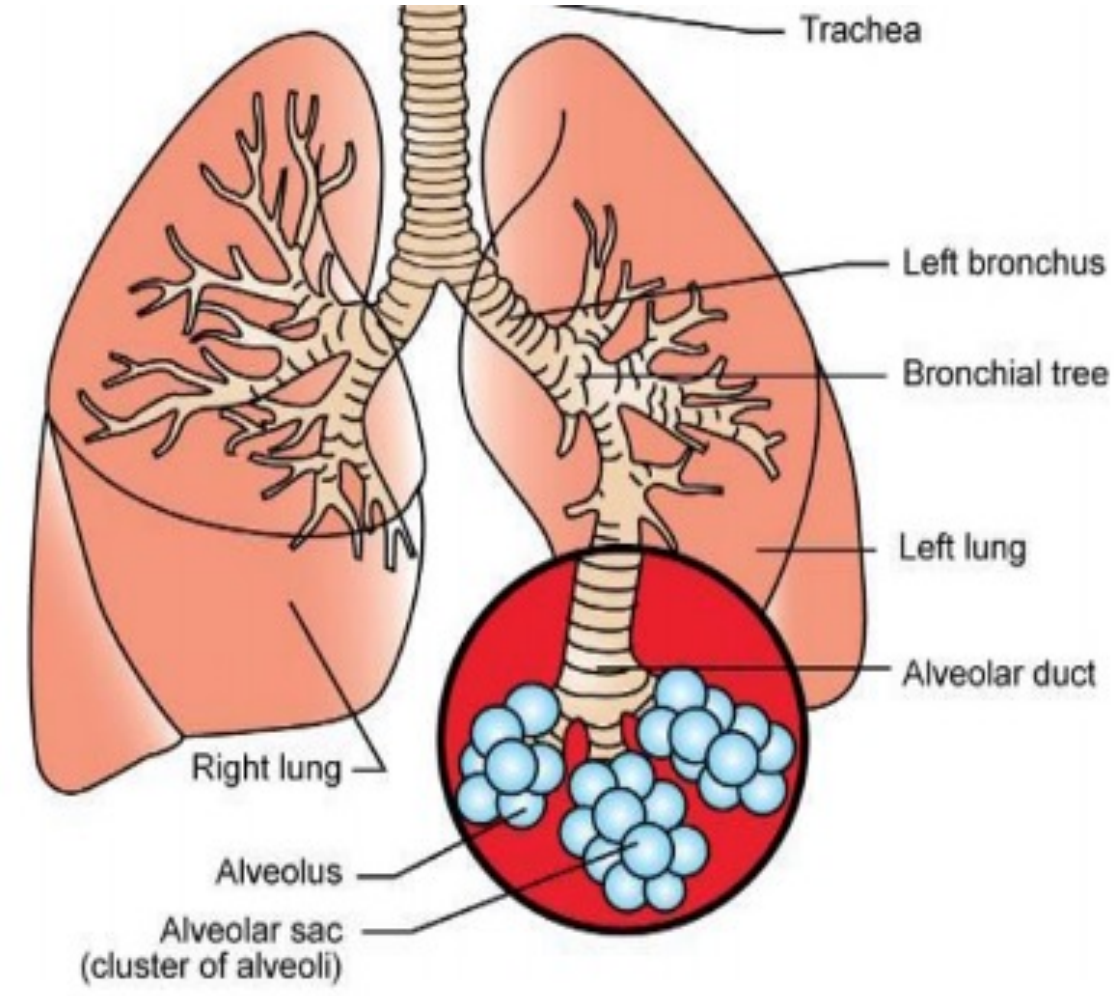


LOWER RESPIRATORY TRACT DISEASES

Carissa Tong, BVM&S, MRCVS
ECC Resident

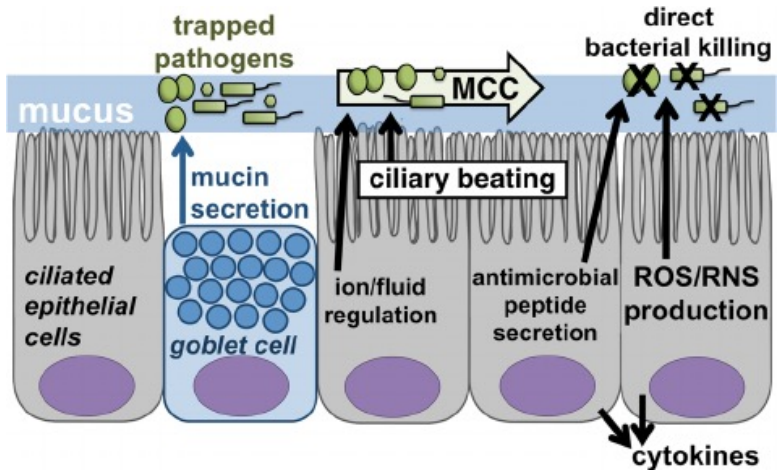
LOWER RESPIRATORY TRACT

- Intrathoracic trachea, bronchi, and pulmonary parenchyma
- Bronchi → Bronchioles, alveolar ducts → Alveoli
- Alveolar ducts end in alveoli that are arranged in sacs like brunches of grapes



NORMAL DEFENSE MECHANISMS

- Bronchi: Mucociliary escalator, antibodies, lysozymes and mucus
  - Mucociliary clearance: Unidirectional movement and removal of deposited particles and gasses dissolved in the mucus via ciliated epithelium
    - Removes particles between 5-10 microns in main bronchi
  - Bronchus-associated lymphatic tissue (BALT): Submucosal collections where lymphocytes are found in high numbers located at the corner where bronchi/bronchioles bifurcate
    - Role in priming adaptive B and T-cell responses

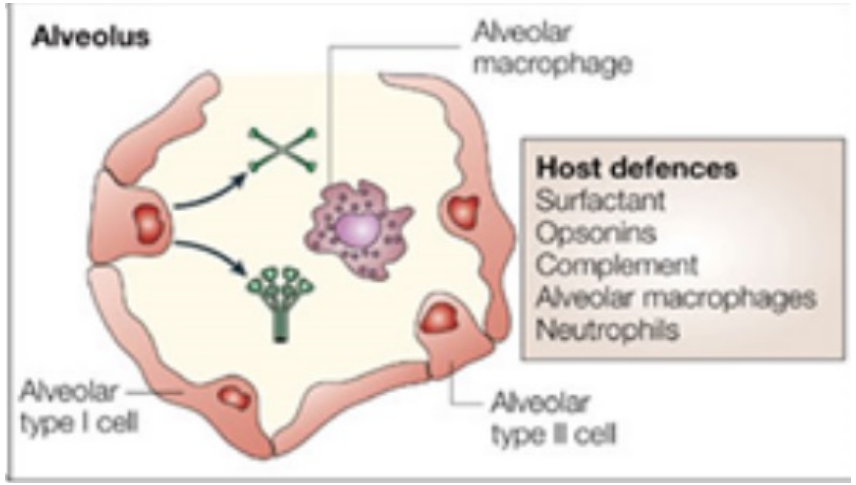


NORMAL DEFENSE MECHANISMS

- Bronchioles: Clara cells, antioxidants, lysozymes, and antibodies

NORMAL DEFENSE MECHANISMS

Alveoli: Alveolar macrophages (inhaled pathogens), intravascular macrophages (hematogenous pathogens), opsonizing antibodies, surfactant, antioxidants



COMMON CLINICAL SIGNS

- Coughing
- Tachypnea
- Dyspnea
- +/- exercise intolerance

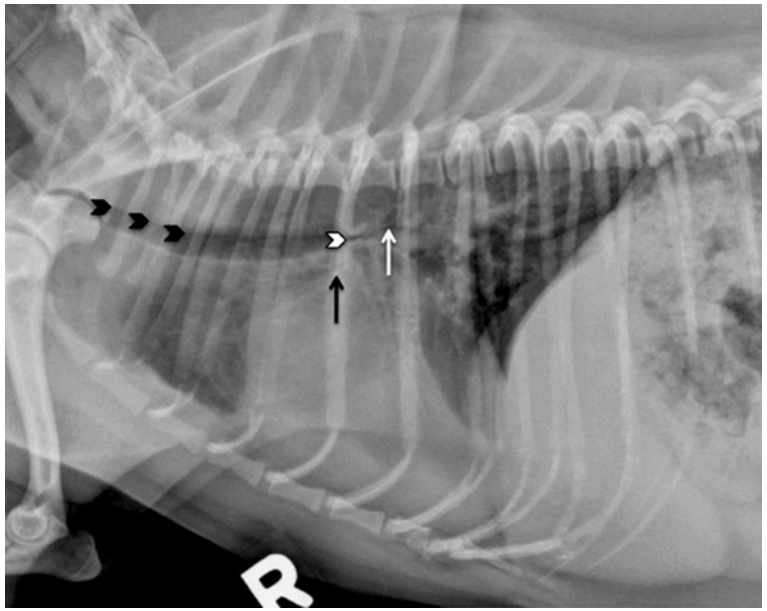
NON-INFECTIOUS DISEASES

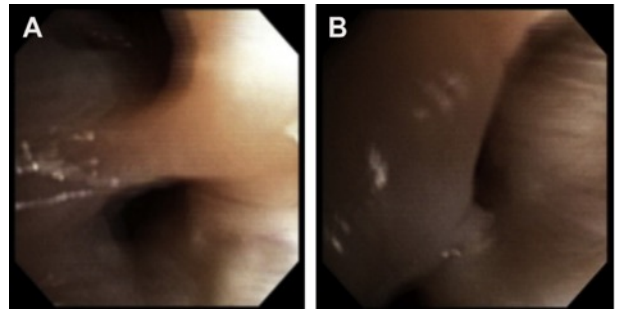
BRONCHIAL COLLAPSE

- Concurrent with tracheal collapse
- **Tracheobronchomalacia** = tracheal and principal bronchial collapse
- **Bronchomalachia** = principal bronchi and lower airway collapse only
  - Reported in 45-85% of dogs with tracheal collapse
  - 87% of dogs with BAS have left cranial lobar bronchus collapse
  - Dogs with LA enlargement can have associated left mainstem bronchi collapse
- Cause is incompletely understood and likely multifactorial
- Inspiratory and expiratory crackles with worsened expiratory effort
  - 17% of dogs have mitral regurgitation on exam

BRONCHIAL COLLAPSE

- Diagnosis
  - CXR may show mainstem bronchus narrowing
  - Fluoroscopy or bronchoscopy best to visualize
  - BAL cytology:
    - Bronchomalacia: eosinophilia or neutrophilia
    - Bronchial collapse: lymphocytosis
- Treatments
  - Bronchial stents used in a case report (Dengate 2014)
  - Bronchodilators: Theophylline
  - Anti-inflammatory steroids
  - Cough suppressants





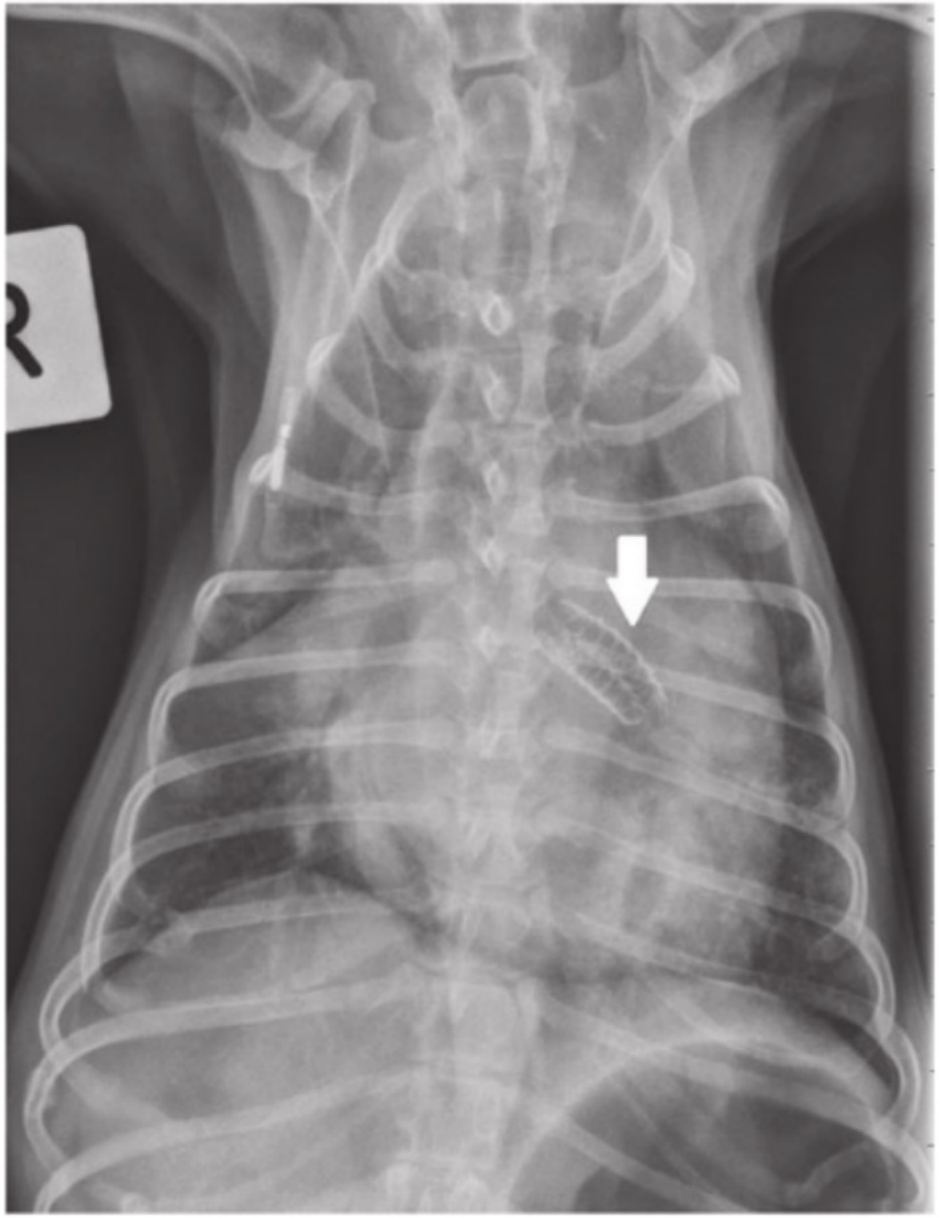


FIG 1. Dorsoventral thoracic radiograph of patient taken 30 minutes after stent placement. The stent is marked by the arrow, within the left mainstem bronchus

