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THE MANAGEMENT OF RESPIRATORY DISEASES IN DOGS & CATS: FOCUSED ON FLUID AND OXYGEN THERAPY

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ABSTRACT

Respiratory diseases in dogs and cats can be classified into respiratory problems brought about as a result of a specific abnormality of the respiratory system; so called primary respiratory disease, and bronchopulmonary problems which occur as a consequence of heart failure; so called secondary respiratory disease. This section will concentrate predominantly on considerations regarding the treatment of primary respiratory diseases. This includes agents used to facilitate bronchodilation, to reduce coughing and various expectorants and mucolytics. In addition, the optimal fluid therapy and various ways of oxygen delivery with complication will be discussed with emphasis In order to understand the indications for, and action of, various drugs used in the treatment of respiratory disease an understanding of normal respiratory physiology is important and these considerations is described in this section for helping to understand further for readers.

Keywords: drugs, respiratory, oxygen therapy, fluid therapy, dogs and cats

NORMAL RESPIRATORY PHYSIOLOGY

Airway Caliber Changes

- The parasympathetic system provides the primary efferent innervation
  - acetylcholine
  - primary neurotransmitter
  - responsible for the baseline tone of mild bronchoconstriction
- The sympathetic system
  - stimulating bronchodilation through β_2-receptors
  - α-adrenergic stimulation can contribute to bronchoconstriction
- Purinergic system
- mediates bronchodilation via vagal stimulation
  - neurotransmitter has not yet been conclusively identified
  - vasoactive intestinal peptide has been implicated in the cat
  - associated with bronchial hyperreactivity (asthma).
- The intracellular mechanisms

- intracellular concentration of cyclic adeno-sine monophosphate (cAMP) and cyclic guanosine mono-phosphate (cGMP)
  - Cyclic AMP-induced bronchodilation
    - decreased by α-adrenergic stimulation
    - increased by β_2-receptor stimulation
  - cGMP-induced bronchoconstriction
    - increased by stimulation of muscarinic
    - indirectly, histaminergic receptors
- Control of bronchial smooth muscle tone
- irritant (or mechanoreceptor), stretch, or J-receptors

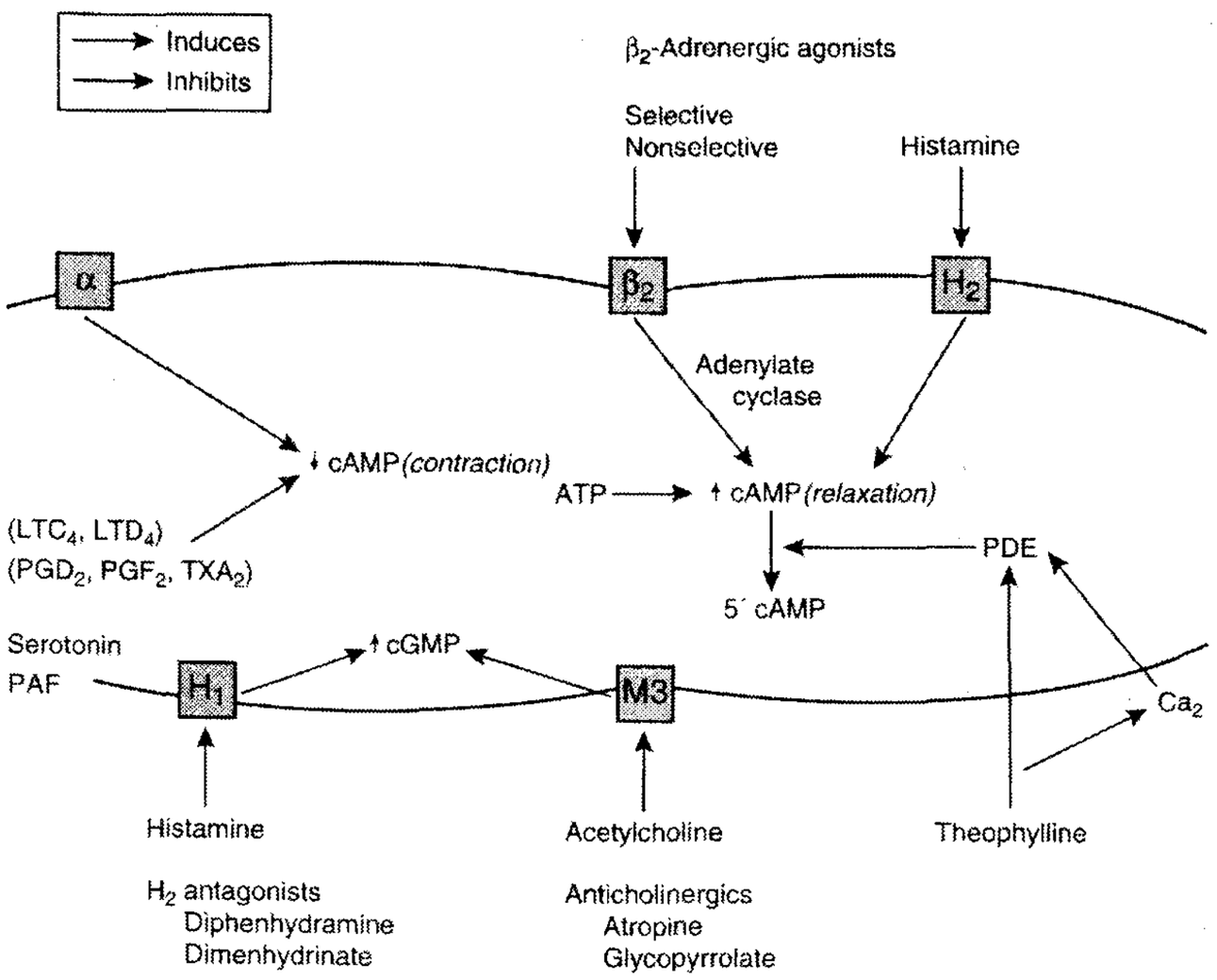

Figure 31–1. Factors determining bronchial smooth muscle tone. Reciprocal changes in cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) determine muscle tone. Contraction occurs when cAMP levels are decreased by events such as α-adrenergic stimulation or when cGMP levels increase in response to muscarinic receptor (M3) stimulation by acetylcholine or H_1-receptor stimulation by histamine. Calcium (Ca^{2+}) and several mediators can also induce bronchoconstriction. Increased cAMP levels induced by β_2-adrenergic or histamine (H_2) receptor stimulation counteract muscle contraction. Inhibition of phosphodiesterase (PDE) also causes increase cAMP. Although the effects of most inflammatory mediators are best counteracted by preventing their release (see Fig. 31–3), several drugs may be used to antagonize smooth muscle contraction regardless of the etiology. LTC, LTD = leukotrienes C and D; PAF = platelet-activating factor; PGD_2, PGF_2 = prostaglandins D_2 and F_2; TXA_2 = thromboxane.

Respiratory Defense Mechanisms

- the cough reflex
- sneeze reflex
- muco-ciliary apparatus
  - ciliary activity increases with β-adrenergic stimulation
  - low-viscosity, watery medium to maintain their rhythmic beat.
  - A more mucoid layer lies on top of the cilia and serves to trap foreign materials
  - too watery or too rigid will result in mucous transport (less than optimal)

- Mucus released by goblet cells
- Goblet cell numbers increase with a subsequent increase in the viscosity of respiration secretion
- Parasympathetic, cholinergic stimulation increases mucous secretion
- β-adrenergic stimulation causes secretion of mucus, electrolytes, and water

- respiratory mononuclear phagocyte system
- phagocytic properties (release of inflammatory mediators)
  - decrease airway caliber size
  - edema
  - chemotaxis
  - increased mucous production
  - bronchoconstriction

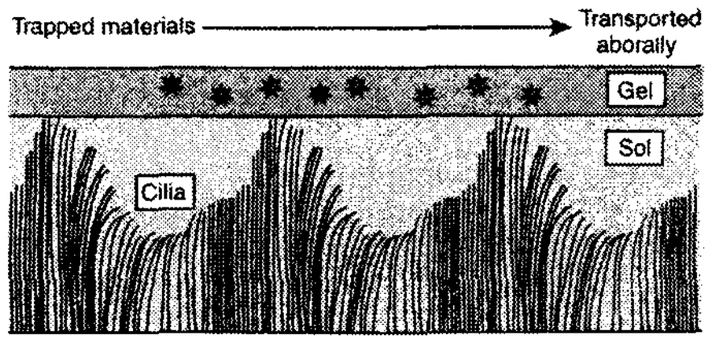

Figure 31–2. The mucociliary apparatus represents the first line of defense for pathogens entering the respiratory tract. Cilia are bathed in a water or sol layer. When the cilia beat in synchrony, the movements send forward (orally) the mucoid or gel layer that lies on top of the cilia. Materials trapped in this layer also move forward to be either swallowed or expectorated.

