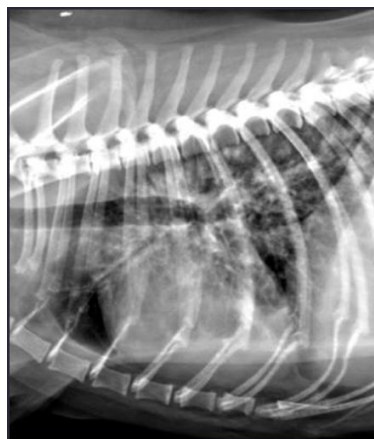




Emergency Club Webinar- Ventilator Therapy in Small Animals

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Respiratory failure and ventilators

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Abbreviation

A – a alveolar to arterial gradient

A/C assist control ventilation

ARF acute respiratory failure

CO cardiac output

CPAP continuous positive airway pressure

FiO₂ inspired oxygen concentration

FRC functional residual capacity

IMV intermittent mandatory ventilation

PaO₂ arterial partial pressure of oxygen

PaCO₂ arterial partial pressure of carbon dioxide

PEEP positive end expiratory pressure

P:F PaO₂/FiO₂

PIP peak inspiratory pressure

PPV positive pressure ventilation

PSP pressure support ventilation

SIMV synchronised IMV

V_t tidal volume

V/Q ventilation to perfusion gradient

Overview of positive pressure ventilation

The main goal of ventilation is to reduce the work of breathing until the cause of respiratory failure is reversed. Positive pressure ventilation (PPV) has been used in human medicine for over 50 years and companion animals have been reaping the benefit of this human advancement. This talk will focus on invasive methods of ventilation as currently there is no evidence to support benefit in cardiopulmonary indices with non-invasive (fitted face mask) in animals.¹ The reported overall survival to discharge of dogs undergoing mechanical ventilation ranges from 20% to 33% for parenchymal disease and 57% to 71% in patients with neuromuscular disease.²

Ventilation is defined as the to-and-fro, valveless pumping of air into and out of the pulmonary system. This requires regulation of the muscular component by the nervous system to allow the alveoli as an oxygen and carbon dioxide exchange membrane to perform its task. During normal ventilation (negative pressure ventilation), pressures in the airways and pleura decrease during inspiration. When one of these ventilator components are compromised i.e. diffusion surface, circulatory failure or muscular or nervous system failure then mechanical ventilation can perform the function of ventilation. During a ventilation compromised patient with hypoxaemia, as much as 30 to 40% of cardiac output (CO) (normal 2-5%) can perfuse through the diaphragm at the expense of vital organs like the brain and kidneys. Excess work of breathing can lead to respiratory fatigue and hyperthermia.

Positive pressure ventilation is contra-indicated in closed thorax pneumothorax until thoracostomy tubes or thoracotomy is performed to relieve the tension pneumothorax.

Indications and predicted outcomes

If the problem is significant enough to warrant you asking the question, then the problem is significant enough to ventilate.

It is important to inform the owner about ventilator outcomes before intubation as it carries a poor prognosis with large financial implications. The indications for PPV can broadly be categorised into two groups: inadequate blood oxygenation because of diffuse parenchymal disease and inadequate elimination of carbon dioxide and differ significantly in their prognosis². Mechanical ventilation is indicated for any patient whose arterial partial pressure oxygen (PaO₂) drops below 50 – 60 mmHg on supplemental oxygen or arterial partial pressure of carbon dioxide (PaCO₂) increases above 50 - 60 mmHg or for any animal that is in danger of impending respiratory failure due to the excessive energy required for ventilation (work of breathing is excessive).³ Therefore ventilated patients are largely divided into two groups, those with difficulty oxygenating (hypoxaemic respiratory failure) and those with difficulty ventilating (hypercapnoeic respiratory failure).

Hypoxaemic respiratory failure, also known as type I acute respiratory failure (ARF), lung failure, oxygenation failure exists when the lungs fail to absorb sufficient oxygen to meet the metabolic needs of the body.³ This can be caused by four classes of disease viz. 1. Insufficient gas exchange at the level of the alveoli and pulmonary vasculature, such as thickening of the diffusion barrier as in the case of acute respiratory distress syndrome (ARDS), 2. Shunting, the diversion of blood around the pulmonary vasculature as in the case of Eisenmenger syndrome or reverse patent ductus arteriosus, 3. Ventilation to perfusion (V/Q) mismatch such a pulmonary thromboembolism (PTE) reducing perfusion or atelectic lung from contusion not ventilating and 4. Decreased inspired oxygen concentration (FiO₂).³ The most common aetiologies in practice that cause hypoxaemic respiratory failure include, pulmonary contusion, near drowning, pneumonia, aspiration of gastric content and cardiogenic pulmonary oedema. Overall, dogs with parenchymal disease have much lower successful weaning, survival and discharge rates than do dogs with hypoventilation. In a study examining outcome of dogs with prolonged PPV, only 22% of dogs with hypoxaemia as the reason to ventilate survived.² Cats are also reported to have a much lower weaning rate than dogs, as are smaller dogs.² Age of the dog impacted outcome with every increase in year of age, would reduce the odds of survival by 10%.² Overall dogs with ARDS did the worst of all groups and severity of lung injury could be predicted by PaO₂/FiO₂ (P:F), with a higher P:F ratio associated with successful weaning.² Overall, brachycephalic dogs are more likely to receive mechanical ventilation than non-brachycephalic dogs, surprisingly the indication was hypoxaemia caused by aspiration pneumonia rather than hypoventilation from airway obstruction⁴. Aspiration pneumonia is a common complication of brachycephalic airway syndrome, but do not fair worse in weaning rates as compared to the general dog population.⁴ In this group of dogs (brachycephalics) weaning is the most challenging aspect if airway obstruction has not been corrected surgically, and the effect of laryngeal paralysis as a consequence of reduced pharyngeal muscle tone. Abrupt hypoxia in these dogs have a strong pharyngeal muscle reflex causing upper airway obstruction, tracheostomy in most instances is unhelpful in successful weaning.⁴ Acute respiratory distress syndrome (ARDS) has been defined in the veterinary literature by a consensus statement as fulfilling five criteria, acute onset of respiratory distress, a known risk factor, pulmonary capillary leak in the absence of increased pulmonary capillary wedge pressure, evidence of inefficient gas exchange with evidence of inflammation.⁵