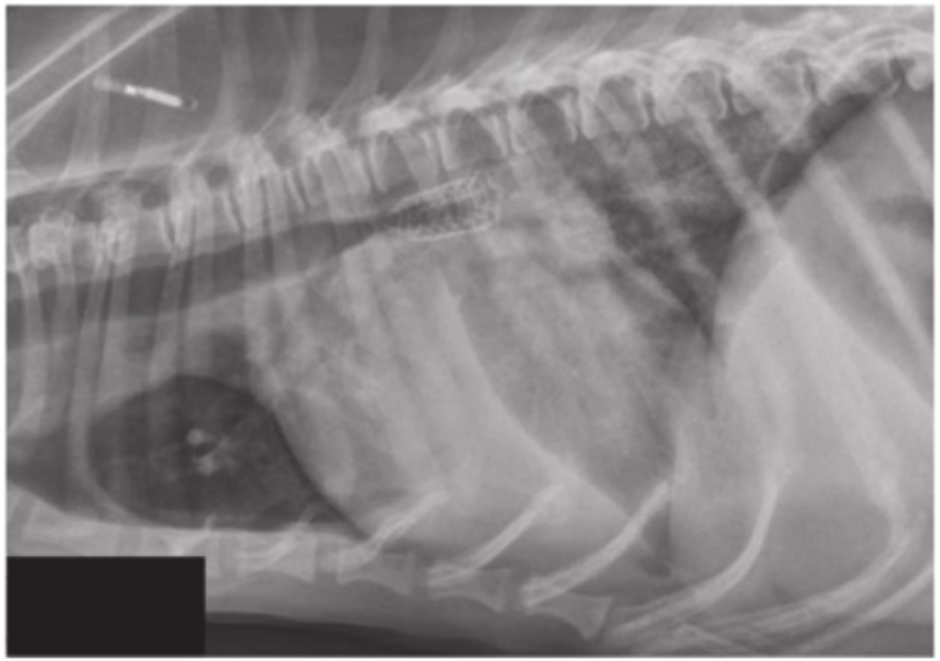
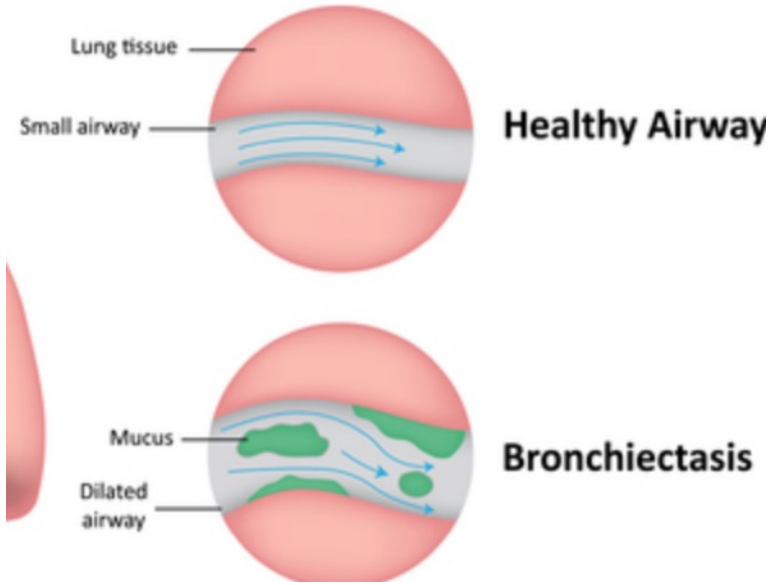


FIG 2. Lateral thoracic radiograph 30 minutes after stent placement

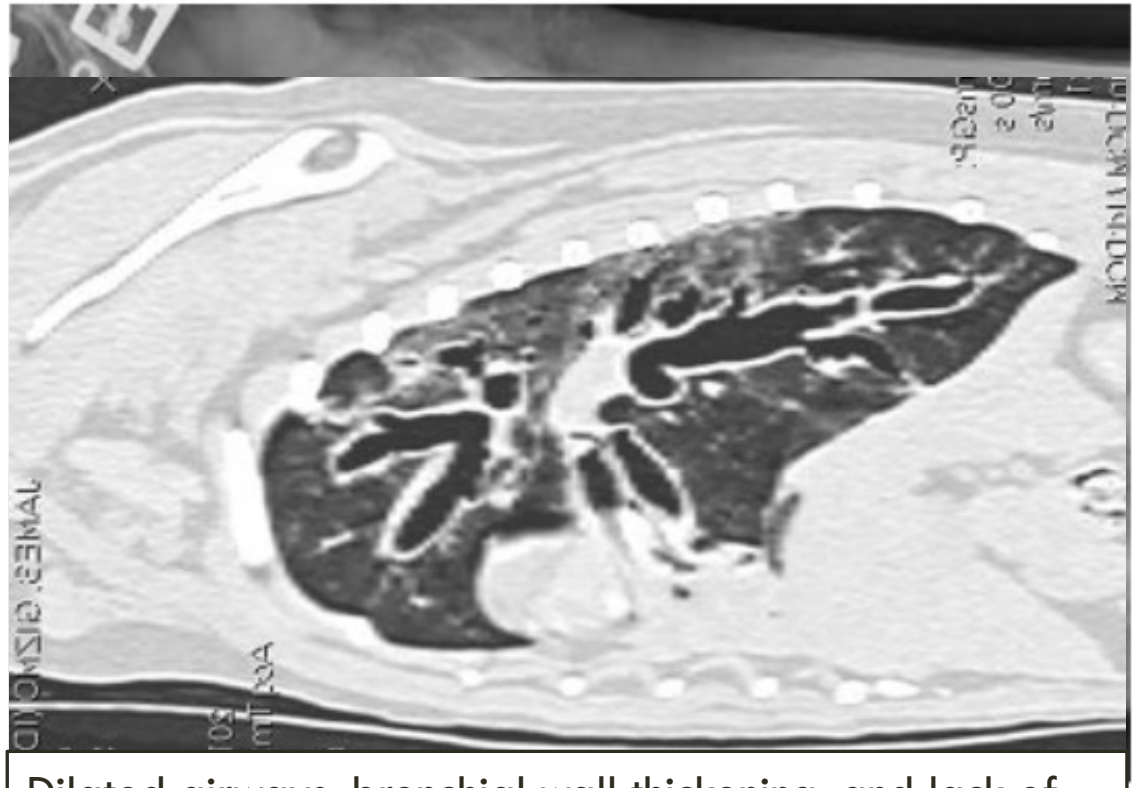
BRONCHIECTASIS



- Pathological destruction of the elastic and muscular components of the bronchial wall leading to chronic abnormal dilation and distortion of the bronchi
  - Concurrent disease in dogs: bacterial pneumonia (50%), chronic bronchitis (33%), eosinophilic lung disease (12%)
  - In cats, it is associated with FLAD
- May be congenital or may develop secondary to acquired disease, with the latter being much more common
- Dogs > cats
  - Retrievers, cocker spaniels, and standard poodles
  - Siamese cats
- No specific PE findings that characterize bronchiectasis

BRONCHIECTASIS

- Definitive dx is challenging –
  Early radiographic lesions are subtle and dilated thickened airways aren't seen easily on CXR
- CT useful to visualize dilated airways, bronchial wall thickening, and lack of peripheral airway tapering
  - BA:PA ratio should be <2, bronchiectasis usually has BA ratio>4
- Bronchoscopy allows visualization and documentation of bronchiectasis



Dilated airways, bronchial wall thickening, and lack of peripheral airway tapering.

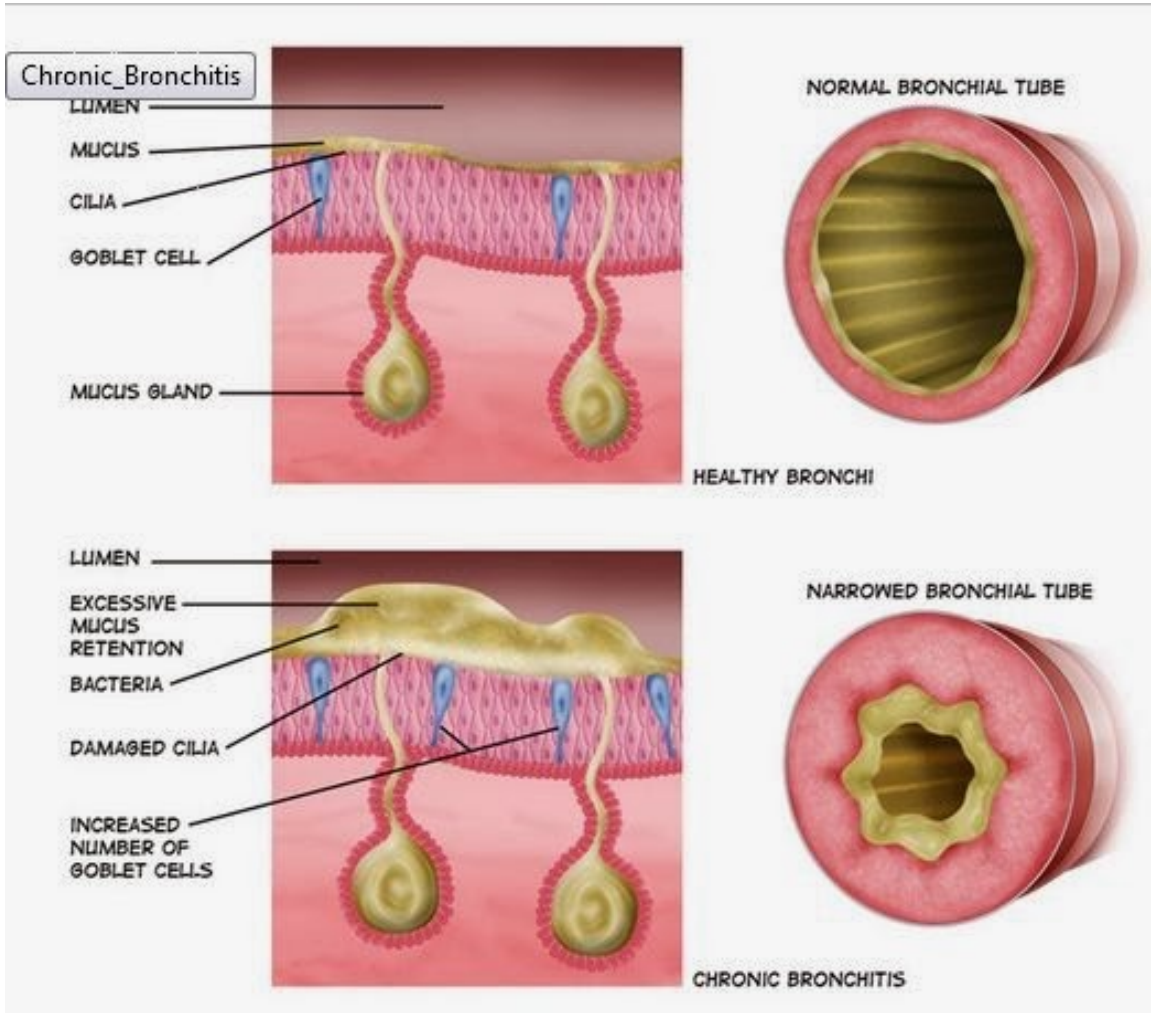
demonstrates diffuse thickening of airway walls and lack of tapering to the bronchi, indicative of bronchiectasis, particularly in the cranial lung lobe (*arrows*).

BRONCHIECTASIS

- Bronchiectasis is irreversible – goal is to control signs and slow progression
- If focal bronchiectasis is seen, surgical lobectomy can be considered
- Prognosis is variable but guarded
  - Bronchiectasis can lead to bronchopneumonia, pulmonary hemorrhage, bronchiolitis obliterans and emphysema, chronic respiratory insufficiency, and cor pulmonale
  - May develop secondary IMGN from chronic antigenic stimuli
  - Chronic ABX use increase risk of dysbiosis and antimicrobial resistance

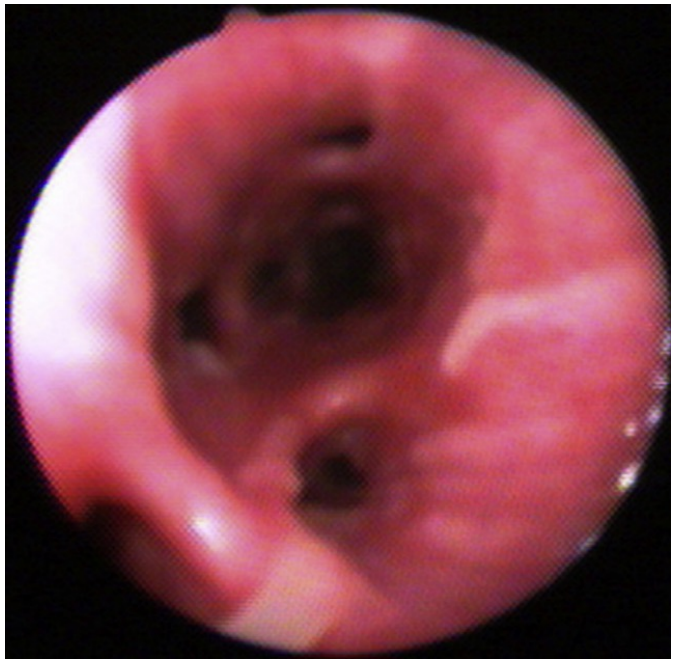
CANINE CHRONIC BRONCHITIS (CCB)

- The most common cause of chronic in mature dogs
- Defined by the presence of a daily cough that occurs for at least 2 months of the year and lack a specific cause
- Persistent infection or chronic inhalation of airborne irritants can result in sustained injury to the bronchial epithelium



CCB: PATHOPHYSIOLOGY

- Chronic inflammation stimulates metaplastic transformation of the ciliary epithelium, hyperplasia and hypertrophy of mucus-secreting glands and cells, and hyperemia and cellular infiltration of the bronchial mucosa
- Neutrophilic inflammation → Release proteases, elastases and ROS → Perpetuates inflammation and airway damage
- Results in airway narrowing:
  - Edema and cellular infiltration
  - Copious intraluminal mucus → Plugs airway
  - Localized endobronchial narrowing from fibrosis of the lamina propria and polypoid proliferations of the mucosa
  - Spasticity of bronchial smooth muscles -> Reactive airway narrowing
  - Collapse of larger bronchi due to weakening of bronchial wall



CCB: ACUTE EXACERBATION

Airway collapse

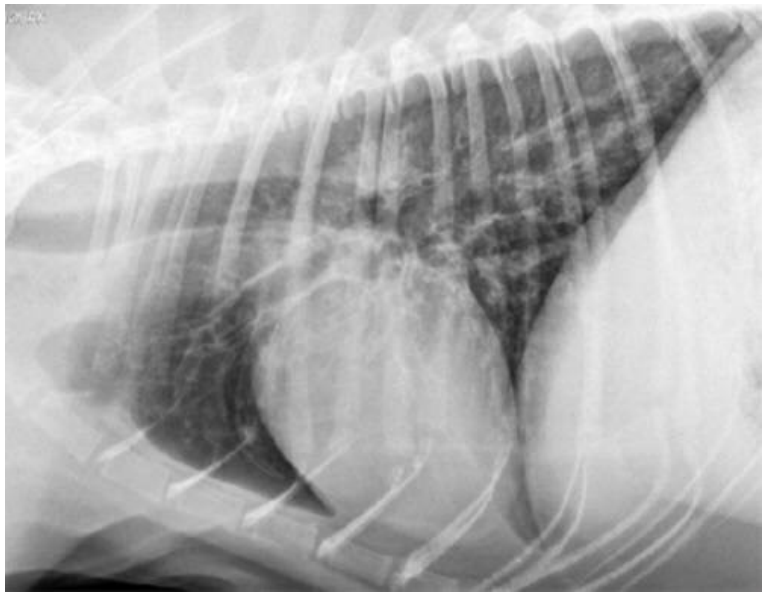
- Sustained inflammation leads to degradation of airway cartilage and loss of airway smooth muscle tone → airway collapse
- Treat with beta 2 agonists (terbutaline IM or inhaled albuterol)

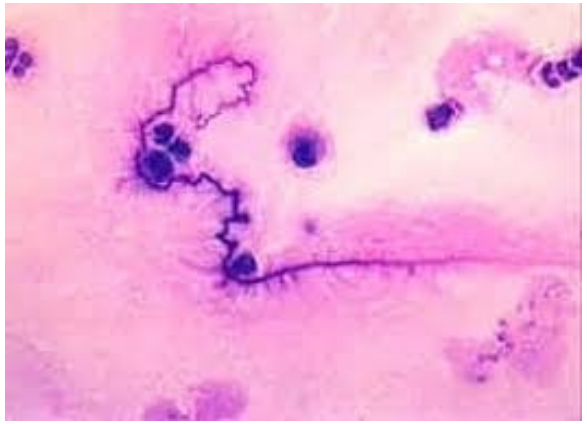
Mucus obstruction

- Hypertrophy of goblet cells and mucus hypersecretion in CCB predisposes this
- Inspissation of mucus precipitated by use of antihistamine, atropine, or diuretics
- Treatment: saline nebulization, injectable mucolytics (NAC?), consider coupage

CCB: DIAGNOSIS

- Middle aged to older, small-breed dogs, cocker spaniels
- Chronic cough, inspiratory crackles, expiratory wheeze/ snap, exercise intolerance
- CXR: Bronchial pattern, +/- hyperinflation
- CT: Bronchial wall thickness (bronchial wall:PA diameter >0.6)
- Bronchoscopy: Irregular mucosal surfaces without glistening, thickened mucosa with granular + roughened appearance, hyperemic mucosal vessels and partial collapse of bronchi during expiration
- BAL cytology: Predominantly non-degenerate neutrophilia excessive mucus and Curschmann's spirals





CCB: TREATMENTS

- Limit inflammation: Anti-inflammatory glucocorticoids
- Limit trigger: Environmental pollutants, allergens
- Maintain lean body weight
- Antitussive
- +/- Bronchodilators?
  - Active bronchoconstriction isn't a component so beta 2 agonists not as helpful
  - Consider methylxanthines (e.g. Theophylline)
- ABX if bacterial pneumonia
- Prognosis: Permanent changes are not reversible but aggressive medical management can help ameliorate signs or slow down/stop progression.