PATHOGENESIS OF INFLAMMATORY RESPIRATORY DISEASES

- Asthma is a pathologic state of the lungs characterized by marked bronchoconstriction and inflammation
- Mediators released during inflammation are the major contributors to the pathogenesis
- changes in mucosal epithelial permeability
- cholinergic bronchoconstriction
- the bronchial tree becomes hypersensitive
- inhibit mucociliary function
- Airway obstruction in chronic disease
  - bronchoconstriction
  - bronchial wall edema
  - accumulation of mucus and cells
  - airways eventually become plugged and ultimately collapse
  - leads to fibrosis → contributes to the collapse, air trapped within the alveoli (emphysema)

INFLAMMATORY MEDIATORS IN THE RESPIRATORY TRACT

Histamine

- Histamine is a vasoactive amine (basophils and mast cells)
- Interaction with the H1 receptor causes an increase in intracellular calcium, and ultimately in cGMP
- Histamine also stimulates cholinergic receptors in the airway

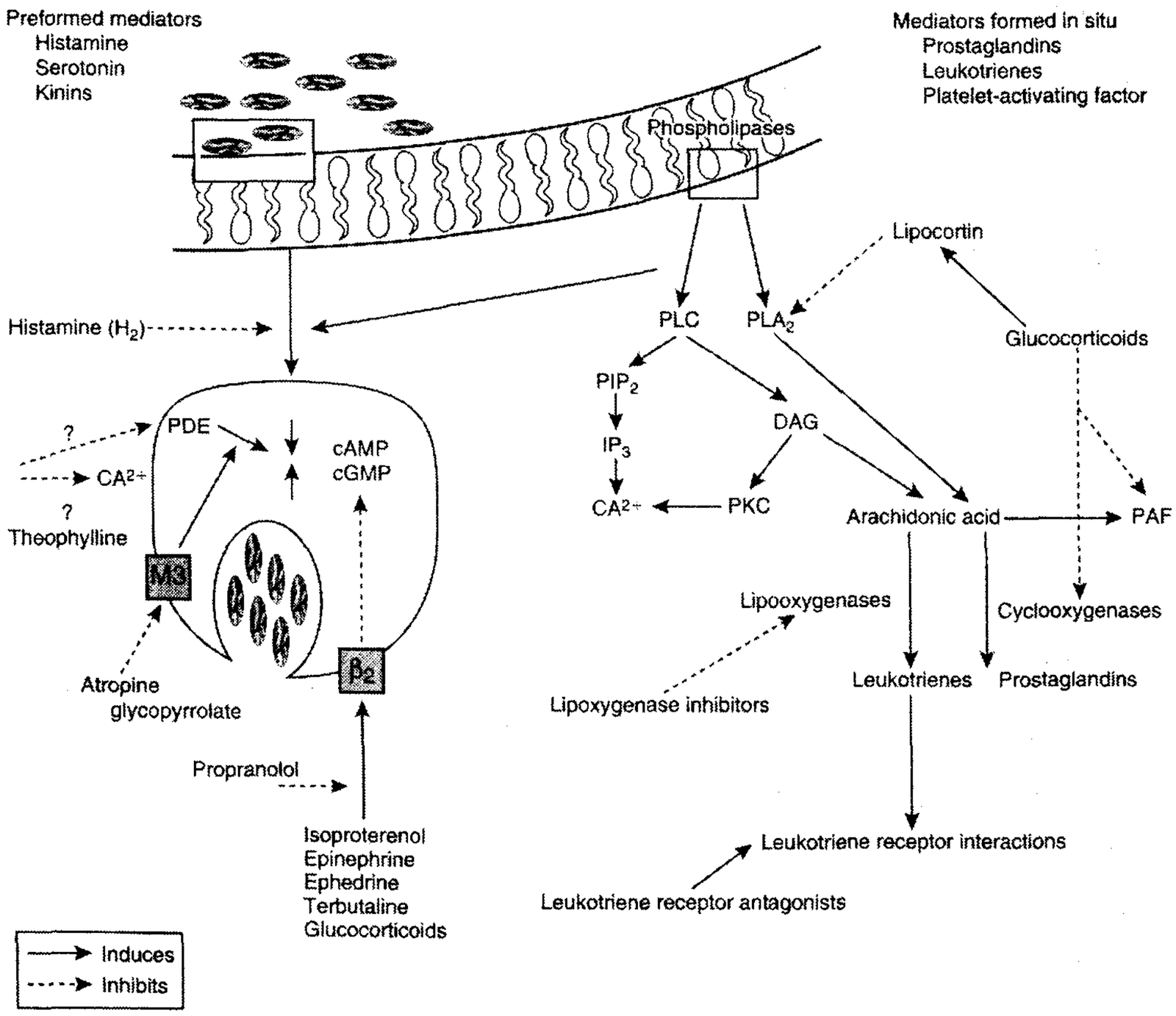

Figure 31-3. The formation of mediators important in the pathogenesis of respiratory disease. Leukocytes and other cells release arachidonic acid metabolites and platelet-activating factor (PAF) after activation of phospholipases by a variety of stimuli. Mast cell degranulation induced by both immune and nonimmune stimuli is also accompanied by arachidonic acid metabolism as well as by the release of performed mediators that are stored in the granules. Intracellular mechanisms that induce mast cell degranulation include increased calcium (Ca^{2+}), increased cyclic guanosine nucleotide (cGMP) mediated by muscarinic (M3) receptors, or decreased cyclic adenosine nucleotide (cAMP) mediated by α-adrenergic receptor stimulation. Drugs used to prevent mediator release include glucocorticoids, which are one of the few classes of drugs that can prevent activation of phospholipases (mediated by lipocortin) and thus release of arachidonic acid metabolites and PAF. Inhibition of prostaglandin synthesis by nonsteroidal anti-inflammatory drugs may prove beneficial but also may lead to increased formation of leukotrienes by providing more arachidonic acid. Leukotriene actions can be blocked either by leukotriene receptor antagonists or by blockade of leukotriene receptors. Mast cell degranulation can be prevented by stimulation of β_2-adrenergic receptors, inhibition of calcium influx or phosphodiesterase (PDE), or prevention of muscarinic (M3) receptor stimulation. Drugs that block β_2-adrenergic receptors are contraindicated in most respiratory diseases. DAG = diacylglycerol; IP_3 = inositol triphosphate; PIP_2 = phosphatidylinositol; PKC, protein Kinase C; PLC, PLA_2 = phospholipases C and A_2.

- Histamine causes constriction in both central and peripheral airways
- Stimulation of H_2 receptors causes an increase in cAMP and bronchodilation
  - Antihistamine drugs that block H_2 receptors may be contraindicated in asthma
- Histamine contributes to bronchial occlusion by mechanisms other than bronchoconstriction
  - Mucous secretion is mediated via H_2 receptor
- Histamine is chemotactic to inflammatory cells, particularly eosinophils and neutrophils

Serotonin

- released during mast cell degranulation
- Not important mediator of human or canine bronchial asthma
- Constriction by interaction with serotonin receptors or enhanced release of

acetylcholine

- cause profound vasoconstriction of the pulmonary vasculature and microvascular leakage

Prostaglandins and Leukotriens

- eicosa-noids formed when phospholipase A_2
- PGD_2, PGF_{2a}, and TXA_2 cause bronchoconstric-tion
- PGEi and to a lesser extent PGIj cause bronchodilation
- Bronchoconstriction induced by PGD_2 is about 30 times as potent as that induced by histamine.
  - Both PGD_2 and TXA_2 have been implicated in immediate bronchial airway hyperreac-tivity
- Lipoxygenases in the lung catalyze the conversion of AA to hydroperoxyeicosatetraenoic acid (HPETEs)
- slow reactive substance, an important mediator released in the lungs during anaphylaxis
- Bronchial smooth muscle contraction and microvascular permeability mediated by LTC_4 and LTD_4 is 100- to 1000-fold more potent than that induced by histamine
- LTs are potent stimulators of mucous release in the dog but appear to be less potent in cat

Platelet-Activating Factor

- potent. dose-independent constrictor of human airways,
- potent chemotactant for platelets and eosinophils
- implicated as the cause of the sustained bronchial hyper-responsiveness (asthmatics)
- The role of PAF in feline and canine respiratory diseases has not been addressed.