CANINE EOSINOPHILIC LUNG DISEASES

Received: 31 March 2019 | Accepted: 15 August 2019
DOI: 10.1111/jvim.15605
STANDARD ARTICLE
Journal of Veterinary Internal Medicine Open Access ACVIM American College of Veterinary Internal Medicine

Eosinophilic bronchitis, eosinophilic granuloma, and eosinophilic bronchopneumopathy in 75 dogs (2006-2016)

Lynelle R. Johnson[1] | Eric G. Johnson[2] | Sean E. Hulsebosch[1] | Jonathan D. Dear[1] | William Vernau[3]

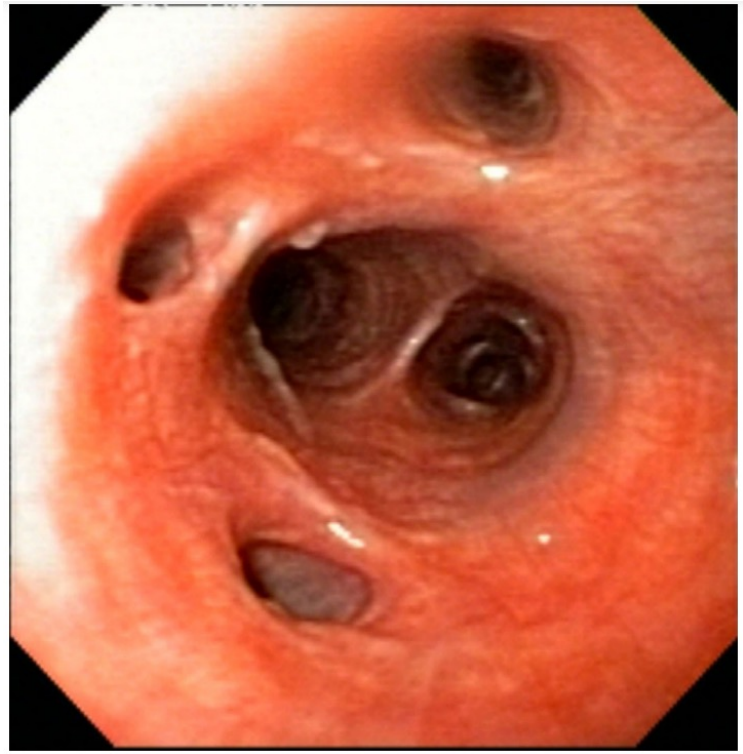
- Pulmonary hypersensitivity with eosinophil infiltration of lungs + bronchial mucosa
- Cause rarely identified – develop in response to parasitic, fungal, or neoplastic diseases or as an immunologic response to an unknown trigger
  - Some cases of EBP are considered idiopathic
- Signalment: Younger (4-6y), Siberian Huskies + Alaskan Malamute overrepresented, more females
- Often in good body condition
- Signs Coughing (90-100%), gagging and retching. Labored breathing, nasal discharge (mucopurulent, yellow-green; up to 50%),. Sometimes pruritus

CANINE EOSINOPHILIC LUNG DISEASES

- Eosinophilic bronchitis (EB)
- Eosinophilic granuloma (EG)
- Eosinophilic bronchopneumopathy (EBP)

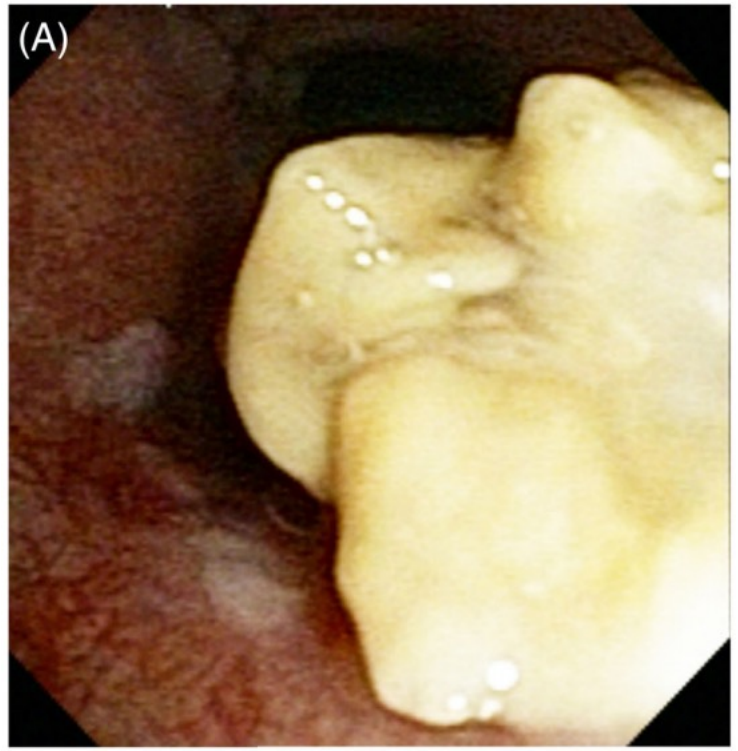
CANINE EOSINOPHILIC LUNG DISEASES

- **Eosinophilic bronchitis (EB)**
  - Normal thoracic radiographs or primarily a bronchial pattern
  - Bronchoscopy: Minimal mucosal irregularities, hyperemia alone, mild or focal mucus, and lack of airway collapse
  - Lower peripheral eosinophil count and lower eosinophil % in BAL (0-20%)
- Eosinophilic granuloma (EG)
- Eosinophilic bronchopneumopathy (EBP)



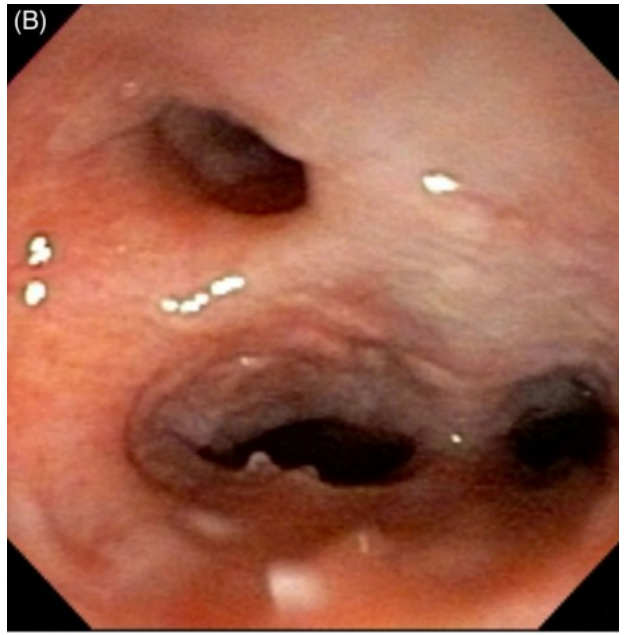
CANINE EOSINOPHILIC LUNG DISEASES

- Eosinophilic bronchitis (EB)
- **Eosinophilic granuloma (EG)**
  - Bronchoscopic evidence of intraluminal eosinophilic mass lesions plugging ≥1 airways
- Eosinophilic bronchopneumopathy (EBP)

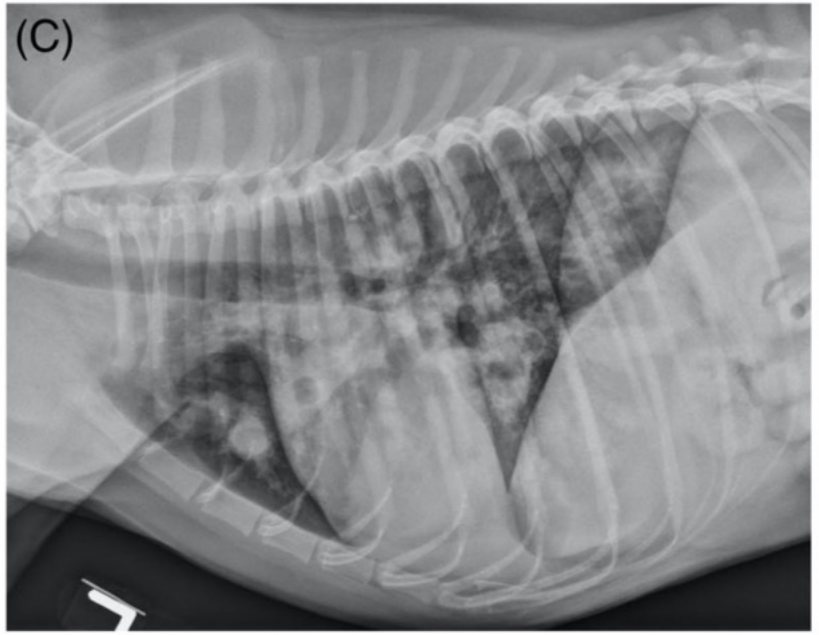


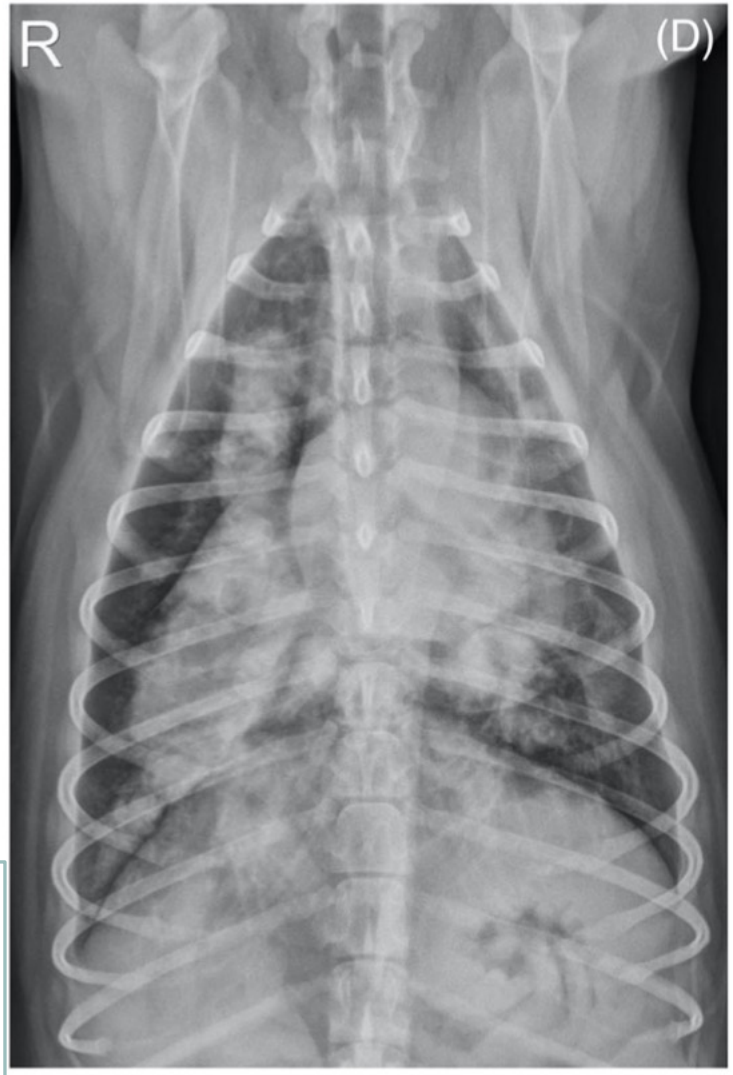
CANINE EOSINOPHILIC LUNG DISEASES

- Eosinophilic bronchitis (EB)
- Eosinophilic granuloma (EG)
- **Eosinophilic bronchopneumopathy (EBP)**
  - CXR: Diffuse, prominent, bronchial pattern
    - 40% have alveolar infiltrates
    - 26% have signs of bronchiectasis
    - 9% have hilar lymphadenopathy
  - CBC: 50% have peripheral eosinophilia and 60% have peripheral leukocytosis
  - Bronchoscopy: Abundant yellow-green mucus or mucopurulent material, thickening with irregularities or polypoid changes to mucosa, exaggerated closure of airway during expiation
  - BAL/ETW: >50% eosinophils in 87% dogs; 20-50% eosinophils in 13% dogs



Airway collapse with nodular epithelial changes





Severe bronchial pattern with bronchiectasis and, in particular, gross enlargement of the right cranial and right caudal lobar bronchi that are filled with soft tissue opacity and are tubular in shape

CANINE EOSINOPHILIC LUNG DISEASES

- For EG + EBP: Increased radiographic detection of bronchiectasis is an indicator of severity
- Treatments:
  - Glucocorticoids starting at 1 mg/kg PO q12h induction dose then try to taper down
    - Most dogs relapse once steroids is discontinued
    - May require very low dose (0.25-0.5 mg/kg PO q48h) to maintain remission
  - Inhaled glucocorticoids can be added in to help taper oral dose

FELINE LOWER AIRWAY DISEASE (FLAD)

- A group of disorder associated with airway inflammation in absence of infection that results in excessive mucus production, epithelial hyperplasia, and airway smooth muscle constriction in asthmatic form of disease
- Feline asthma and chronic bronchitis
  - Clinically very similar
  - Grotheer 2020: Not possible to differentiate the two based on age, blood eosinophilia, Cx (cough, dyspnea, abnormal auscultation findings) and radiographic findings
- Reported triggers: Scented hair sprays, clay-based litters, scented air fresheners, or cigarette smoke
- Most common cause of a chronic cough in cats
- Differentials: Heartworm-associated respiratory disease, lungworm, Toxocariasis

FELINE CHRONIC BRONCHITIS

- Infrequently associated with resp distress as bronchoconstriction isn't a component
- Associated with neutrophilic inflammation
- Etiology: results from a previous insult (e.g. infection or inhaled irritants that damaged the airway)

  Young to older cats, no gender or breed predisposition

  Majority have daily cough

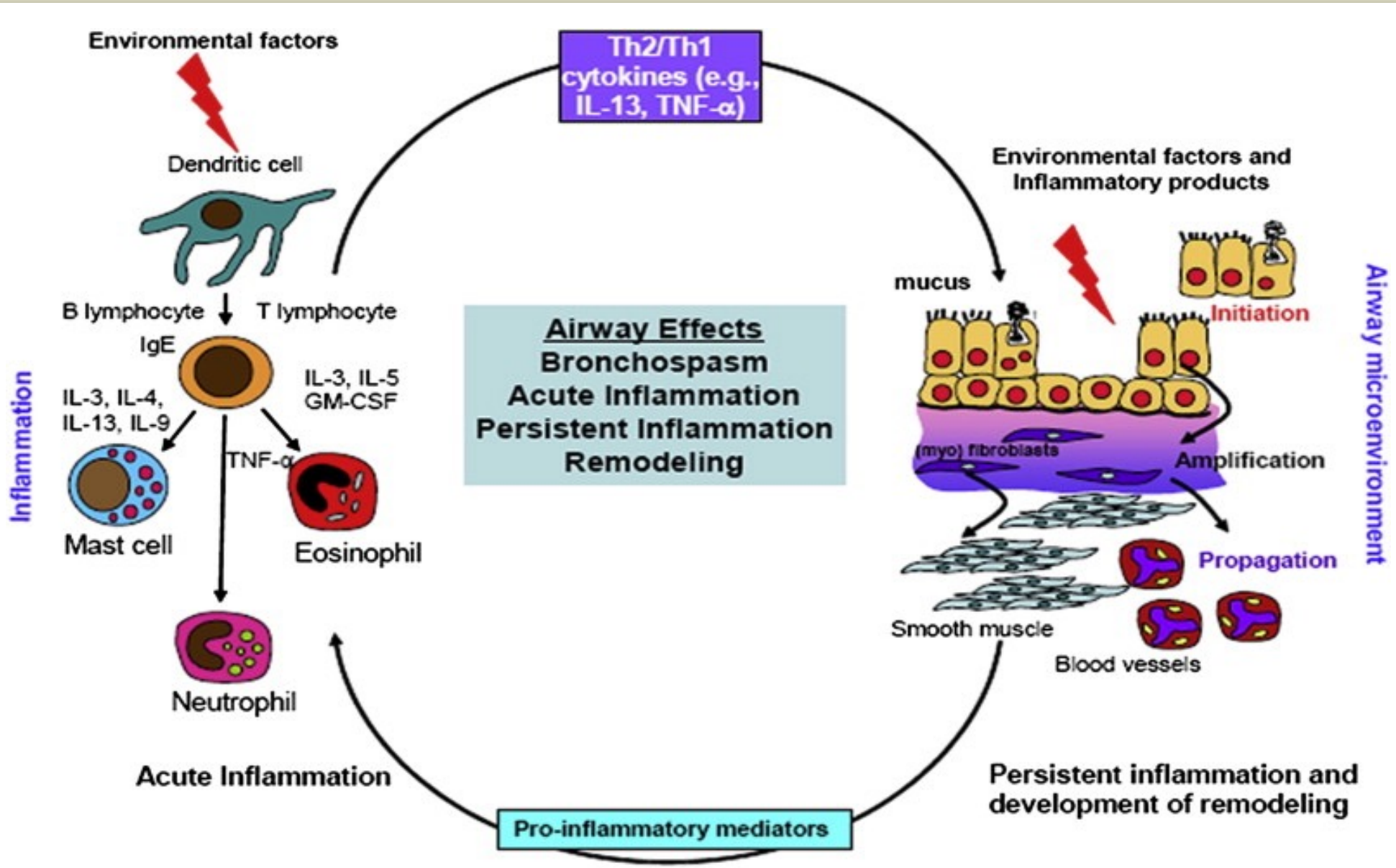
- Diagnosis:
  - CXR: Bronchial pattern
  - Airway cytology: Non-degenerate, non-septic neutrophilia)

FELINE ASTHMA

- Reversible obstructive airway disease manifesting as extensive narrowing of the airways with excessive airway mucus, resulting in respiratory distress.
- Affects 1-5% of cats
- Thought to be allergic
  - Environmental aeroallergnes: house dust mites, grass allergen, pollens
  - Predisposing factors: city/urban cats, smoking households
- 3 hallmarks:
  - Airway inflammation
  - Airway hyperresponsiveness
  - Airflow limitation (reversible)

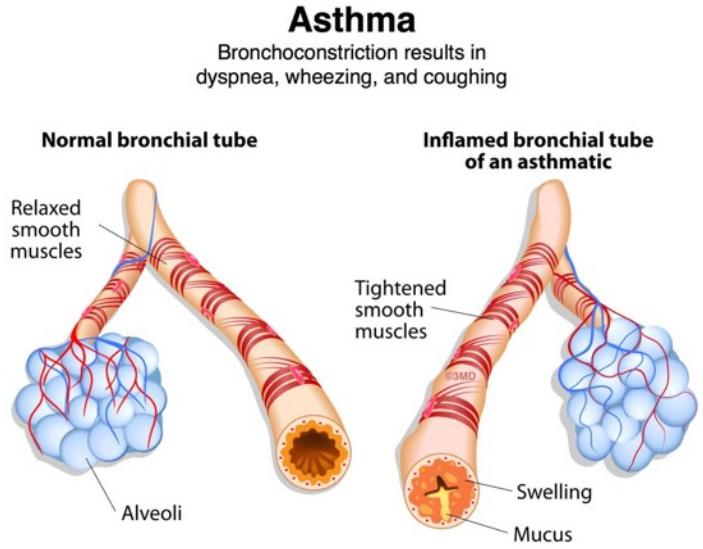
FELINE ASTHMA: PATHOPHYSIOLOGY

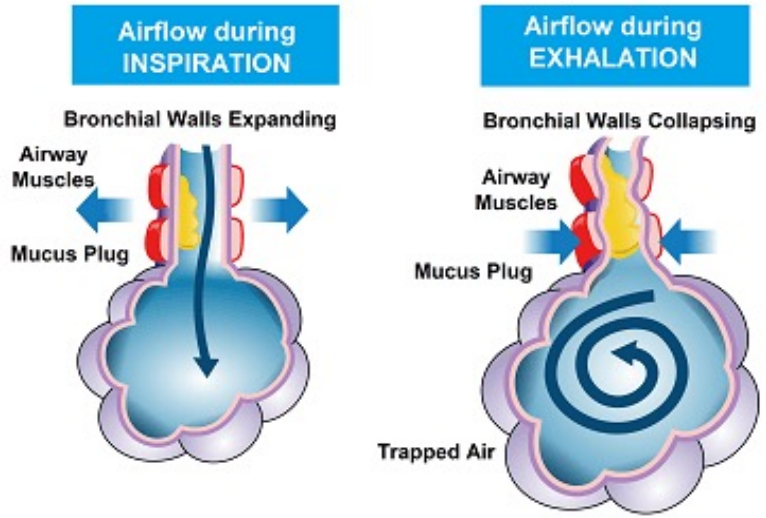
- Type 1 hypersensitivity reaction
  - Dendritic cells in resp tract engulf particle, migrate to LN and presents to TH1 cells
  - TH1/TH2 interaction results in IgE production
  - IgE binds to receptors on mast cell and basophils → Sensitization
- On re-exposure, IgE cross-linking occurs on surface of sensitized mast cells → Mast cell release histamine, leukotrienes, eosinophilic chemotactic factor, and bradykinin
  - Mast cells trigger bronchoconstriction, mucus hypersecretion, increase capillary permeability, promote granulocyte + eosinophil release
- Inflammatory mediators induce bronchoconstriction
- Late-phase inflammation (hours later via arachidonic acid pathway) lead to pulmonary mucosal edema, smooth muscle hypertrophy of bronchi and bronchioles, accumulation of secretions and airway narrowing


Environmental factors
Dendritic cell
B lymphocyte
T lymphocyte
IgE
IL-3, IL-4,
IL-13, IL-9
IL-3, IL-5
GM-CSF
TNF-α
Mast cell
Eosinophil
Neutrophil
Inflammation
Acute Inflammation
Th2/Th1
cytokines (e.g.,
IL-13, TNF-α)
Airway Effects
Bronchospasm
Acute Inflammation
Persistent Inflammation
Remodeling
Environmental factors and
Inflammatory products
mucus
Initiation
(myo) fibroblasts
Amplification
Propagation
Smooth muscle
Blood vessels
Airway microenvironment
Persistent inflammation and
development of remodeling
Pro-inflammatory mediators

FELINE ASTHMA: PATHOPHYSIOLOGY

- Mucus hypersecretion maybe due to hyperplasia and/or hypertrophy of mucus secreting cells
  - Mucus can be transported up tracheobronchial tree → mucus plug
- Expiratory phase is affected
  - Increased airflow resistance results from bronchospasm, mucus plug, and turbulent airway
  - Increased air trapping





FELINE ASTHMA

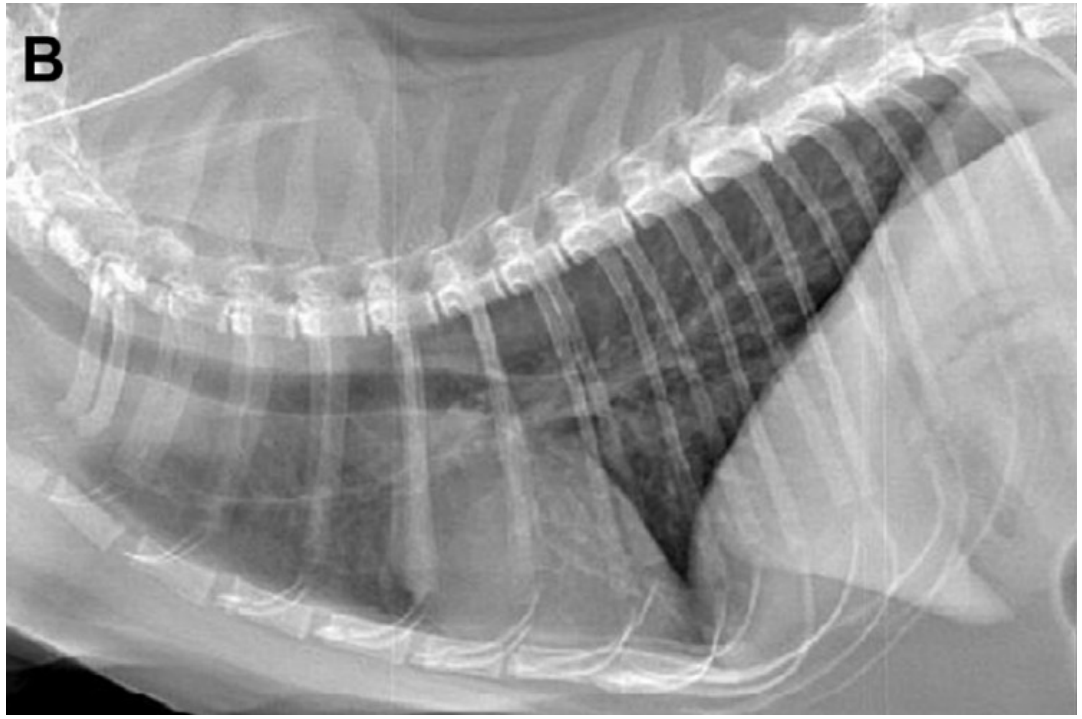
Cough, increase RE, open-mouth breathing, tachypnea, vomiting

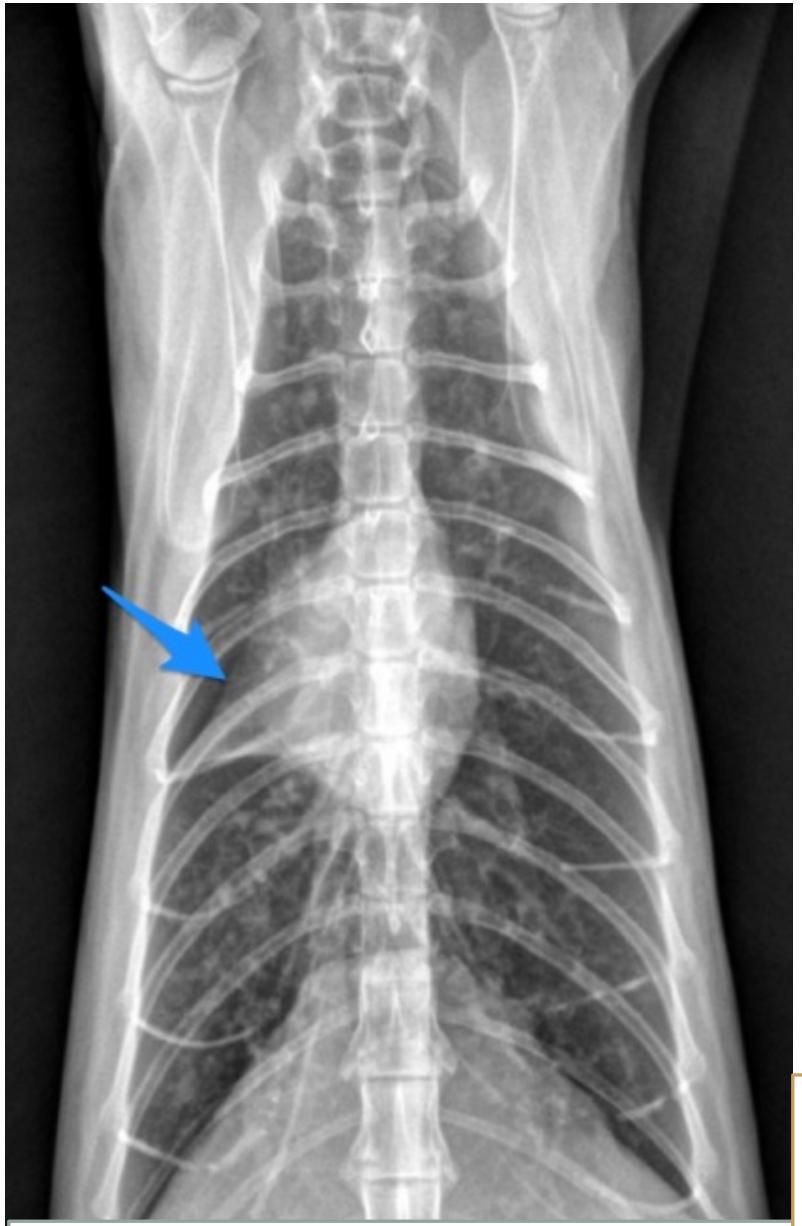
- Frequency of coughing does not equate degree of airway inflammation

- Exam findings: inducible cough on tracheal palpation, expiratory wheezes, increased abdominal push on expiration
  - Crackles, wheezes, increased breath sounds all possible
- Status asthmaticus: Acute respiratory distress due to bronchoconstriction of hyperresponsive airways
  - Open-mouth breathing
  - Peri-respiratory arrest possible