DRUGS USED TO MODULATE THE RESPIRATORY TRACT

Bronchodilators and Anti-inflammatory Drugs

- most drugs that induce bronchodilation & reduce inflammation
- Bronchodilators reverse airway smooth muscle contraction by increasing cAMP, decreasing cGMP, or decreasing calcium ion concentration
- decrease mucosal edema & are anti-inflammatory
- β-receptor agonists, methylxanthines & cholinergic antagonists.

Table 31–2. Doses of Drugs Used To Treat Respiratory Diseases

Drug	Route	Dose	Frequency (Hours)
β-Agonists*			
Epinephrine	IM, IV, SC	0.1 mg/cat or 20 μg/kg	
	SC	0.1 ml/kg of 0.001 solution	30 min†
Ephedrine	IM, PO	2–5 mg total (C)	
		5–15 mg (total) (D)	
Isoproterenol	PO	0.44 mg/kg (C), 10–30 mg (D)	6–12
	IM, SC, IV	0.1–0.2 mg total	6
	Aerosol	0.5 cc of 1:200 dilution	4 × 3
Metaproterenol	PO	0.5 mg/kg	6
	Aerosol		4 × 3
Albuterol	Aerosol	200 μg‡	
	PO	50 μg/kg	8
Terbutaline	PO	0.625–1.25 mg total (C)	12
		1.25–5.0 mg (D)	8–12
Isoetharine	Aerosol	0.5–1.0 mL of 1:3 saline dilution	8
Anticholinergics			
Atropine	IV, IM, SC	0.02–0.04 mg/kg	As needed
Glycopyrrolate	IV, IM, SC	0.01–0.02 mg/kg	As needed
Methylxanthines		10 mg/kg (D)	6–8 (D)
Aminophylline	PO	5–6 mg/kg (C)	12 (C)
	IV infusion§	2–5 mg/kg	8–12
			Over 30–60 min
Theophylline base	PO	4 mg/kg (C)‖	12 (C)
		5–10 mg/kg (D)	6–8 (D)
		Slow-release anhydrous	
		20 mg/kg (C)	12 (C)
Oxytriphylline	PO	10–15 mg/kg¶	8–12
			6–8
Glucocorticoids			
Prednisolone	PO	1–2 mg/kg	6–12**
Prednisolone sodium succinate	IV, IM**	2–4 mg/kg	4–6
Dexamethasone	IV, IM**	0.2–2.2 mg/kg	
Triamicinolone	PO	0.25–0.5 mg total	24**
Beclomethasone dipropionate	Inhalant	200 μg total‡	6–8
Megestrol acetate	PO	5 mg total	24 × 4, then weekly × 4
Antitussives			
Codeine	PO	1–2 mg/kg	8
		0.2–2 g	
		15–60 mg	
Hydrocodone	PO	0.22 mg/kg	6–12
Butorphanol tartrate	SC, IM	0.055–0.11 mg/kg	As needed
	PO	0.5–1.0 mg/kg	6–12
	SC	0.55 mg/kg	
Dextromethorphan	PO	1–2 mg/kg	6–8
Morphine	IM, SC	0.1 mg/kg	6–12
Decongestants			
Chlorpheniramine	PO	0.22 mg/kg (D)	8
	PO	2–4 mg total (C)	24
		1/4 to 1/2 slow release (C)	24
Diphenhydramine	PO	2–4 mg/kg	8
Dimenhydrinate	PO	12.5 mg total (C)	8
	PO	8 mg/kg (D)	
Hydroxyzine	PO	2 mg/kg (D)	6–8
Pseudoephedrine			

Abbreviations: C = cat; D = dog; IM = intramuscular; IV = intravenous; PO = orally; SC = subcutaneous.
*Use cautiously in cats with cardiac disease.
†Up to a total dose of 0.5 mL.
‡Human dose.
§Emergency treatment.
‖Based on 80% theophylline.
¶Based on 65% theophylline.
**Taper doses to minimum effective dose.

β-Receptor Agonists

- most effective bronchodilators
- cAMP for activation of specific protein kinases→cause relaxation of airway smooth muscle
- stimulate secretion of airway mucus→ less viscous secretion and enhanced ciliary activity
- β_2-receptors blocker contraindicated in animals with bronchial disease

Nonselective β-Agonists

- epinephrine, ephedrine & isoproterenol
- epinephrine and ephedrine cause α-adrenergic activity (cause vasoconstriction and systemic hypertension)
- *may* contribute to airway constriction
- Aerosolization reduces the adverse effects of nonselective

β2-Selective Agonists

- not generally associated with the undesirable effects
- Metaproterenol (analogue terbutaline)
- Albuterol
- Oral doses are thus higher than parenteral doses
- can cause β1 side effects at high doses
- Albuterol & isoetharine (aerosolization)
- Chronic use: can result in refractoriness due to down-regulation of β-receptors

Methylxanthine Derivatives

- Theophylline, aminophylline
- attributed to inhibition of phosphodiesterase (PDE), and increased concentrations of cAMP
- antagonism of the inhibitory neurotransmitter adenosine
- Broncho-dilation through interference of calcium mobilization
- Theophylline:
  - inhibits mast cell degranulation and thus mediator release
  - increases mucociliary clearance
  - prevents microvascular leakage
  - A major advantage: increased strength of respiratory muscles
  - Rapid absorption → slow-release products but limited dose sizes available in small animal
  - Theophylline is metabolized by demethylation in the liver

- the elimination rate constant of theophylline is less in cats (0.089/h) than dogs (0.12/ h), resulting in a longer half-life in the cat (7.8 h) compared with the dog (5.7 h) thus necessitating a smaller dose in cats
- Rapid infusions or infusions of undiluted aminophylline can cause cardiac arrhythmias, hypotension, nausea, tremors, and acute respiratory failure.

Anticholinergic Drugs

- Anticholinergic drugs compete with acetylcholine at muscarinic receptor sites
- In the respiratory tract, reduce the sensitivity of irritant receptors and antagonize vagally mediated bronchocon-striction.
- have not proved clinically effective in the treatment of bronchial diseases in animals
- limited to treatment of bronchoconstriction associated with organo-phosphate toxicity or in animals in status asthmaticus unresponsive to bronchodilator therapy
- M3 receptors release acetylcholine, whereas M2 receptors block its release
- Nonselective blockade of muscarinic receptors by atropine and ipratropium may actually potentiate acetylcholine release by antagonizing the effects of M2-receptor stimulation
- Drugs specific for M3 receptors may ultimately lead to successful treatment of bronchial disease with anticholinergics drugs.

Atropine

- Aerosolized atropine, a prototype anticholinergic drug, affects predominantly the central airways, whereas both central and peripheral airways are affected if the drug is administered intravenously
- In the respiratory tract, atropine reduces ciliary beat frequency, mucous secretion, and electrolyte and water flux into the trachea
- The primary indication for atropine in small animals is facilitation of bronchodilation in acutely dyspneic animals.
- It is the treatment of choice for life-threatening respiratory distress induced by anticholinesterases.
- A combination of atropine with either β-adrenergic agonists or glucocorticoids will cause better bronchodilation than either drug alone

Ipratropium bromide

- is a synthetic anticholinergic
- is pharmacodynamically superior to atropine
- does not cross the blood-brain barrier
- is not well absorbed after aerosolization (limits the likelihood of adverse effects)

Glycopyrrolate

- can also be used as a bronchodilator in small animals
- onset of action is slower than that of atropine
- its half-life is 4 to 6 hours compared with 1 to 2 hours for atropine

Mast Cell Stabilizers

◆ stabilize mast cells are most effective in syndromes associated with marked mast cell activity

Cromolyn

- mechanism of action of cromolyn is not certain
- inhibit calcium influx into mast cells, thus preventing mast cell degranulation and the release of histamine and other inflammatory mediators
- is most useful as a preventative before activation of inflammatory cells
- is not significantly absorbed after oral administration and is characterized by a short half-life
- effective therapy depends on frequent aerosolization (limits its utility in the treatment of small animal diseases)

Calcium Antagonists

- The efficacy has yet to be identified
- Their potential benefits include prevention of mediator release, smooth muscle contraction, vagus nerve conduction, and infiltration of inflammatory cells