FELINE ASTHMA: DIAGNOSTICS

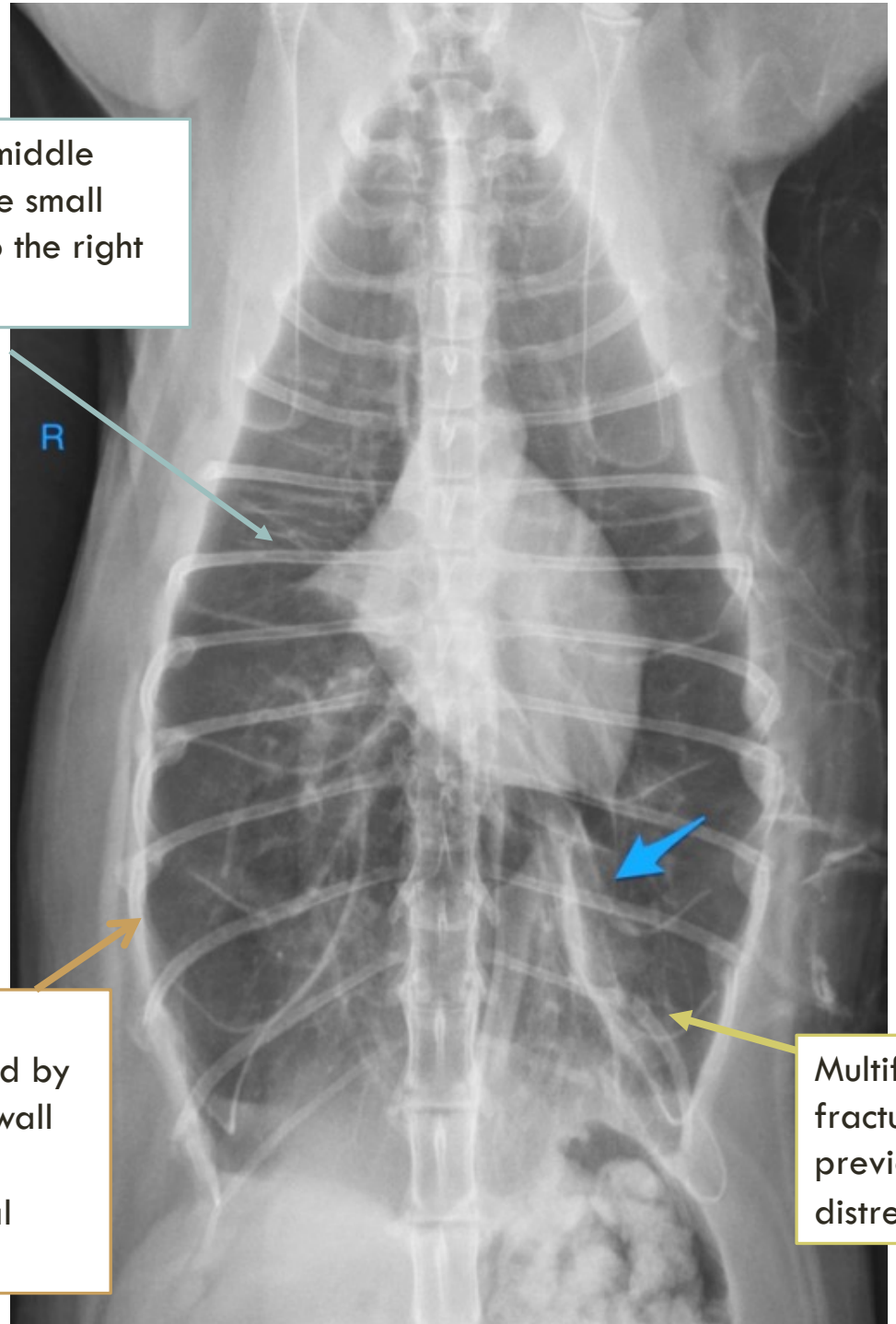
- CBC: only 9% of cats have peripheral eosinophilia in one study
- CXR: thickening of airway, flattening of diaphragm, air trapping or hyperlucency
  - 11% have an alveolar pattern/consolidation in right middle lung lobe (when a mucus plug obstructs a large airway and cause distal atelectasis)
- Bronchoscopy: Nonspecific findings – excessive mucus accumulation, stenosis of bronchial openings and nodular epithelial irregularities, airway hyperemia, airway collapse, and bronchiectasis
  - Bronchi of heathy cats are NOT sterile – bacterial culture only significant if >2000 CFU/mL in cats
- Airway cytology: >17% eosinophils





Collapse of the right middle lung lobe creating a faint triangular alveolar pattern projecting to the right of the heart (blue arrow).

The collapsed right middle lobe representing the small triangular opacity to the right of the heart



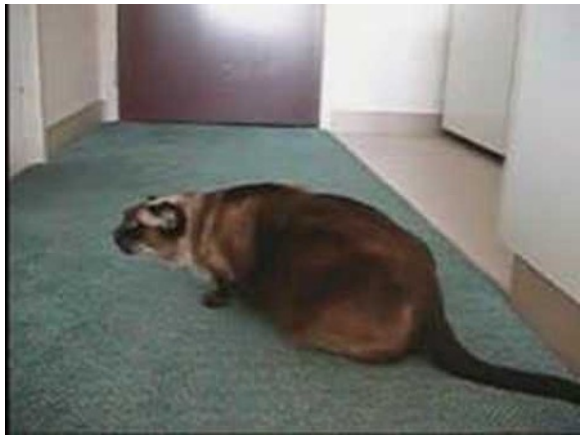
The lungs are severely hyperinflated evidenced by bellowing of the chest wall and tenting of the diaphragm at the costal attachments

Multifocal healed rib fractures likely due to previous respiratory distress.

ASTHMA VS BRONCHITIS

Parameters	Asthma	Chronic bronchitis
Age at initial dx	Young-middle, avg 4 years	Young-older
Sex	Female	Either
Breed	Any; Siamese?	Any
Cx	-Episodic resp distress w/ increase abdominal effort -Some cough daily -Some paroxysmal cough -No hx of coughing before status asthmaticus possible	-Majority of them cough daily -Resp distress occurs at end-stage disease
Resp to acute bronchodilators	Rapid, sig. decr in RR/RE is seen, d/t reversible bronchoconstriction	-Minimal since airflow obstruction tends to be permanent -Not reversible
CXR	-Bronchial to bronchointerstitial pattern -Hyperinflation: Flattening of the diaphragm, expanded lung fields, hyperlucent lungs, and increased distance from the caudal aspect of the cardiac silhouette to the diaphragm +/- collapsed right middle lung lobe, caudal rib fx +/- spontaneous pneumo -Normal CXR don't r/o LAD	-Bronchial to bronchointerstitial pattern -Less likely to see hyperinflation
Cytology from lower airway	Eosinophilic (>17%)	Predominantly neutrophils – nondegenerative and nonseptic

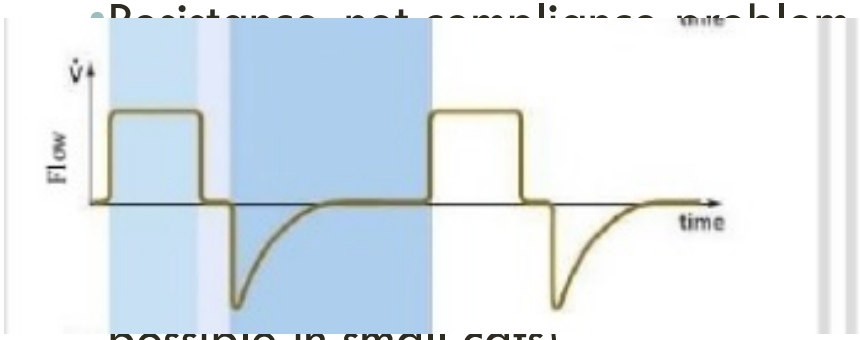
ACUTE MANAGEMENT

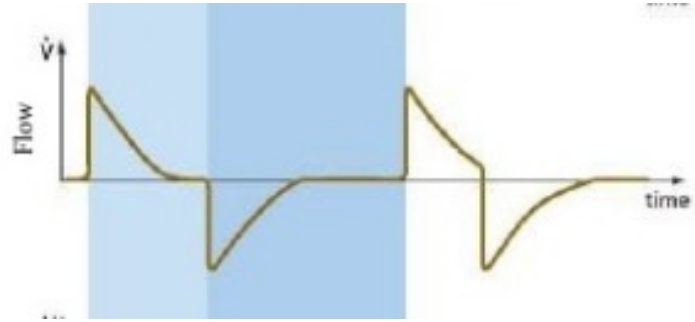


1) Oxygen supplementation
2) Minimal handling
3) Injectable beta 2 agonists
4) Anti-inflammatory steroids

FELINE ASTHMA: VENTILATION?

- Status asthmaticus – severe cases may require mechanical ventilation
- Resistance, not compliance problem





possible in small cats)

- Aim for decelerating waveform in expiration
- Aim for lower peak airway pressure – at risk of pneumothorax
- Overall survival for cats undergoing PPV is 15% (Lee 2005)

TREATMENTS NON-INFECTIOUS AIRWAY DISEASES

1) Treat inflammation with steroids
2) Treat bronchoconstriction with bronchodilator
3) Reduce cough with antitussives
4) +/- antibiotics
5) +/- anxiolytics

GLUCOCORTICOIDS

- Oral prednisolone or inhaled fluticasone
- Not recommended to start pre-scope for feline asthma as it will reduce ingress of eosinophils into the airway, changing the cytology results
- Inhaled fluticasone takes 10-14 days to reach optimal levels
  - Start oral prednisolone concurrently first 2-4 weeks, then taper off
- Injectable can be considered in dyspneic cats in the acute setting, but in repeated doses, more likely to result in adverse effects (hyperglycemia, CHF)

BRONCHODILATORS

- Reduces bronchoconstriction in acute crisis
- 2 main classes
  1) Beta-2 agonists
  2) Methylxanthines

BETA-2 AGONISTS

- MoA: Stimulation of b2 receptors causes an increase in intracellular AC and ultimately decrease intracellular [Ca2+] leading to smooth muscle relaxation of the bronchial wall
- Inhaled route have minimal systemic effects
  - Albuterol inhaler: 88 mcg/dose, 2 puffs 7-10 breaths q12h for cats
- Terbutaline 0.01 mg/kg SQ/IM
  - Quick onset (15-30min)
  - May cause transient tachycardia
  - Hypokalemia possible

METHYLXANTHINES

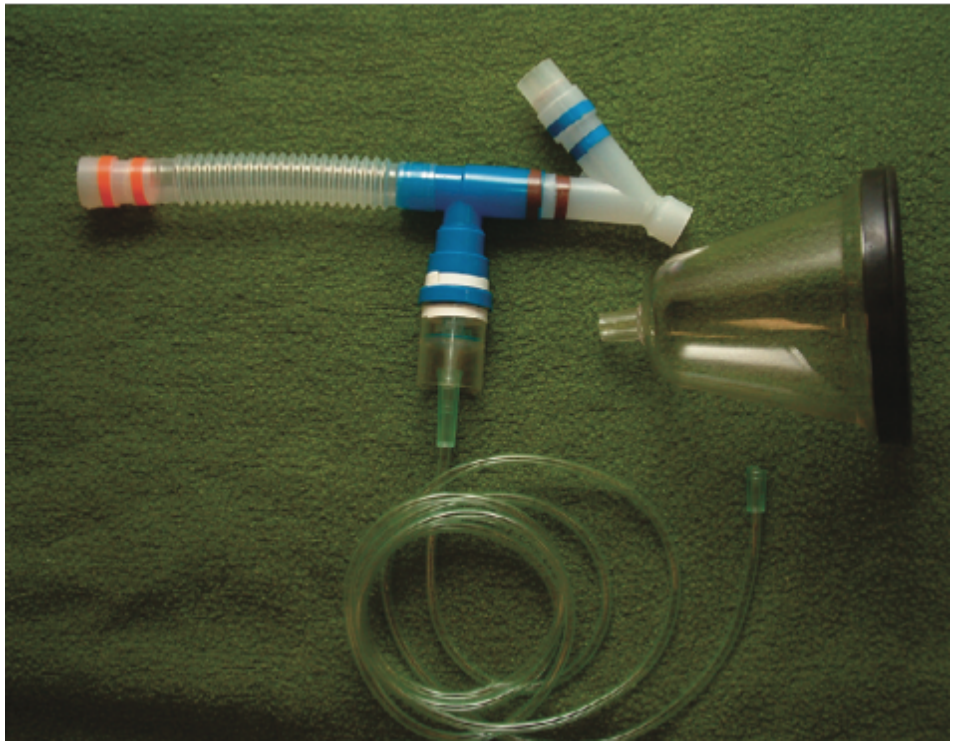
- Effects
  - Bronchodilator via PDEIII smooth muscle relaxation
  - Suppress airway response to stimuli, suspect associated w/ PDE inhibition
  - Anti-inflammatory (Unknown MoA)
  - Increase mucociliary transport speed
  - Inhibits mast cell degranulation
  - Weak chronotropic and inotropic action
  - Centrally mediated respiratory stimulation
- Injectable aminophylline or oral theophylline
- If using concurrently with fluoroquinolone, dose reduced by 30%
- Side effects: tachyarrhythmias, restlessness, CNS stimulation, increase gastric acid secretion, GI upset

ANTITUSSIVES

- Indicated in non-productive cough or chronic coughing is impacting QoL
- Opioids (hydrocodone, butorphanol, diphenoxylate) most commonly used
- MoA: Decrease responsiveness of cough center to afferent stimuli and decrease perception of peripheral irritation via mu-opioid receptors; increase mucus clearance via mu-receptor stimulation
- Diphenoxylate and hydrocodone are formulated with atropine (anti-cholinergic)
  - Mild bronchodilation
  - Decreases mucus secretion

INHALED MEDICATIONS

- Manage respiratory disease while minimizing adverse, systemic effects
- Aerosol therapy or nebulization = production of a liquid particular suspension within a carrier gas (aerosol)
- Factors determining effects:
  - Mass median diameter (MMD)
  - Rate of gravitational fall (sedimentation)
  - Tendency of particles to resist change in airflow speed and direction (inertial impaction)
  - Inherent random motion of particles created by collision with gas molecules (Brownian diffusion)



DELIVERY SYSTEMS

1) **Jet nebulizers (atomizers)**: Delivers high velocity gas that comminutes the solution in nebulizer compartment into a mist → mist travels through tubing and facemask that is attached to the patient
2) **Ultrasonic nebulizers**
3) **Metered dose inhalers (MDI)**: Plastic mouthpiece and holder attached to a sealed aerosol canister with a metered valve that releases a precisely measured dose of medication when cannister is pressed into the actuator
   - Once actuated, medication is propelled through the nozzle to form a spray
   - MDIs connected to a spacer to allow patients to breathe independently of the device

NOVEL TREATMENTS FOR ASTHMA

- Omega-3 FA
- Allergen-specific immunotherapy
- Mesenchymal stem cell therapy
- Cyclosporine
- Cyproheptadine

PARASITIC DISEASES

FELINE HEARTWORM DISEASE

- Cats are more resistance to heartworm than dogs and usually has low worm burden

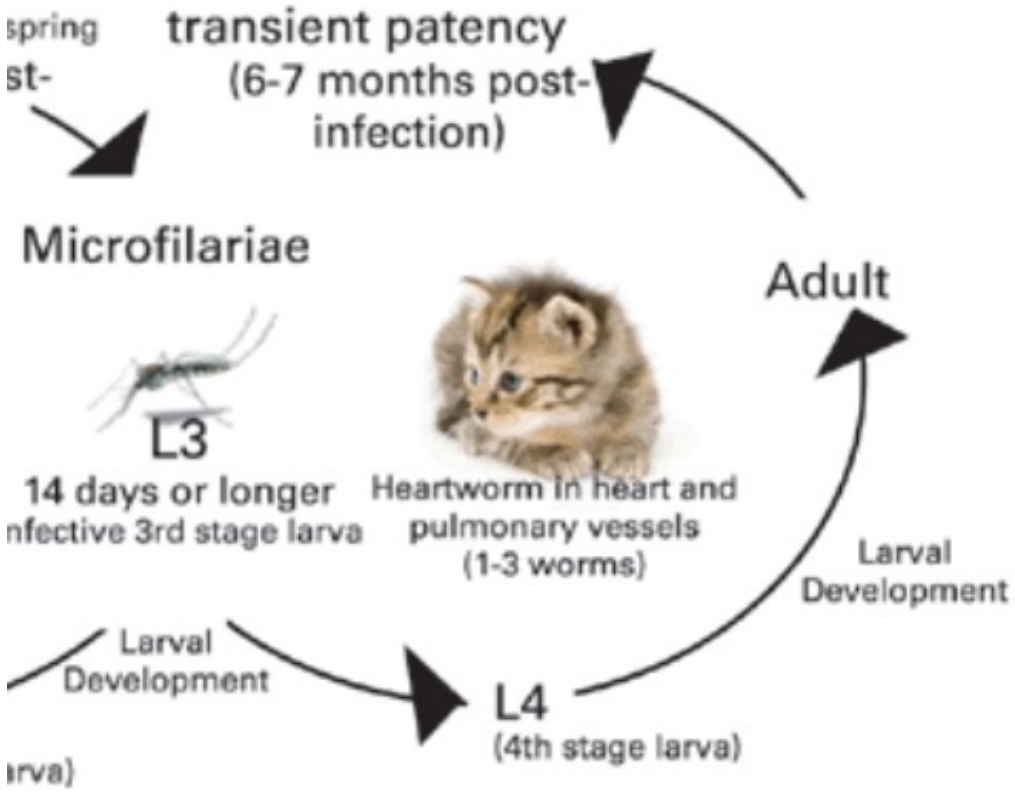
- Dyspnea, coughing, vomiting unrelated to eating but up to 28% asymptomatic