Drugs that Target Inflammatory Mediators

Drugs that Target Leukotrienes

- Leukotrienes are very potent causes of inflammation in the lungs, causing marked edema, inflammation, and broncho-constriction
- Zafirlukast (Accolate) is an LT receptor antagonist
- zileuton (Zyflo) is a lipoxygenase inhibitor
- appear to be effective for dogs

Nonsteroidal Anti-inflammatory Drugs

- The role needs to be defined
- Although NSAIDs effectively block PGs through inhibition of cyclooxygenase, they do

not appear to have any effect on lipoxygenase and therefore production of LTs

- NSAIDs nonselectively block all PGs, including those that provide some protection during periods of bronchoconstriction
- the use of NSAIDs for the treatment of respiratory diseases in small animals is limited to aspirin therapy as treatment for thromboembolism associated with heart-worm disease
- The use of selective TXA2 inhibitor for selected feline respiratory disease

Antihistamines

- have not proved clinically useful in the control of small animal
- act to block target receptors from responding to histamine
- do nothing to prevent release of histamine or other mediators from any inflammatory cell
- The newer antihistamines (Hi), loratadine and cetirizine, are exceptions, drugs that also decrease histamine release from basophils
  - have not been studied for efficacy or safety in animals
- The use of H2 blockers may be detrimental in animals with chronic disease because of their effects on airway secretions
- The role of H_2 receptors in bronchodilation, mucous secretion, and inflammation suggests that H_2-receptor blockers should also be used with caution
- Cyproheptidine: an antiserotinergic, Because feline airways are exquisitely sensitive to the constrictor effects of serotonin, this drug may prove particularly useful in cats either alone or as an adjunct to bronchodilators or glucocorticoids

ANTITUSSIVES

- is to decrease the frequency and severity of cough without impairing mucociliary defenses
- the underlying cause should be identified and treated
- Cough suppressants should be used cautiously and are contraindicated if the cough is productive
- Cough reflex can be blocked peripherally, either by facilitating removal of the irritant with mycolytics or expectorants or by blocking peripheral receptors to induce bronchodilation, or it can be blocked centrally at the cough center in the medulla

Narcotic Antitussives

- depress the cough center sensitivity to afferent stimuli
- be associated with strong sedative properties, as well as constipation

Codeine

- is the prototype narcotic antitussive
- is one of the most effective drugs
- Compared with morphine, codeine is equally effective as a cough suppressant but is less suppressing to other central centers and causes less constipation

Hydrocodone

- is a more potent antitussive than codeine but causes less respiratory depression
- is probably the most commonly used antitussive for dogs

Butorphanol

- is probably more commonly used as an analgesic
- it is 100 times more potent than codeine and 4 times more potent than morphine
- Therapeutic concentrations cause minimal cardiac or respiratory depression

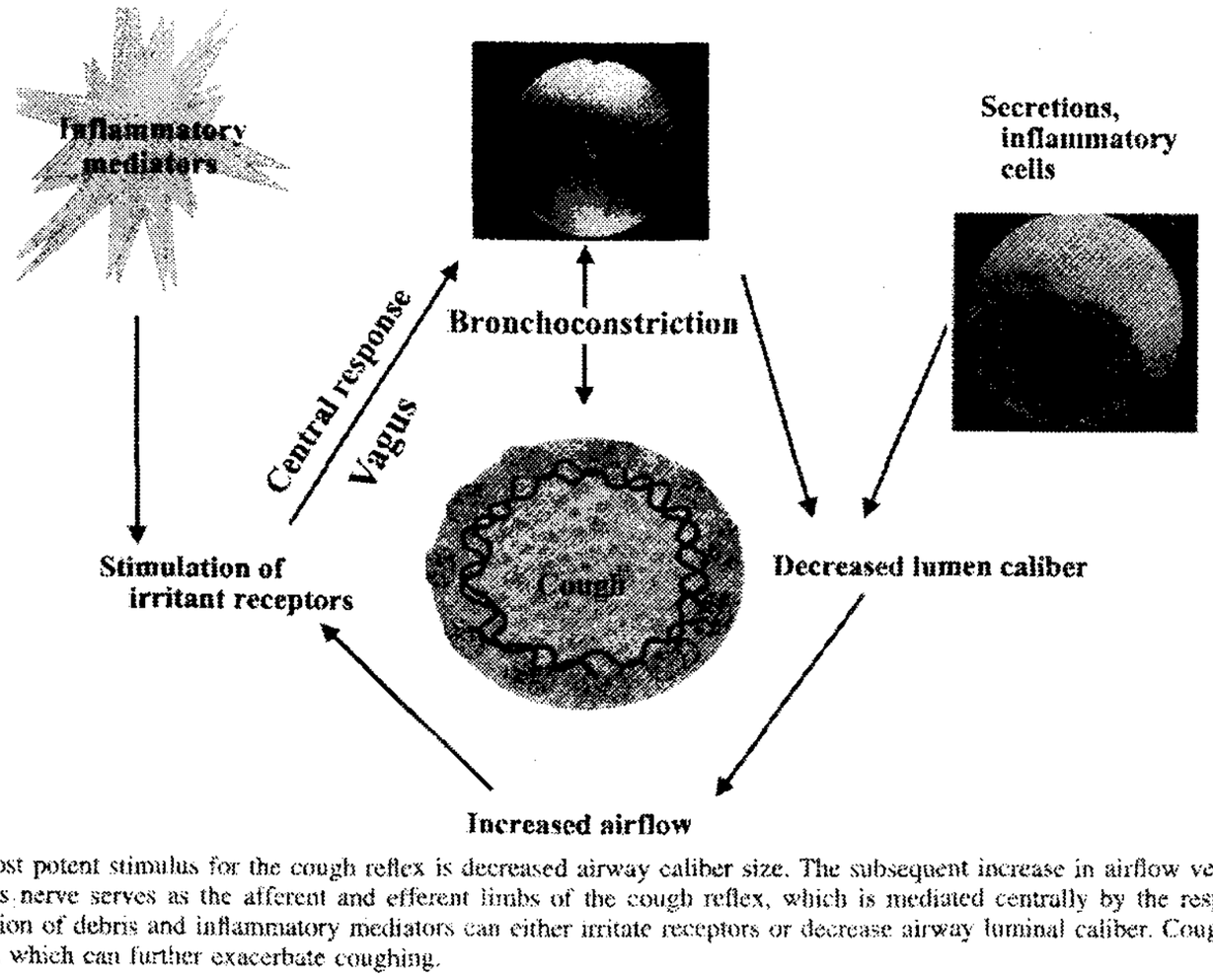

Figure 31–4. The most potent stimulus for the cough reflex is decreased airway caliber size. The subsequent increase in airflow velocity irritates stretch receptors. The vagus nerve serves as the afferent and efferent limbs of the cough reflex, which is mediated centrally by the respiratory center in the medulla. Accumulation of debris and inflammatory mediators can either irritate receptors or decrease airway luminal caliber. Cough is accompanied by bronchoconstriction, which can further exacerbate coughing.

Non-narcotic Antitussives

Dextromethorphan

- is a semisynthetic derivative of opium that lacks its narcotic properties
- L-isomer has antitussiu activity (similar to codeine in potency)

- fully effective within 30 minutes after oral administration
- its antitussive efficacy is equal to codeine
- the combination of dextromethorphan with a bronchodilator is superior to dextromethorphan alone

Noscapine

- is a non-addictive opium alkaloid that has antitussive effects similar to codeine

Peripheral Bronchodilators

- Ephedrine peripherally induces bronchodilation and as both a bronchodilator and decongestant

MUCOKINETICS

- facilitate the removal of secretions from the respiratory tree
- indicated for conditions associated with viscous to inspissated pulmonary secretions such as are commonly associated with chronic bronchial diseases
- induced by drugs that improve ciliary activity (e.g., β-receptor agonists and methyl-xanthines) or by drugs that improve the mobility of bronchial secretions by changing viscosity
- Viscosity can be decreased by hydration (e.g., sterile or bacteriostatic water or saline), increasing pH (e.g., sodium bicarbonate), increasing ionic strength (sodium bicarbonate and saline), or by rupture of sulfur (S-S) linkages in the mucus (e.g., acetylcysteine or iodine)
- Hydrating agents can be administered parenterally (i.e., isotonic crystalloids) or by aerosolization
- The efficacy of aerosolization in liquefying airway secretions is controversial
- Bland aerosols such as water and saline can actually be detrimental to mucociliary function

Acetylcysteine (N-acetyl-L-cystein)

- is the mucolytic drug most widely used by humans
- efficacious after aerosolization
- oral administration has become the preferred route
- the mechanism of acetylcysteine reflects destruction of mucoprotein of the disulfide bonds by a free sulfhydryl group

- N-acetylcysteine serves as a precursor to glutathione, a major scavenger of free oxygen radicals associated with inflammation
- Acetylcysteine is often used in combination with aerosolized antimicrobials because it may improve antibacterial penetration of infected mucus
- Installation of a 10% to 20% solution has also been used to clean and treat chronic sinusitis
- is associated with few adverse effects

EXPECTORANTS

- potassium iodide are common ingredients
- increase the fluidity of respiratory secretions through several mechanisms
- often used as adjuvants for the management of cough by facilitating removal of the inciting cause
- Bronchial secretions are increased by vagal reflex after gastric mucosa irritation (iodide salts) and directly through sympathetic stimulation or by volatile oils that are partially eliminated via the respiratory tract

Iodide Preparations

- Potassium iodide is a saline expectorant capable of increasing secretions by 150%
- should not be used in pregnant or hyperthyroid animals or in milk-producing animals

Stimulant Expectorants

- are used more commonly for coughing associated with chronic bronchial diseases
- Guaiacol and its glyceryl ether guaifenesin
- Neither the volume of viscosity nor respiratory secretions appear to change after treatment with guaifenesin

DECONGESTANTS

- The indications include sinusitis of allergic or viral etiologies and reverse sneezing or other complications of postnasal drip
- Two major categories of drugs used as decongestants are the histamine (H1) receptor antagonists (e.g., dimenhydrinate, diphenhydramine, chlorpheniramine, and hydroxyzine) and the sympathomimetic drugs (i.e., α-adrenergic agonists; ephedrine, pseudoephedrine, phenylephrine)
- given topically to avoid the systemic effects associated with oral therapy

- Stimulation of α_2-receptors concentrated on precapillary arterioles results in vascular smooth muscle vasoconstriction.
- Sympathomimetic drugs mimic norepinephrine
- The mechanism of rebound hyperemia is not clear but may result from secondary β-adrenergic effects, as β-receptors up-regulate or desensitize α-receptors
- Regardless of the cause, repeated contraction of the vasculature can result in ischemia and mucosal damage, perhaps due to loss of nutrition
- Oral treatment of sympathomimetic drugs can be associated with a number of adverse reactions
- Antihistamines are effective for the treatment of allergic rhinitis in human patients

AEROSOLIZATION AS A ROUTE OF DRUG ADMINISTRATION

- are to directly deliver drugs to the respiratory tract and to facilitate liquefaction and mobilization of respiratory secretions
- Factors that determine the amount of drug administered via aerosolization include the particle size generated by the aerosolizer, the technique of delivery (i.e., mask *vs* endotracheal tube and nose *vs* mouth), flow rate of the delivery gas, and patient factors
- The optimum particle size for particle (and drug) deposition in the trachea is 2 to 10 um, whereas that in peripheral airways is 0.5 to 5.0 um
- Less than 10% to 20% of aerosolized drug in small animals probably reaches the tracheobronchial tree, and even less will reach the peripheral airways and the lungs
- The more tortuous the airways traversed by an aerosol, the smaller the percentage delivered
- With progression of chronic disease, therapy may become less effective as the respiratory pattern of the animal becomes shallow and rapid
- Administration of an aerosol by mask reduces drug delivery to the tracheobronchial tree because particles will be deposited in the nasal turbinates and oropharynx
- The utility of aerosolization may be further limited because of stimulation of irritant receptors and reflex bronchoconstriction.
- Either animals should be pretreated with a β-adrenergic or methylxanthine broncho-dilator 10 minutes before aerosolization or a bronchodilator should be included in the aerosolized medicament (e.g., 100 mg aminophylline)
- Care should be taken not to overhydrate and flood the respiratory tract
- Treatments of approximately 30 to 45 minutes should be repeated every 4 to 12 hours

Oxygen Supplementation and Humidification

- ❑ Oxygen (0_2) therapy plays a critical role in the treatment of hypoxemia and respiratory failure
- ❑ Patient response to oxygen therapy varies significantly depending on the underlying cause
- ❑ Several potential complications can be associated with oxygen supplementation

Indications for Oxygen Therapy

- ❑ Oxygen delivery to the tissues depends on
  - ■ Hemoglobin concentration
  - ■ Oxygen saturation of hemoglobin
  - ■ Cardiac output
  - ■ The total oxygen content of the blood = The oxygen saturation of the hemoglobin + the amount of oxygen dissolved in the blood (Pao_2)

CLINICAL SIGNS

- ❑ Clinical signs of respiratory distress and hypoxemia may include anxiety, an extended head and neck, open mouth breathing, abducted elbows, increased respiratory effort or abdominal effort, and tachypnea
- ❑ Clinical signs of hypoxia may also include tachycardia, psychomotor incoordination, gastrointestinal upset, and restlessness.
- ❑ Cyanosis is not a sensitive indicator of hypoxemia, however, because it is not evident until the Pao_2 is less than 50 mm Hg and because it cannot be detected in patients with severe anemia (i.e., packed cell volume less than 15%)
- ❑ Arterial blood gas analysis, pulse oximetry, and calculation of alveolar-arterial oxygen tension (A-a) gradients can help

HYPOXEMIA

- ❑ is defined as decreased levels of oxygen in air, blood, or tissue
- ❑ An inadequate supply of oxygen to the tissues can result from hypoxemia (subnormal oxygena-tion of arterial blood)
  - ■ reduced oxygen carrying capacity of red cells
  - ■ decreased tissue blood flow
  - ■ increased tissue demand for oxygen
  - ■ impaired tissue extraction of oxygen

- Hypoxemia can be caused by
  - a low fraction of inspired oxygen (Fio_2)
  - hypoventilation
  - venous admixture due to diffusion impairment
  - intrapulmonary shunt
  - ventilation-perfusion (V/Q) mismatch
- The most common causes of impaired pulmonary gas exchange are ventilation-perfusion mismatch and physiological shunt secondary to alveolar collapse
- Oxygen supplementation should be considered in patients with a Pao_2 of less than 70 mm Hg or an arterial hemoglobin saturation (Sao_2) of less than 93%

DECREASED OXYGEN DELIVERY TO TISSUES

- Oxygen delivery to the tissues is affected
  - by anemia
  - hemoglobin abnormalities (e.g., carboxyhemoglobin or methemoglobin)
  - decreased tissue perfusion (e.g., as occurs in patients with shock)
  - Increased tissue oxygen demand occurs in animals with increased body temperature or metabolic rate (fever, heat stroke, malignant hyperthermia, sepsis, and seizures)
- Oxygen therapy may be helpful in treating patients with head trauma because many suffer from cerebral ischemia secondary to increased intracranial pressure and reduction in cerebral perfusion

Oxygen Administration Techniques

- **FACE MASK**
  - is a short-term method of oxygen delivery that can be initiated quickly, requires minimal set up, and allows convenient access to patients
  - a flow rate of 1 L/min (small dog)
  - a flow rate of 5 to 10 L/min (large dog)
  - The stress of holding a face mask.