Signs present during 2 stages of disease:

1. Arrival of HW in pulmonary vasculature (3-4 months post infection) → heartworm associated respiratory disease (HARD) → Vascular, interstitial and alveolar inflammatory reaction

2. During death of adult worms → Release of heartworm debris initiating a secondary inflammatory response → fatal ALI

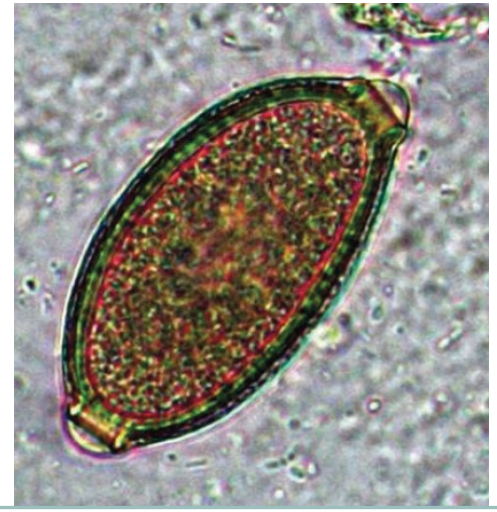
- Dx: ELISA testing more reliable



PARASITIC BRONCHITIS

- Caused by intestinal parasite migration or primary pulmonary parasites → triggers parenchymal or lower airway allergic inflammatory response
- Migratory parasites: *Toxocara canis* >>> *Ancylostoma caninum* (dog), *Atronhyloids stercoralis* (dogs + cats)
- Canine lungworm disease: *Crenosoma vulpis, Filaroides hirthi, Oslerus osleri, +/- Angiostrongylus vasorum ("French lungworm")*
- Feline lungworm disease: *Aelurostrongylus abstrusus* and *Capillaria aerophilia* >> *Troglostrongylus brevior*

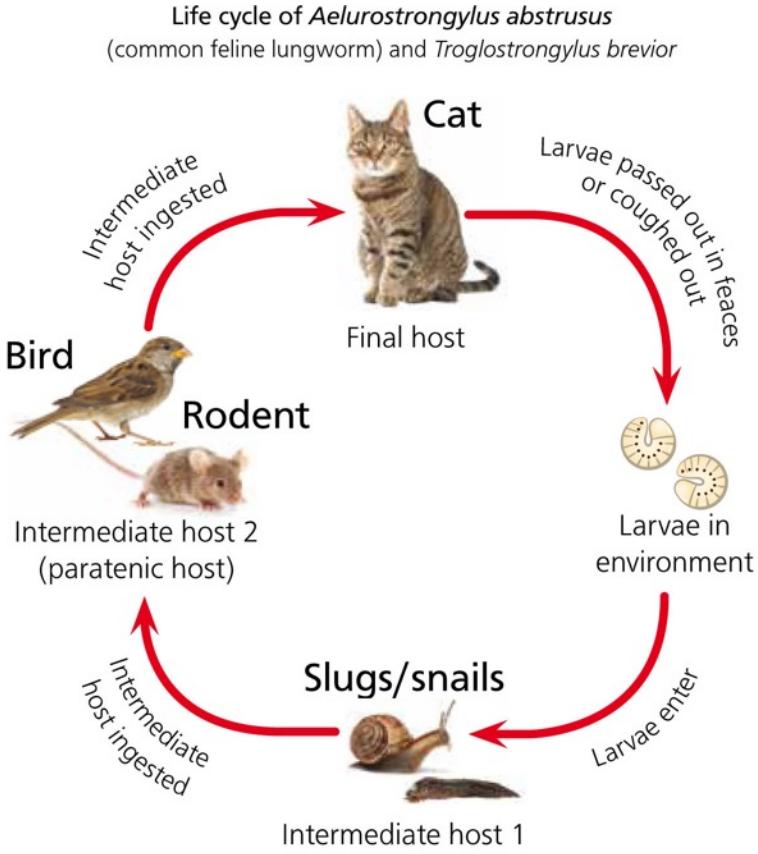
(a) Aelurostrongylus abstruse
(b) Troglostrongylus brevior



Egg of Capillaria aerophila

FELINE LUNGWORM

- Indirect life cycle
- Adult female worms lay eggs on cats → hatch into L1 and migrate and reach pharynx → coughed up and swallowed
- L1 fecally excreted into environment → develop to L3 infective stages in mollusks
- Intermediate hosts ingest infected mollusks
- Cats become infected by ingesting intermediate hosts
- Mild form with low worm burden is asymptomatic
- Clinical signs related to inflammatory response triggered by egg shed by female worms and migration of L1 along the bronchial tree, producing lesions in the alveoli, bronchioles, and local arteries



Parasite	Method of transmission	Special features	Clinical findings	Diagnosis	Treatment
Filaroides hirthi	Fecal–oral	Young dogs in confinement or kennels	Cough	L1 in feces (Baermann)	Ivermectin 1 mg/kg once weekly × 2 Albendazole 50 mg/kg BID for 5 days Fenbendazole 50 mg/kg/day for 3 weeks
Aelurostrongylus abstrusus	Ingestion of intermediate host (snail, bird, or rodent)	Outdoor cats or hunters	Cough	L1 in feces (Baermann) or tracheal wash cytology	Fenbendazole 50 mg/kg daily for 10 days
Capillaria aerophila	Ingestion of eggs or intermediate host (earthworm)			Eggs in fecal float (whipworm-like)	Fenbendazole 50 mg/kg daily for 10 days Ivermectin 0.2–0.2 µg/kg SQ for 1–2 doses
Oslerus osleri	Regurgitative feeding	Dogs exposed to wild canids?	Obstructive respirations, cough	Nodules at carina	Unknown
Crenosoma vulpis	Ingestion of intermediate host (mollusk)		Chronic cough	L1 in feces (Baermann) or BAL fluid cytology, worms in the airways or bronchial nodules	Fenbendazole 50 mg/kg/day for 7–10 days
Paragonimus kellicotti	Ingestion of crayfish	Hunters	Cough, tachypnea, pneumothorax	Large operculated egg in tracheal wash cytology or feces (sedimentation or zinc sulfate centrifugation flotation)	Praziquantel 25 mg/kg PO TID for 2–3 days Fenbendazole 50 mg/kg PO for 10–14 days
Larval migration	Perinatal	Young animals	Cough, tachypnea	Fecal flotation for ascarid eggs, eosinophilic airway wash	Fenbendazole 50 mg/kg daily for 10 days

INFECTIOUS DISEASES

CANINE INFECTIOUS RESPIRATORY DISEASE COMPLEX (CIRDC)

- Otherwise known as infectious tracheobronchitis (ITB) or kennel cough
- Acute onset contagious respiratory disease
- Dogs are more likely to develop signs the longer they're in a group-housing environment
- Signs: Paroxysmal, harsh cough; serous ocular discharge; nasal discharge +/- sneezing
- Diagnosed with respiratory panels (real-time PCR) to detect CPIV, CAV-2, CRCoV, CHV, CIV, *B. bronchiseptica* and *Mycoplasma* spp by swabbing the subconjunctival space and oropharynx
  - False -ve results are common due to transient/low-level shedding and sample degradation
- Only treat with ABX if systemically unwell and signs persistent >7-10 days

Canine Infectious Respiratory Disease

Krystle L. Reagan, DVM, PhD*, Jane E. Sykes, BVSc (Hons), PhD

Organisms	Incubation period (d)	Locations	Cx	Vaccination?
Bordetella bronchiseptica	2-6	Adhere to respiratory cilia	Asymptomatic to mild upper resp signs to severe bronchopneumonia	Parenteral inactivated; attenuated live intranasal
Mycoplasma cynos	3-10	Trachea, lung	Asymptomatic or pneumonia	No
Streptococcus equi subsp zooepidemicus	Days?	Lungs	Subclinical, mild upper resp, or severe rapidly progressing fatal hemorrhagic pneumonia	No
Canine adenovirus 2 (CAV-2)	3-6	Nonciliated bronchiolar ep cells, ep cells of upper resp tract, mucous in trachea+ bronchi, type 2 pneumocytes	Mild upper resp signs Harsh cough x2w	Attenuated live parenteral and mucosa vacc, x-protect for CAV-1
Canine distemper virus	3-6	Lymphoid + tonsil -> lymphatics	Resp signs + lethargy + neuro + GI signs	Parenteral attenuated live + recombinant vaccines *CORE*
Canine herpersvirus-1 (CHV-1)	6-10	Ep cells of upper resp mucosa	Subclinical or mild resp signs in adult; ocular changes; severe fatal disease in neonates	No
Canine influenza virus	2-4	Bronchi, bronchioles, alveoli	Variable: subclinical to severe dz + 2ry bacterial infection	Parenteral inactivated vax for H3N2, H3N8 or both
Canine parainfluenza virus (CPIV)	3-10	Respiratory ep cells	Highly contagious Upper resp signs 6-10d	Attenuated live parenteral and mucosal vaccines
Canine resp coronavirus (CRCoV)	Days?	Respiratory lymphoid tissues	Variable: subclinical to mild	
Other viruses: Canine pneumovirus, canine bocavirus, canine hepacivirus – their role in induction of dz is unclear				

BORDETELLA BRONCHISEPTICA

- Gram negative coccobacilli
- Airborne transmission, HIGHLY contagious!
- Pathogenesis:
  - Inhaled → Adhere to respiratory cilia via adhesion molecules (fimbrial adhesions, filamentous hemagglutinin, pertactin, and lipopolysaccharides)
  - It evades the host defense via virulence factors via outer capsules, O antigen (protects it from phagocytosis and complement-mediated attacks)
  - Once colonized, it alters the respiratory ep cell function → excessive mucus secretion, impairment of local innate defense → predisposes host to opportunistic infections
- Can be shed for at least 1 month but up to several months reported

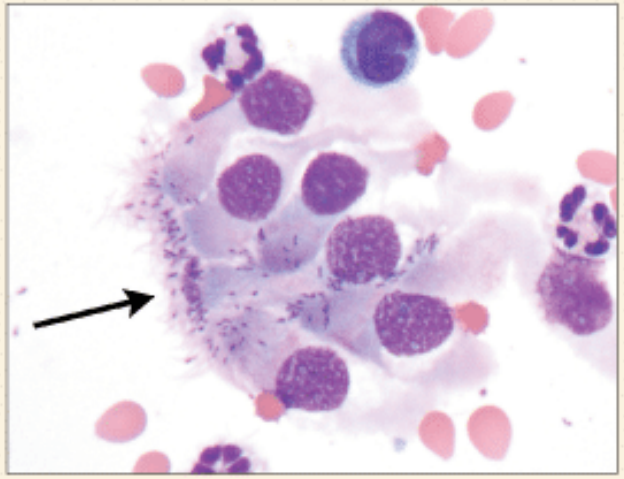


Figure 3. *Bronchoalveolar lavage fluid cytology demonstrating characteristic cytologic appearance of* Bordetella bronchiseptica*; note the adherence of the coccobacilli to the ciliated respiratory epithelial cells (100×).* Courtesy Tamara Hancock, DVM

BRONCHOPNEUMONIA

- Inflammation of the pulmonary parenchyma, arising in the bronchi or bronchioles
- 36-57% of dogs with pneumonia have a concurrent predisposing disorder
  - Impaired mobility
  - Upper airway disorders
  - Esophageal dysmotility
  - Others: Congenital abnormalities, immunocompromise, seizures, tracheostomies
- Various causes: Aspiration (SD presentation next), bacterial, viral, fungal, protozoal, parasitic

Table 22-1 Factors Predisposing to or Associated with Pneumonia in Dogs and Cats

Factor	Comment
Impaired Patient Mobility	
Unconsciousness (natural or via general anesthesia)*	Attenuation, loss of reflexes (gag, cough)
Mechanical ventilation	Natural defense mechanisms of the upper airway bypassed by intubation and mechanical ventilation; normal movement and coughing prevented
	Regurgitation or aspiration of oropharyngeal bacteria may contribute
Weakness, paresis, paralysis*	—
Upper Airway Disorders	
Laryngeal mass or foreign body*	Successful laryngeal examination possible in many/most unsedated dogs using only a bright light source (Finnoff transilluminator), especially in dogs with marked dyspnea from upper airway obstruction
Laryngeal paralysis*	
Laryngeal or pharyngeal surgery*	Aspiration pneumonia (without overt clinical signs)—a common postoperative complication in animals with laryngeal paralysis (see Chapter 23)
Regurgitation Syndromes	
Esophageal motility disorder*	Dynamic esophagram (barium swallow) required for diagnosis
	Important if other tests do not identify an underlying cause for pneumonia
Esophageal obstruction*	Foreign body sometimes visible on thoracic radiographs
	Caution necessary with barium swallow procedures (barium aspiration risk); endoscopy may be preferable
Megaesophagus*	Often identifiable on plain thoracic radiographs
Other Factors	
Bronchoesophageal fistula	Usually acquired via trauma (e.g., perforating esophageal foreign body)
Cleft palate	Congenital abnormality that may cause ingesta to enter nasal cavity with subsequent aspiration
Crowded or unclean housing	Persistence and concentration of infectious organisms in environment contributors to risk
Forceful bottle feeding*	Aspiration possible when care provider squeezes the nursing bottle during suckling or if hole in nipple is too large
Gastric intubation*	—
Immune compromise	Specific conditions: anticancer or immunosuppressive chemotherapy; concurrent illness, including feline leukemia, feline infectious peritonitis, diabetes mellitus, or hyperadrenocorticism; primary ciliary dyskinesia; immunoglobulin or leukocyte defects or deficiencies
Inadequate vaccination	Viral, bacterial, or parasitic infection with secondary opportunistic bacterial pneumonia
Induced vomiting*	—
Seizures*	Must differentiate pneumonia radiographically from noncardiogenic pulmonary edema
Tracheostomy*	—

BACTERIAL BRONCHOPNEUMONIA

- Opportunistic bacteria belonging to the normal oropharyngeal flora overcomes normal defense mechanisms
- In puppies, Bordetella most common (49%)
- Middle aged Irish wolfhounds predisposed to recurrent pneumonia and associated with focal bronchiectasis (Viitanen 2019)
- Mycoplasma is most commonly cultured from BAL in cats (Dear 2021)