- **FLOW-BY OXYGEN**
  - is a simple, quick, and easy method of short-term oxygen supplementation in emergencies
  - is less effective than mask oxygen but may be tolerated better by dyspneic

animals

- at a flow rate of 2 to 5 L/min with the hose held 2 to 4 cm from the nose (or mouth in panting animals)
- Disadvantages of this technique include the requirement for constant supervision, the inability to achieve high enough inspired oxygen concentrations in some cases

NASAL OXYGEN

- is a practical and effective way of raising tracheal O_2 concentration and Pao_2
- is useful for tolerant patients that are anticipated to require several days of oxygen therapy
- Passing a nasal catheter can be stressful for the patient, so severe respiratory distress may preclude its safe placement
- Patients with upper respiratory signs attributable to the nares, and brachy-cephalic breeds, should not be considered for nasal catheterization
- Low nasal flow rates of 50 to 100 ml/kg/min should be adequate to increase the mean tracheal 0_2 concentration to 40% to 50%
- A nasal catheter flow rate of 0.75 L/min
- Nasal oxygen therapy offers several advantages
  - The patient has freedom of movement
  - is accessible for monitoring without discontinuing oxygen supplementation
  - is also relatively inexpensive and not as wasteful as flow-by oxygen and oxygen cages.
- Side effects include
  - the possibility of nasal mucosal hemorrhage in coagulopathic animals
  - gastric distension at very high flow rates (greater than 5 L/min)
  - nasal discharge
  - epistaxis
  - sneezing

ELIZABETHAN COLLAR OR HOOD OXYGEN

- is applied snugly to the neck with the tip of an oxygen line placed inside the collar on the animal's neck. The front circle of the collar is then covered with a piece of clear plastic wrap and a small opening is made at the top of the

canopy to allow the escape of CO_2 and humid and warm air

- Oxygen should be administered at a high flow rate for the first 1 to 2 minutes to fill the canopy quickly, then a maintenance rate of 0.75 to 1 L/minute
- The advantages of canopy or hood oxygen include
  - the accessibility of the patient
  - its effectiveness
  - the potential for long-term use
  - lack of humidification requirements because the airways are not bypassed
- several disadvantages including
  - oxygen leakage
  - hyperthermia
  - high humidity
  - potential CO_2 retention
  - lack of patient cooperation
  - potential variability in oxygen concentration within the hood

INTRATRACHEAL OXYGEN

- can be delivered through an endo-tracheal tube, tracheostomy tube, or transtracheal catheter
- Intratracheal oxygen supplementation is highly effective in producing desired Fio_2 and Pao_2 levels
- An intra-tracheal flow rate of 10 ml/kg/minute should ensure 97% hemoglobin saturation
- The advantages of this method include
  - higher oxygen concentration with a lower flow rate than intranasal routes
- Disadvantages include
  - the stress of placing the catheter
  - possible tracheal irritation leading to discomfort
  - kinking of the catheter at the skin entry point
  - displacement of the catheter→ subcutaneous insufflation of oxygen

OXYGEN CAGE

- provides a sealed compartment with mechanisms to regulate oxygen

concentration, ambient temperature, humidity, and elimination of expired CO_2.

- This is a noninvasive, nonstressful method of supplementing oxygen that allows accurate monitoring and control of the environment
- Disadvantages include the expense of purchasing the cage, oxygen waste, and isolation of the patient from the clinician
- Ambient temperature should be maintained at approximately 22° C (70° F) with a relative humidity of 40% to 50%

❑ **MECHANICAL VENTILATION**

- Ventilatory support is usually required in patients with either ventilatory failure or failure of pulmonary oxygen exchange due to lung disease
- Patients with high Fio_2 requirements for extended periods, respiratory fatigue or arrest, coma, increased intracranial pressure, or failure to respond to oxygen supplementation may require positive pressure ventilation

Monitoring the Response to Oxygen Therapy

❑ Clinical signs are important tools for monitoring

❑ Serial assessments of respiratory rate, respiratory effort, auscultation, mucous membranes, capillary refill time, and pulses

❑ More objective tests included

- arterial blood gas analysis
  - ◆ is the most objective technique to monitor the oxygenation and ventilatory function
  - ◆ samples should be obtained while the patient is breathing room air
  - ◆ normal values for Pao_2 and $Paco_2$ are 85 to 100 mm Hg and 35 to 45 mm Hg
  - ◆ Animals with Pao_2 values less than 70 mm Hg may require oxygen supplementation
  - ◆ those with a persistently elevated $Paco_2$ of 50 mm Hg or greater may require mechanical ventilation
- calculation of oxygen tension based indices
  - ◆ The A-a gradient is calculated from arterial blood gas results and is a sensitive measure of the efficiency of pulmonary gas exchange
    - ● estimates the adequacy of oxygen transfer from the alveolus to the pulmonary capillary blood

- reference range for the A-a gradient is less than 10 mm Hg (as much as 20 mm Hg in normal dogs)
- Gradient values greater than 30 mm Hg suggest clinically significant impairment of gas exchange.

◆ the Pao_2:Fio_2 ratio is a clinically relevant estimate of intrapulmonary shunt
- most useful in animals being supported by positive pressure ventilation
- reference range in normal dogs is 432 to 564
- less than 200 suggests serious lung disease (expected to have a positive response to oxygen supplementation)
- less than 100 indicate profound failure of gas exchange, a potentially poor response to oxygen therapy, and the probable need for positive pressure ventilation.

■ pulse oximetry
◆ is a noninvasive method of monitoring the oxygen saturation of hemoglobin (Sao_2)
◆ Based on the oxyhemoglobin saturation curve, an Sao_2 of 90% is equivalent to a Pao_2 (60 mm Hg)

Complications of Oxygen Therapy

OXYGEN TOXICITY

■ caused by lipoperoxidation of essential intracellular sulfhydryl groups and poly-morphonuclear cell infiltration
■ Formation of oxygen radicals causes direct endothelial and epithelial cell damage, leading to increased endothelial permeability, cyto-toxicity, and inflammatory activity
■ Atelectasis, interstitial and alveolar edema, pleural effusion, and changes in cell function and structure
■ The degree of oxygen exposure (i.e., lethal compared with sublethal doses) alters the end result
■ Lethal exposure
- initiation, inflammatory, and destructive phases result in the patient's death due to fulminant respiratory failure

■ Sublethal exposure
- initiation, inflammatory, proliferative, and fibrotic phases result in varying degrees of permanent parenchymal change

HYPERCARBIA

- Injudicious use of oxygen therapy leads to chronic hypercapnia (hypercarbia)
- In patients with chronic lung disease and a chronically high work of breathing, ventilatory drive results from hypoxic stimulation of peripheral chemoreceptors
- As the hypoxemia is relieved with oxygen supplementation, decreased ventilatory drive may result in a dramatic decrease in ventilation and severe hypercarbia may occur
- If the oxygen supplementation is then stopped, profound hypoxemia follows, and it may take many minutes to unload the large amount of CO_2 retained in the tissues

ABSORPTION ATELECTASIS

- If an airway becomes totally obstructed, absorption atelectasis of the lung distal to the airway obstruction may occur
- Since the sum of the partial pressures of gas in venous blood is less than atmospheric pressure, the trapped gas is gradually reabsorbed, resulting in collapse of alveoli and atelectasis
- Nitrogen slows the absorption process because of its relatively low solubility compared with oxygen
- Therefore in patients breathing high oxygen concentrations, the rate of absorption is accelerated

OTHERS

- Suppression of erythropoiesis
- pulmonary vasodilation
- systemic arteriolar vasoconstriction

Fluid Therapy in Animals with Lung Disease

- ❑ All patients with lung disease are not at risk of developing pulmonary edema.
- ❑ Rather, pulmonary edema can worsen, or can develop in addition to another primary lung disease
- ❑ if the patient's lungs are susceptible to elevations in pulmonary capillary hydrostatic pressure
  - Ex) higher rates of intravenous fluid administration
  - conditions that predispose to high pressure pulmonary edema (e.g., left-sided heart failure or insufficiency)
  - the various forms of increased permeability pulmonary edema

- Marked increases in hydrostatic pressure (i.e., intravascular volume overload) will result in pulmonary edema even when microvascular permeability is normal, irrespective of the type of fluid used
- When pulmonary microvascular permeability is increased, the fluid-retaining effect of the intravascular colloid osmotic pressure is reduced or lost, and relatively *small rises in pulmonary capillary hydrostatic pressure can then result in extensive fluid loss into the lung.*
- With high-pressure edema, increases in lung weight do not occur until pulmonary capillary pressures reach approximately 25 mm Hg
- With increased permeability edema, lung weight increases at pulmonary capillary pressures of 12 mm Hg
- In normal lungs
  - the pulmonary endothelium is relatively permeable to protein compared to other tissues
  - albumin and hetastarch molecules equilibrate rapidly with the interstitial space
  - If the increase in permeability is small, then colloid molecules will remain within the intravascular space and reduce lung water or limit its increase
  - If the increase in endothelial permeability is sufficient so that the majority of colloid molecules can pass through the pulmonary capillary endothelium, then colloid therapy may worsen pulmonary edema.
  - When administering colloid to a patient with the potential for increased pulmonary microvascular permeability it therefore makes sense to use hydroxyethyl starch, the colloid with the largest average molecular weight.
- In dogs with experimental increased permeability pulmonary edema, aggressive infusions of saline and dextran 70 caused no increase in lung weight when left atrial pressure was kept constant
- When left atrial pressure was allowed to increase, lung weight increased with both crystalloid and colloid infusion
- Smoke inhalation: dogs were given 50 ml/kg/hr of lactated Ringer's solution for 2 hours
  - had a 50% increase in lung water
  - human ARDS patients
    - the early stages: cardiorespiratory function providing that wedge pressures of 18 mm Hg were not exceeded
    - the later stages: with worsening pulmonary microvascular permeability,

colloids worsened lung function

- Patients with mild to moderate increases in pulmonary microvascular permeability may benefit from colloid infusion
- If respiratory signs worsen after colloid infusion, then it is probably inadvisable to continue colloid therapy
- Once pulmonary edema is established, *towards careful fluid restriction*
- Restriction of fluid therapy in the patient with pulmonary edema must be weighed against the potential risks (e.g., compromised renal or cardiovascular function and multiple organ failure)
- Attention has been focused on the factors involved in the formation of pulmonary edema (i.e., increased hydrostatic pressure and increased permeability)
- Fluid is cleared from the pulmonary parenchyma
  - via the bronchial circulation
  - via pulmonary lymphatics
  - by drainage into the pleural space and visceral pleural veins
  - Because the former two drain into the right side of the heart, increased cranial vena caval pressure may retard pulmonary fluid clearance
- Aggressive volume expansion in patients with uncontrolled hemorrhage is associated with increased bleeding and a higher mortality rate
- Pulmonary hemorrhage appears to be exquisitely sensitive to volume expansion.
  - Aggressive fluid resuscitation almost always worsens pulmonary bleeding, and this author considers aggressive volume expansion to be absolutely contraindicated in this patient population
- When most animals first present in left-sided heart failure, it is usually safest to treat with cage rest, oxygen supplementation, and diuresis, and not to administer any intravenous fluids for at least the first 12 to 24 hrs
  - Subsequently, animals that will not voluntarily drink sufficient amounts and that become dehydrated may be placed on low intravenous fluid rates (e.g., half of normal maintenance fluid rates) using half strength (0.45%) saline
  - Sodium overload must be avoided in these patients because they are likely to avidly retain sodium as a result of reduced effective circulating blood volume and activation of the RAAS system
  - Although administration of fluids by the subcutaneous route has less immediate effects on the intravascular compartment, it can still be associated with volume overload in susceptible patients such as those with heart disease or oliguric renal

failure

- Never hypotonic fluids given by the subcutaneous route
  - electrolytes to diffuse into the subcutaneous fluid pocket → worsening hypovolemia

- Patients with heart disease that results in diastolic dysfunction (e.g., HCM) may be more preload dependent
- In these cases, dehydration and reduced preload may precipitate life-threatening reductions in cardiac output; therefore avoidance of dehydration by use of judicious fluid therapy may be necessary
  - If possible, require intravenous fluid therapy should have a central venous catheter placed to allow monitoring of central venous pressure
- Fluid therapy in animals with pulmonary edema secondary to left-sided heart failure is potentially dangerous because of the risk of increasing the already elevated pulmonary hydrostatic pressure, and worsening pulmonary edema
- Lower intravascular plasma protein reduces the hydrostatic pressure at which high-pressure edema occurs
  - In dogs with a plasma protein concentration reduced to 47% of normal, lung water begins to accumulate at left atrial pressures of only 11 mm Hg, compared with 24 mm Hg in dogs with a normal plasma protein concentration
  - Hypoproteinemic animals in heart failure may benefit from carefully increasing the intravascular COP via colloid administration
  - Extreme caution to avoid increases in pulmonary capillary hydrostatic pressure

  - Colloid support in the patient with left-sided heart failure should only be considered in animals with significant hypoproteinemia in a critical care environment with invasive monitoring capabilities.

DRUG THERAPY OF SPECIFIC DISEASES OF THE RESPIRATORY TRACT

Therapy of Fungal Infections of the Nose

- Nasal aspergillosis:
  - Medical management accompanied by surgical debridement
  - Topical therapy includes flushing the nasal mucosa with povidone-iodine solutions (10%) every 8 hours for 6 to 8 weeks after surgery; a 10% solution of clotrimazole in polyethylene glycol, instilled in nasal tubes and administered twice daily or in direct contact for 1 hour during surgical exploration; or

enilconazole (10%) at 5 mg/kg instilled into nasal tubes twice daily for 7 to 14 days

- Topical therapy should be accompanied by systemic therapy with itraconazole

Therapy of Disorders of the Trachea

Tracheitis

- Resolution of underlying causes
- Cough can be controlled with peripheral or central antitussives or a combination thereof
- Humidifying secretions (liquification of mucoid material) becomes increasingly
- nebulization four to six times a day or exposure in a steam-filled bathroom for 15 to 20 minutes three times daily
- Physical therapy (coupage) should be implemented after liquifaction of secretions
- Short-term therapy with short-acting glucocorticoids
- Antibiotics are indicated for infectious tracheitis/tra-cheobronchitis

Hypoplastic Trachea

- Slight or moderate tracheal hypoplasia may respond to bronchodilator therapy
- Recurrent infections (bacterial) should be anticipated because of a poorly functioning mucociliary tract
- Although prophylactic antibiotic therapy is discouraged, antibiotic therapy during active infection should be anticipated
- Drugs that facilitate muco-ciliary clearance should be considered on a daily basis
- The use of bronchodilators should be considered
- Supportive actions should also include weight control, avoidance of smoke and other environmental contaminants, and avoidance of actions or drugs that cause immune compromise

Tracheal Collapse

- control of the cough with bron-chodilators and centrally acting antitussives
- Mucokinetic drugs may also be helpful
- Short-term glucocorticoid therapy may be important to minimize the inflammatory response to damage induced by paroxysmal coughing
- Nebulization may be helpful, but pretreatment with bronchodilators is

probably important

- The use of bronchodilators should be considered for their effects on peripheral airways
- Bronkoelixir, an old product containing phenobarbital as a sedative and theophylline as a bronchodilator, may prove beneficial
- Digitalization reportedly has been beneficial in some patients that do not respond to other therapies

Therapy of Bronchial Diseases

Canine Infectious Tracheobronchitis

- bacterial organism most commonly associated with kennel cough
- Therapy of uncomplicated cases is supportive
- Antitussives, in relative order of efficacy (least to most), include dextromethorphan (antitussives), butorphanal, and hydrocodone
- Hydrocodone may be associated with sedation, which may be beneficial in cases of paroxysmal coughing.
- Antimicrobial therapy in uncomplicated cases (lasting 7 to 10 days) has not been shown to decrease the time course of the disease
- most antimicrobials used empirically (i.e., amoxicillin) generally do not penetrate bronchial secretions in sufficient quantities to be effective. For the same reason, prophylactic therapy should be used cautiously.
- antibiotic therapy (in addition to other supportive therapy) is indicated for complicated infections or for dogs whose coughing persists after 2 weeks
- Antimicrobials recommended empirically include chlor-amphenicol, tetracyclines (both include *Mycoplasma* species in their spectrum), and amoxicillin.
- Animals that fail to respond to antimicrobial therapy may benefit from the addition of aerosolization with gentamicin (pretreat with bronchodilators).

Feline Bronchial Diseases

- Treatment should include environmental management
- Administration of drugs should be accompanied by oxygen therapy and rest.
- Glucocorticoids are recommended by some authors as initial therapy; however, the lag time to effect may lead to the additional use of bronchodilators as a prudent initial choice
  - β_2-Adrenergic agonists preferred

  - Parenteral rather than oral administration will ensure the most rapid onset of action
- Subcutaneous epinephrine can be administered at presentation and, if the patient responds, repeated every 30 minutes for several doses
- Terbutaline can also be administered subcutaneously either in lieu of epinephrine or for animals that fail to respond to epinephrine
- Aminophylline can be infused intravenously (2 to 5 mg/kg in 5% dextrose or saline) in animals that fail to respond to β-agonists
- The addition of atropine or glycopyrrolate may facilitate bronchodilation
- Glucocorticoid therapy should be initiated in conjunction with bronchodilators in cats with bronchial asthma
- The hydration status of the patient should be assessed at presentation and corrected if indicated
  - Overzealous fluid therapy can prove detrimental, however, and should be avoided
- Oral bronchodilator and glucocorticoid therapy can begin when the patient is stabilized
  - Repositol forms of glucocorticoids should be avoided because of the risk of exacerbation of disease
  - Intermittent high doses of intravenously administered or aerosolized glucocorticoids, and particularly beclomethasone di-propionate, in conjunction with oral maintenance glucocorticoids can be used to treat animals whose disease exacerbates
- Addition of bronchodilator therapy should be considered for animals that do not respond sufficiently to glucocorticoid therapy
- Bronchodilators may decrease the amount of glucocorticoids necessary to control clinical signs
- Oral theophylline is the bronchodilator most commonly used for long-term bronchodilator therapy in dogs and cats
- The use of cyproheptidine and leukotriene receptor antagonists as anti-inflammatories should be considered in cats that have not sufficiently responded to or cannot tolerate glucocorticoid or bronchodilator therapy