Bacteria commonly isolated from canine patients with pneumonia

Organism	Isolates
B. bronchiseptica	22-71%
E. coli	11-51%
Klebsiella pneumoniae	2-25%
Pasteurella spp	3-21%
Mycoplasma spp	30-70%
Streptococcus spp	6-21%
Staphylococcus spp	7-20%
Anaerobes	5-17%
Enterococcus spp	4-11%

VIRAL PNEUMONIA

- Induces inflammation of respiratory epithelium + parenchyma and immunosuppression
- Creates ideal environment for secondary bacterial colonization
- CIRDC most common in dogs
- Feline herpesvirus-1 or calicivirus most common in cats

LIPID PNEUMONIA

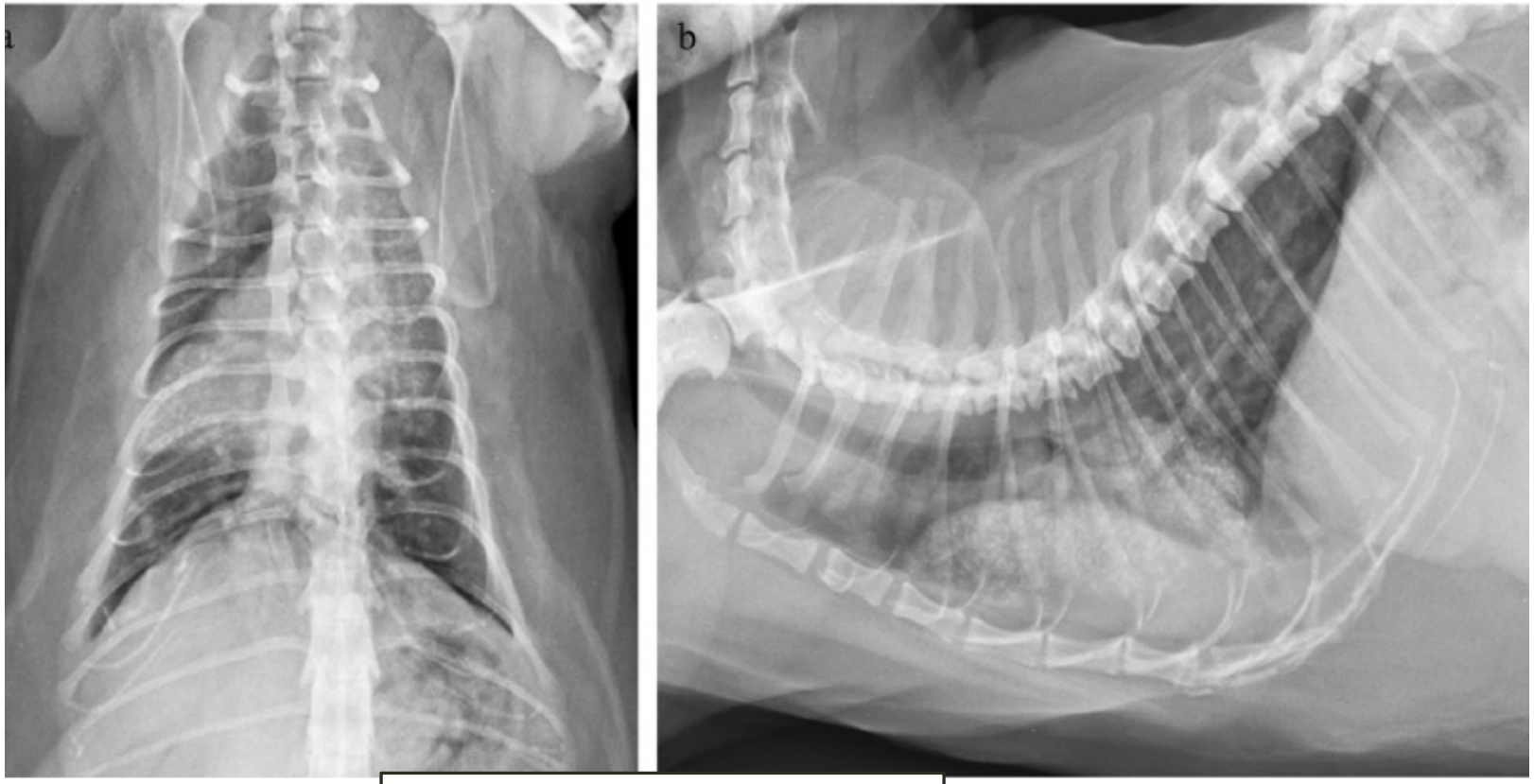
- Characterized by intra-alveolar lipid and lipid-laden macrophages in the alveoli
- **Exogenous** lipoid pneumonia is caused by a chronic FB rection to fatty substances in the alveoli, e.g. after aspirating laxative mineral oils
  - Technically a type of aspiration pneumonia
  - One recent feline case series (Mallol 2019): Dystrophic mineralization occurred secondary to chronic history of constipation and "forced fed" oral mineral oil
- **Endogenous** lipoid pneumonia (EnLP) is caused by pneumocyte injury leading to alveolar lipid deposition.
  - Most commonly associated with obstructive pulmonary neoplasia or other types of obstructive pulmonary disease
  - Others: parasitic lung disease, heartworm disease, plant material aspiration, some idiopathic
  - One recent case report in dogs (Perez-Accino 2020) and one older study in cats (Jones 2000)

ENDOGENOUS LIPOID PNEUMONIA (ENLP)

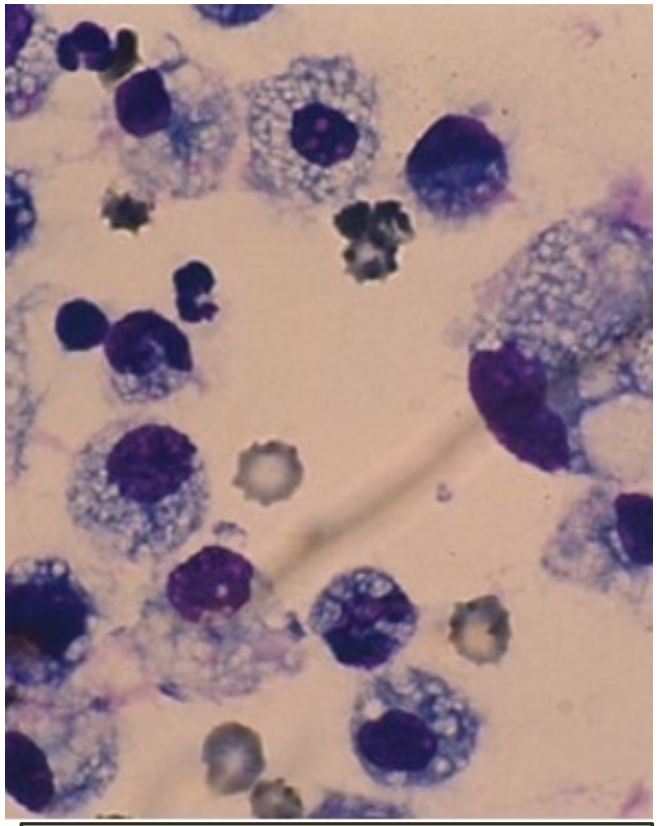
- Pneumocyte injury leads to cellular degeneration → Release of membrane cholesterol and cholesterol esters and proliferation of type II pneumocytes → Overproduction of surfactant with a high cholesterol content.
- Lipids are then phagocytosed by macrophages → Classic histologic pattern of alveoli filled with foamy macrophages, incites an inflammatory response

The mainstay of therapy for EnLP is to treat the underlying cause

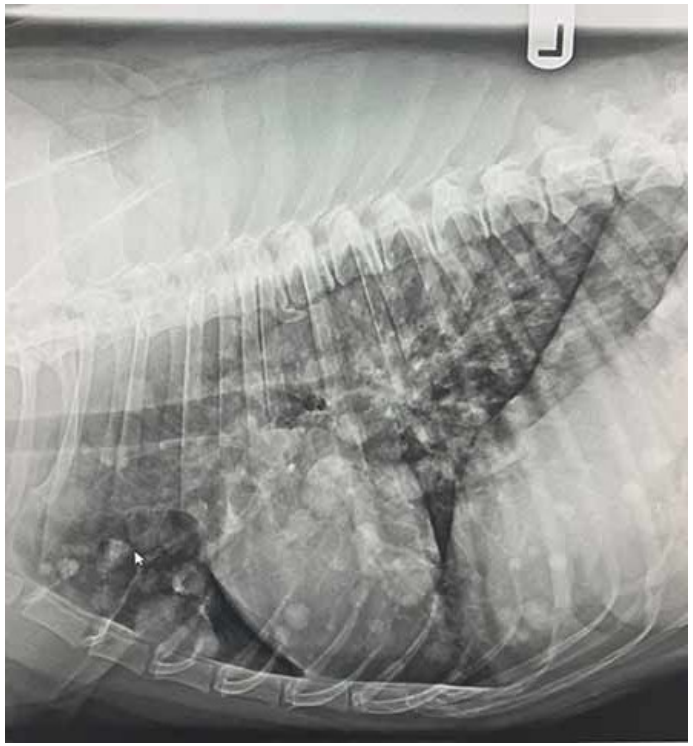
- If localized, consider lobectomy
- "Treat" the underlying neoplasia
- Prednisone/prednisolone used in people

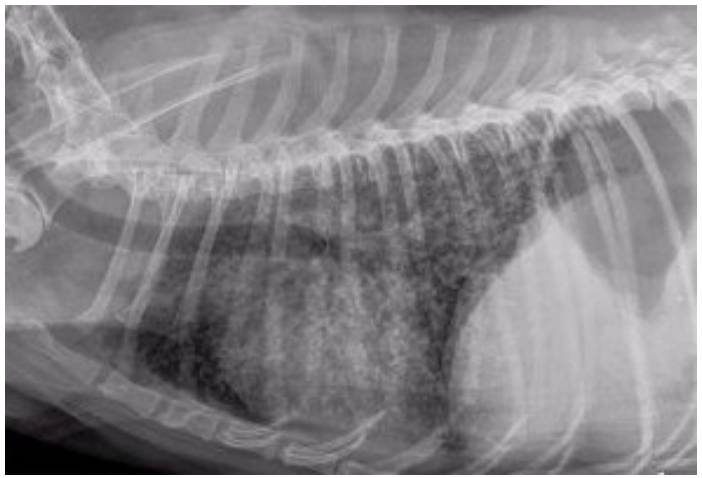


Mineralised ‘sponge-like’ pattern



Activated macrophages with lipid droplets within the cytoplasm



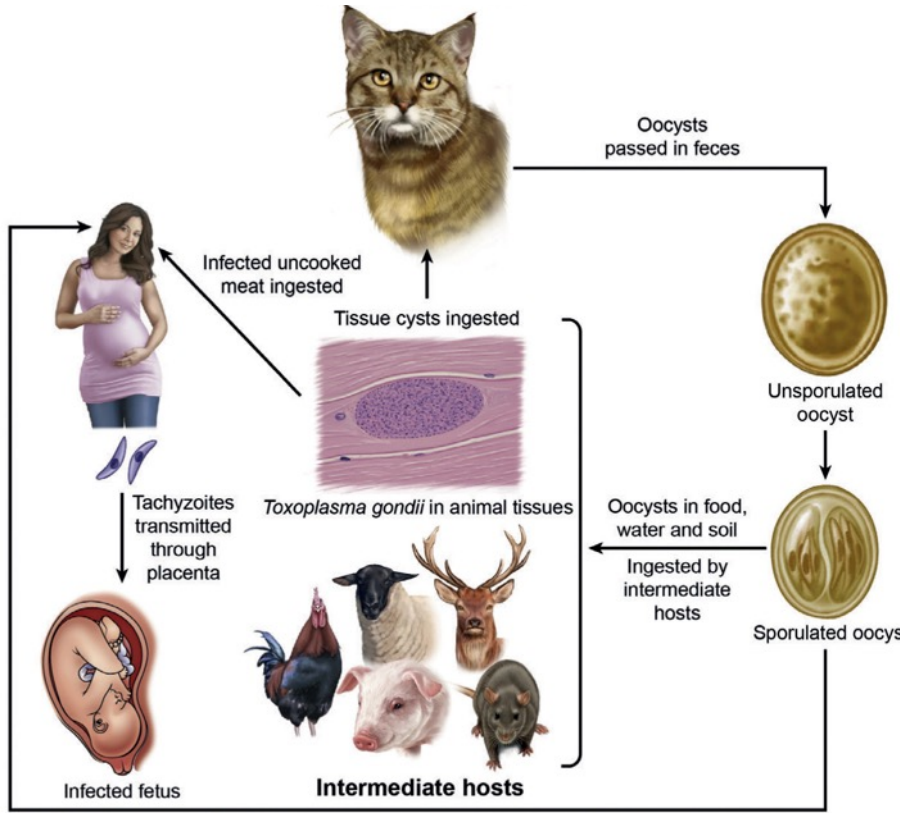


FUNGAL PNEUMONIA

- Fungal pneumonia: Aspergillus, Histoplasma, Blastomyces, Coccidioides, Cryptococcus (refer to previous BR)
- Inhalation of air-borne fungal spores most common
- Cats: Crypto > histo > blasto
- Dogs: Aspergillosis in mesocephalic + dolichocephalic dogs more common

TOXOPLASMA PNEUMONIA

- Toxoplasma gondii
  - Obligate intracellular coccidian
  - 3 stages: oocyst, tachyzoites, bradyzoites
  - Transmitted via ingestion of feces or water/tissue containing tachyzoites or bradyzoites
- Cats are definitive host
- More severe infection if transplacentally infected kittens
  - Jepatitis or cholangiohepatitis, pneumonia, and encephalitis
- Pneumonia (98%) is the main sign of generalized toxoplasmosis
- Other signs: CNS, ocular (uveitis, choreioretinitis), GI upset, cholangitis, lymphadenopathy



TOXOPLASMA PNEUMONIA

- CXR: Diffuse bronchointerstitial, patchy alveolar pattern +/- pleural effusion
- Diagnose via serology to detect IgG and IgM
  - **IgM**: Titre > 1:64 indicates recent or active infection
  - IgG: A ≥ 4-fold increase in titers in paired serum samples taken 2–4 weeks apart indicates recent or active infection
- Tx: Clindamycin x 4 weeks minimum