Canine Bronchitis

- The eradication of the underlying cause is paramount to therapeutic success

- Medical management of chronic airway disease in dogs should be accompanied by weight loss and physical therapy
- Allergic bronchitis is not a common or easy diagnosis in dogs
  - glucocorticoids are indicated
- Bronchodilator therapy provides the mainstay of medical management of chronic bronchitis in many dogs
- Night-time (rather than day time) administration of short-acting theophylline products is not indicated for dogs
- Both terbutaline and albuterol can be used for dogs and might be considered in combination with theophylline for nonresponders for which therapeutic concentrations of theophylline have been maximized or on an alternate basis with theophylline
- Control of inflammation may be facilitated by the use of N-acetylcysteine; additionally, its expectorant and muco-lytic effects also should prove beneficial
- Leukotriene receptor antagonists should be considered as well
- Glucocorticoids should be used only if cytologic examination indicates a large mononuclear or predominantly eosinophilic component to the inflammation
- Antimicrobial therapy should target *Bordetella*
- The potential of infection with *Mycoplasm* should not be overlooked
- The role of antitussives in the treatment of diseases depends on the character of the cough
- Antitussives are generally indicated if the cough is nonproductive
- In the case of productive cough
  - the use of expectorants or mucolytics may actually exacerbate cough
- Hydration of respiratory secretions is critical to effective mucociliary transport function
  - diuretics are contraindicated, and daily water intake must be maintained

Therapy of Pulmonary Diseases

- Supportive therapy should include bronchodilators and a means to maintain airway hydration (mucokinetics or mucolytics)
- N-acetylcysteine should be considered for both its anti-inflammatory and mucolytic actions
- Bronchodilators should not be used indiscriminantly
  - They may also be associated with ventilation-perfusion mismatching
- Diuretics are contraindicated unless vascular overload has led to pulmonary edema.

- Oxygen is a consistent supportive therapy for the hypoxic animal
    - positive-pressure ventilation is indicated for patients with poor pulmonary compliance
- Physical therapy (coupage) is indicated in conditions associated with accumulation of respiratory secretions
- Glucocorticoids are indicated for selected acute and chronic inflammatory conditions
    - Methylprednisolone is often recommended for immediate short-term therapy because of its ability to scavenge oxygen radicals.

Bacterial Pneumonia

- Antimicrobial therapy can begin once cultures have been collected
- Although chloramphenicol and trimethoprim-sulfonamide combinations are inexpensive drugs likely to be effective against these organisms as well as gram-positive cocci
- Amoxicillin-clavulanic acid and first-generation cephalosporins are also good to excellent choices
- Enrofloxacin should also be effective against both gram-positive and gram-negative organisms

Mycotic Pneumonia

- Treatment of mycotic pneumonia is generally considered a life-threatening situation
- Treatment is prolonged, costly, and often includes drugs whose use is limited by toxicity
- Treatment is recommended even for mild infections with itraconazole or, less ideally, ketoconazole
- For severe diseases, amphotericin B should be combined with an imidazole
- Likewise, with increasing severity of infection, or in the presence of renal disease, amphotericin B should be combined with an imidazole for treatment of blastomycosis.
- Resistance of coccidioidomycosis to amphotericin B may lead to itraconazole as the drug of choice
- Ketoconazole is a less ideal drug for treatment of coccidioidomycosis
- Treatment with an imidazole can continue after amphotericin B has been discontinued and should continue for several months beyond resolution of clinical

signs of disease

- Amphotericin B, ketoconazole, or itraconazole is indicated for treatment of cryptococcosis

Parasitic Disease

- In cases of severe inflammatory response, a single treatment with a glucocoricoid may be life saving
- Other supportive therapy includes bronchodilators
- *Paragonimus kellicotti* may respond to praziquantel or fendbendazole
- *Aelurostrongylus* infection may be self-limiting; Fenbendazole and ivermectin
- *Capillaria aerophila* also may be self-limiting; treatment with fenbendazole or ivermectin, levamisole
- *Fileroides hirthi*; Albendazole or fenbendazole

Immune-Mediated Diseases

- Medical management should be accompanied by removal of any suspected allergen
- Immunosuppressive doses of glucocorticoids are indicated for animals that do not respond to environmental changes
- An exception is made for eosinophilic granulomatosis, for which cytotoxic drugs (cyclophosphamide) are indicated
- For nongranulomatous disease, glucocorticoid therapy may need to be long term
- Combination therapy should include cyclophosphamide and immunosuppressive doses of prednisone

Therapy of Vascular Diseases

Pulmonary Hypertension

- is most commonly a secondary problem
- focus on eradication of the underlying cause
- precapillary; alveolar hypoxia caused by lung disease or high altitude)
- postcapillary; congenital heart disease with left to right shunting of blood or acquired heart disease
- Dirofilariasis is probably the most common cause of pulmonary hypertension in dogs
- bronchial asthma might be a cause in cats
- no drugs have been found that can be used in the clinical environment to cause

pulmonary arterial dilation while avoiding systemic arterial vasodilation

- use of pulmonary vasodilators is generally accompanied by undesirable systemic hypotension and tachycardia.

Pulmonary Edema

- Diuretics are indicated for treatment of pulmonary edema associated with volume overload
  - Drugs that cause sodium and chloride excretion (i.e., furosemide) may be more effective, particularly in cases of sodium and water retention
  - Diuretics are contraindicated for patients that are hypovolemic
- Pulmonary edema associated with volume overload; venous dilators can be used to increase the capacitance of the vascular system
  - Topically applied nitro-glycerin or morphine sulfate (0.1 mg/kg intravenously as needed)
- Methylxanthines such as theophyl-line might be helpful in the short term because they also bronchodilate
- Glucocorticoids might be indicated to decrease inflammation and support bronchodilation, although their use is controversial
- Among the glucocorticoids, methylprednisolone should be considered

Miscellaneous

Aspiration Pneumonia

- Oxygen therapy, bronchodilatory therapy, and positive-pressure ventilation are indicated, the latter particularly for patients with poor pulmonary compliance
- Bronchoscopy can be used to guide removal of visible foreign material
- Glucocorticoids might be used to minimize the inflammatory response during the initial phase of therapy; methylprednisolone and an N-acetylcysteine might be considered to minimize oxygen radical damage
- Routine antibiotic coverage is controversial; antibiotic therapy might be more appropriately held until evidence of infection exists

Near Drowning

- Standard supportive therapy for near drowning includes oxygen, positive-pressure ventilation, and therapy for shock
- Bronchodilators may be of benefit

- Use of glucocorticoids is controversial; however, use of methylpredniso lone is appealing
- N-acetylcysteine therapy may be useful for its oxygen radical scavenging effects as well as other benefits.
- Use of antimicrobials should probably be reserved for evidence of infection
- Supportive therapy should also target the advent of cerebral edema

Smoke Inhalation

- Oxygen therapy is critical for removal of carbon monoxide; the half-life of carboxyhemoglobin reduces from 4 to 0.5 hours in the presence of 100% oxygen
- Other supportive therapy includes airway hydration (as needed), bron-chodilators, and, if indicated, positive-pressure ventilation
- Short-term administration of glucocorticoids (methylpred-nisolone preferred) may be of benefit to minimize inflammation and oxygen radical damage and to facilitate bron-chodilation.

Empyema

- Empyema refers to the accumulation of infectious inflamnatory material within the pleural space
- Empirical therapy should include drugs effective against anerobic organisms
- Clindamycin is recommended for treatment of empyema in cats but could also be considered for dogs
- Both clindamycin and amoxicillin/clavulanic acid can be combined with a number of drugs effective against gram-negative organisms, including amikacin or enrofloxacin.
- The use of pleural lavage as supportive therapy is controversial
- Certainly lavage is more indicated in the initial stages of therapy to remove inflammatory debris that might be blocking lymphatic or other drainage pathways
- Addition of heparin may help reduce fibrin formation as well as potentiate phagocytosis of the debris by macrophages
- Use of proteolytic enzymes in lavage fluid is unsupported.