GENERAL POINTS ABOUT PNEUMONIA

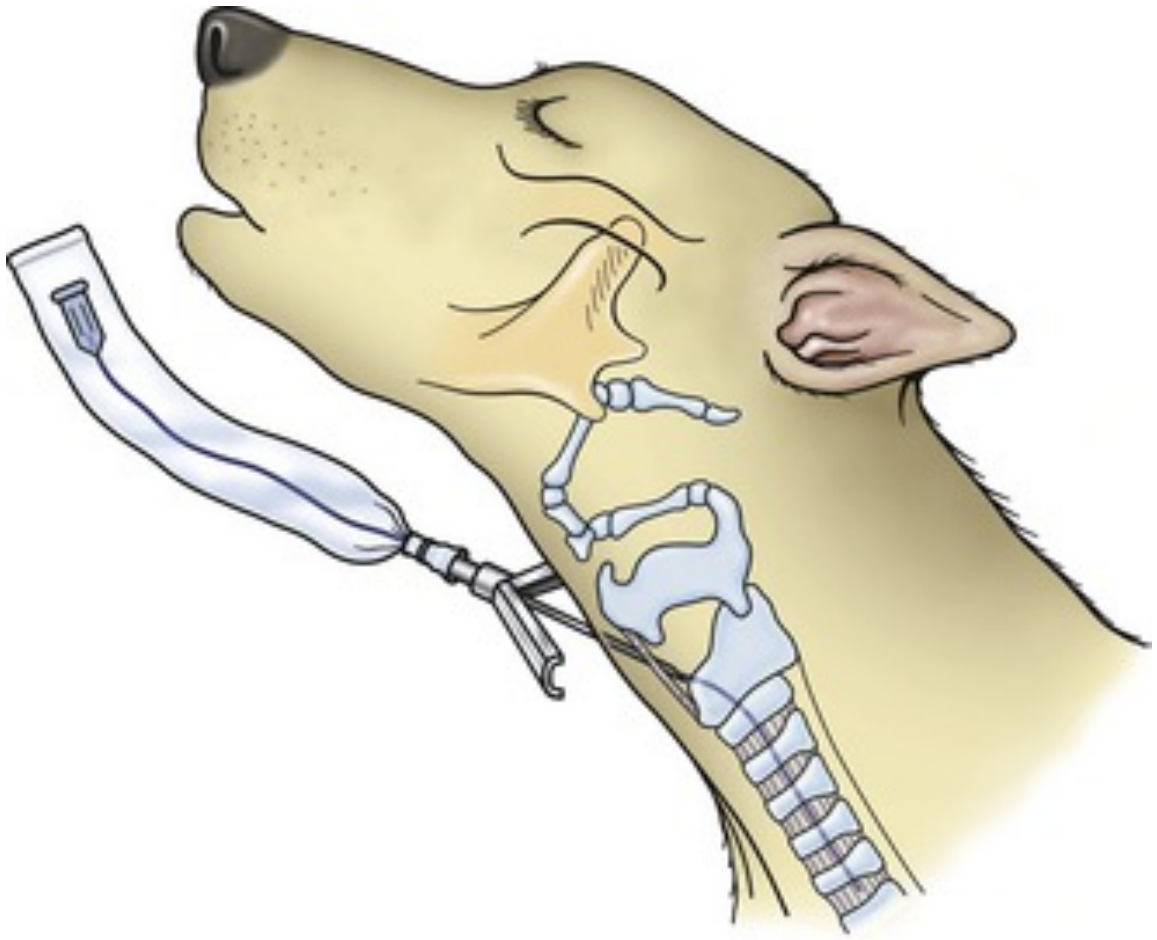
- Exam findings are variable depending on severity
  - From minimally symptomatic to moderate distress, hypoxemia, and peri-arrest
  - 68% of dogs have abnormal lung sounds
  - 36% of cats have no signs
  - Compared to dogs (47%), cats (8%) with infectious pneumonia rarely cough
- CXR mainstay for diagnosis
- On CBC, only 57% of dogs have inflammatory leukogram
- Airway sampling is recommended in recurrent infection

AIRWAY SAMPLING

1) US-guided percutaneous lung aspirates
2) Transtracheal wash (TTW)
3) Endotracheal wash (ETW)
4) Bronchoalveolar lavage (BAL)

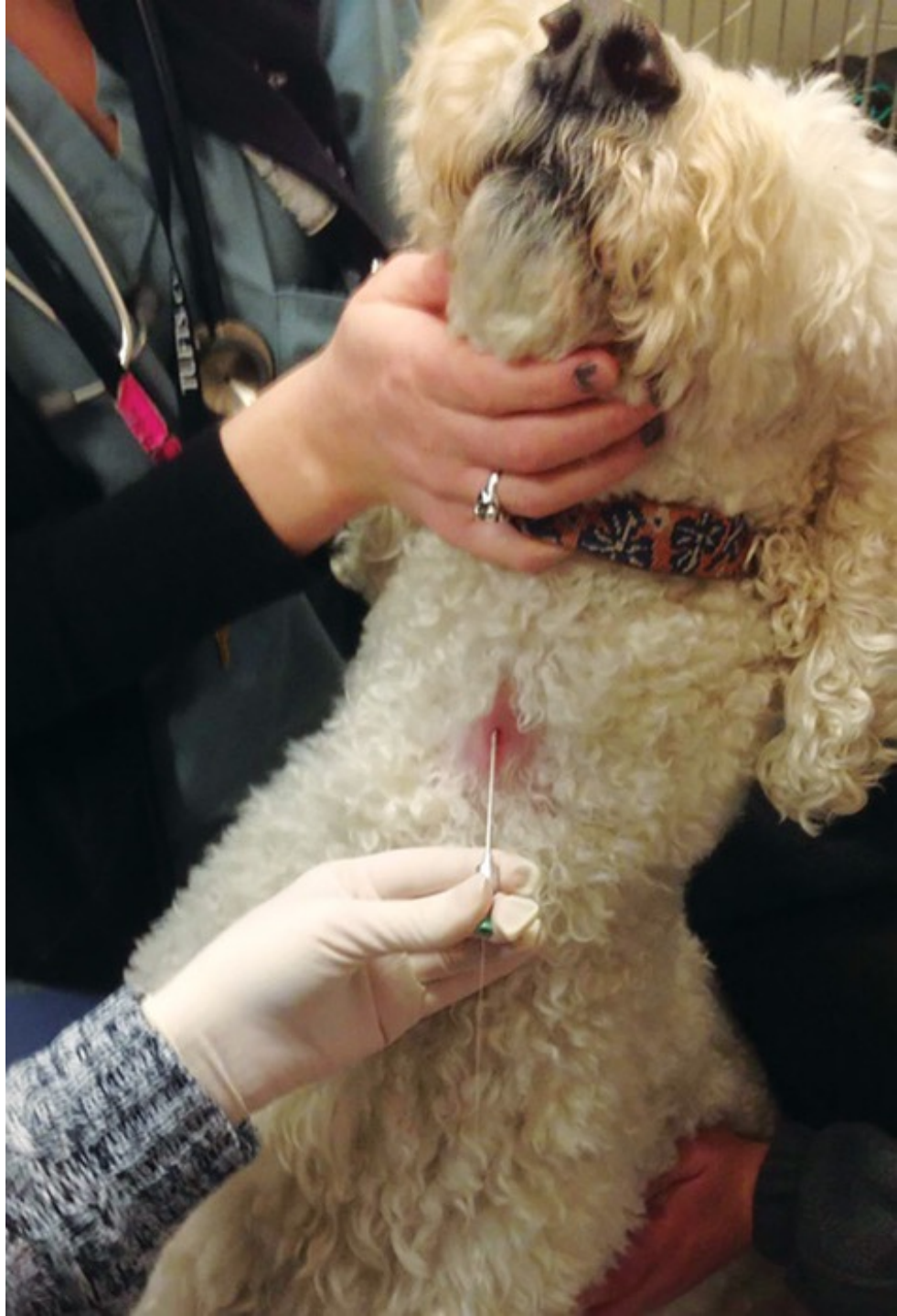
TRANSTRACHEAL WASH

- Bronchial and/or alveolar disease
- Performed under sedation with local anesthetic
- Better in medium to large breed dogs
- Use a through the needle catheter e.g. Intracath or MILA makes tracheal wash kits
- Complications: SQ emphysema, tracheal laceration, hemorrhage, hypoxemia and bronchospasm



TRANSTRACHEAL WASH

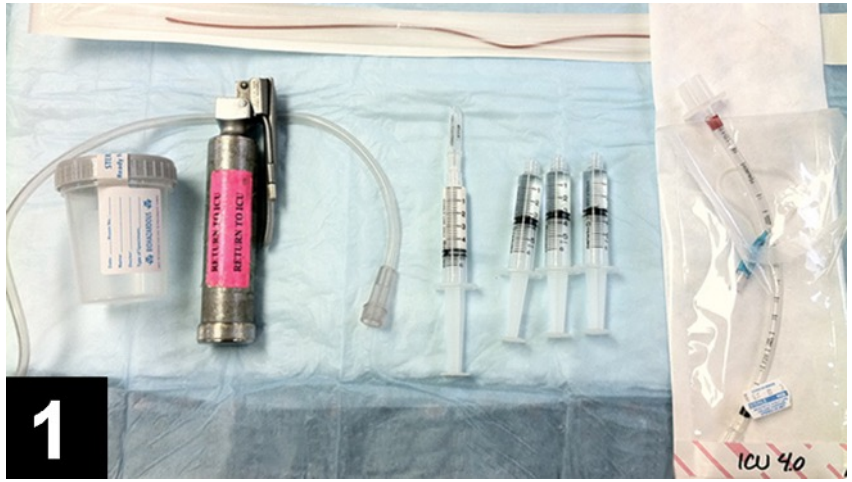
1. Clip and prep site over the lower cervical trachea then infuse lidocaine
2. Insert needle through skin into tracheal lumen (perpendicular to trachea) and advance catheter through needle down to approx. level of carina
3. Place needle guard and remove stylet
4. Infuse sterile saline aliquots (up to 3 times), gentle coupage
5. Patient will often cough. When they do, aspirate the fluid back
6. Sample placed in appropriate containers for submission



ENDOTRACHEAL WASH

- Easy, quick, straight forward
- Brief general anesthesia

1. Intubate with sterile endotracheal tube
2. Place sterile red rubber *or* suction catheter through ET tube and instill saline aliquots (up to 3 times)
3. Brief coupage
4. Manually aspirate or suction catheter and specimen trap to suction cannister
5. Sample placed in appropriate containers for submission

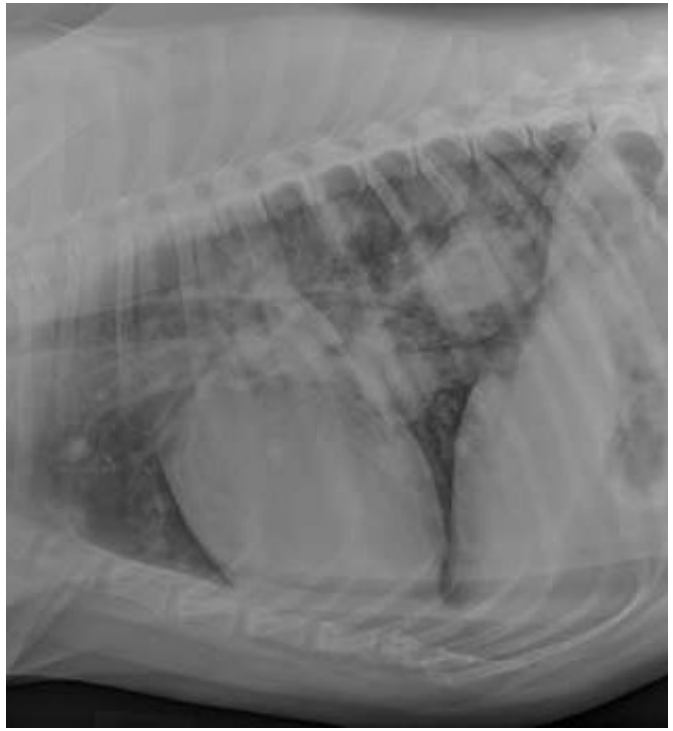


BRONCHOALVEOLAR LAVAGE

- Samples all alveoli dependent on the bronchus where the scope or catheter is lodged
- Obtains a deep sample: The small airways, alveoli and sometimes interstitium
- Preferred if suspecting neoplasia or fungal disease
- Requires general anesthesia
- Can be performed blind (essentially similar to ETW)
- If performed with bronchoscopy, recruit your internist friend! :)
  - Recommend wedging bronchoscope into the bronchi of interest to optimize fluid retrieval

NEOPLASIA

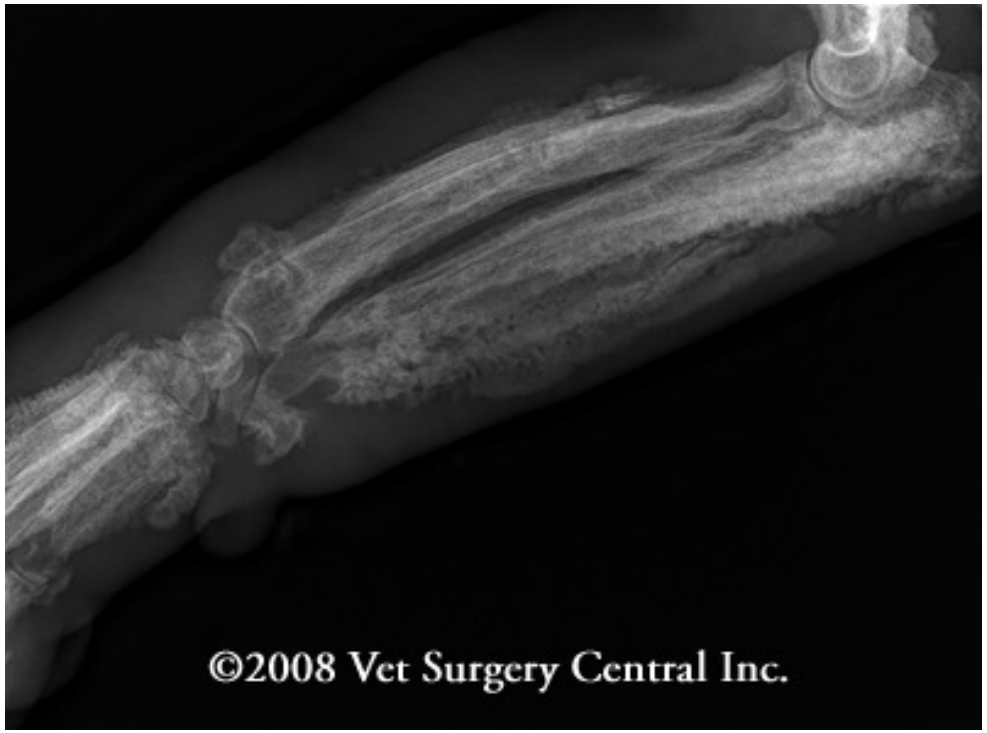
PULMONARY NEOPLASIA



- Neoplasia of the lower respiratory tract are uncommon
- Primary lung tumours make up 1% of all canine tumours
- Female cats predisposed whereas no gender predilection seen in dogs
- Carcinomas are the most common in both dogs and cats
  - Histiocytic sarcoma possible as primary tumour
- Metastatic lung tumours: Mammary adenocarcinoma, OSA, hemangiosarcoma, oral melanoma
  - May occur as its own or with concurrent mets to other organs – via lymphatics, airway, hematogenous, or transpleural

PULMONARY NEOPLASIA

- Coughing (most common in dogs, uncommon in cats), dyspnea, lethargy, weight loss
  - 25% of dogs have no signs
  - Tachypnea/dyspnea usually indicate massive tumour burden or secondary to pleural effusion
- Paraneoplastic syndromes
  - Lameness from hypertrophic osteopathy (HO)
  - Paraneoplastic leukocytosis reported in in one dog
  - Hypercalcemia of malignancy reported in both species



PULMONARY NEOPLASIA: DIAGNOSTICS

- CXR or CT
- Dogs: Single or multiple well circumscribed masses, diffuse lung pattern, or lobar consolidation
- Cats: Ill-defined pulmonary nodules, alveolar disease, pleural effusion, or a combination
- Definitive diagnosis via US-guided lung aspirates or histopath from lung lobectomy
- Barret 2014:
  - Histiocytic sarcomas are significantly larger than other tumour types, most likely to be in left cranial and right middle lung lobe, usually has internal air bronchogram
  - Adenocarcinoma most likely in left caudal lung lobe

PULMONARY NEOPLASIA: PROGNOSIS

- Bronchoalveolar adenocarcinomas carry better prognosis than other lung tumours
- MST 361 days for dogs
  - Better if the lung was peripheral, small, no LN involvement and if the patient is asymptomatic
- MST 115 days for cats
  - Worse if LN met or distant mets, degree of tumour differentiation is prognostic (well differentiated 23 months vs undifferentiated 2.5 months)

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THANK YOU