The existence of ARDS in cats is questionable. ARDS will develop with 24-48 hr of an inflammatory process or tissue trauma. There are thought to be three stages of ARDS, exudative, proliferative and fibrotic.

Patients suffering from hypercapnoeic respiratory failure have normal lung parenchyma but lack sufficient ventilation of the pulmonary system. This manifests in respiratory acidosis due to elevated PaCO₂.³

The aetiologies for this condition include pathology at the level of the central nervous system such as general anaesthesia, opioid overdose, damage to the efferent nerves of the respiratory muscles such as cervical cord injuries and lower motor neuron (LMN) disease including polyneuropathies and neuromuscular junctionopathies.⁶ Acute lower motor neuron diseases include polyradiculoneuritis, botulism, tick paralysis, myasthenia gravis, polymyositis, severe hypokalaemia, organophosphate or aminoglycoside toxicity and snake envenomation.⁶ Many of these dogs may have hypoxaemia as a complication of the disease (organophosphate toxicity or tick paralysis) or as a result of aspiration pneumonia due to laryngeal paralysis. In human patients with LMN disease the mechanism of ARF is multifactorial, with the 4 contributors being upper airway dysfunction, inspiratory muscle weakness, expiratory muscle weakness and pulmonary complications associated with this condition. In a study examining outcome of dogs with LMN disease as a cause of hypercapnoea, the majority suffered from myasthenia gravis followed by polyradiculoneuritis as the next most common aetiology. In the author's hospital setting (OVAH) the most common reason for ventilating a patient with LMN would include neurotoxic snake envenomation, organophosphate toxicity and cervical cord damage. Dogs would have a history of weakness; neurological clinical findings would include decreased spinal and cranial nerve reflexes (including laryngeal paralysis), tetraplegia (possibly ascending)². The indications in this group of dogs for ventilation included hypercapnoea, hypoxaemia, widened alveolar to arterial (A-a) gradient in dogs not receiving arterial oxygen (normal reference < 15 mmHg).⁶ Interestingly hypercapnoea is a late event in hypoventilation in humans and the decision to ventilate is made much earlier in the course of the disease when vital capacity and maximum inspiratory and expiratory pressures are reduced. Approximately a third of all dogs in this study developed ventilation associated pneumonia (VAP) or ventilator associated pneumothorax. All VAP were multi-drug resistant bacteria. In addition post-mortems in non-survivors detected oesophageal and gastric ulcers. Many dogs were euthenised due to lack of clinical response of the neurological disease and cost constraints rather than ventilation failure. In this study a total of 6 out of 14 dogs were successfully weaned from the ventilator with a mean of 55 hours of ventilation but only 3 surviving (discharged) due to relapse or tracheostomy complications. The main complicating factors were iatrogenic complications, which are far less frequently found in human ventilation due to improved experience. An earlier study demonstrated much higher survival rates in dogs with hypoventilation: 86% of dogs with toxicosis, 57% of dogs with LMN disease, 50% survival after cervical cord disease.² Further, only a 7% incidence of pneumothorax was reported in this study. The intermediate syndrome of organophosphate poisoning (OP) was introduced into the veterinary literature in 2002.⁷ The most common presentation of OP is an acute cholinergic crisis (salivation, lacrimation, urination, diarrhoea, emesis, muscle stiffness and possibly seizures). Chronic OP has been reported to present as a polyneuropathy several weeks after the intoxication, known as OP-induced delayed neuropathy (OPIDN) characterised by weakness, ataxia and proprioceptive deficit disorders of the hindlimbs.

A third syndrome called intermediate syndrome that develops 7 to 96 hours after an acute cholinergic crisis, causing muscle weakness of the forelimbs, neck flexor muscles and respiratory muscles. The aetiology is thought to be prolonged acetylcholine esterase inhibition. Hypoventilation is the most significant complication in the intermediate syndrome of OP in dogs and in a case report SIMV for five days was used as supportive care and life-saving initially with intubation and later with tracheostomy.⁷

Criteria for diagnosing respiratory failure⁶

Arterial blood gas needs to be conducted on blood collected from the dorsal pedal or the femoral artery. A pre-filled heparin (1:1000 U/ml) syringe should be used, avoiding dilution. The sample should be analysed immediately and within 2 hours if stored in ice. The most important parameter to assess is the PaO₂, ideally PaO₂ should be five times inspired oxygen (FiO₂) or a PaO₂/FiO₂ ratio. At sea level PaO₂ (of the partial pressure the oxygen molecules in the blood exert) should be > 80 mmHg.

Hypoxaemic respiratory failure

PaO₂ < 60 mmHg at an FiO₂ > 0.5 or a PaO₂ < 40 mmHg on any FiO₂, SPO₂ < 90%, A-a gradient > 25 mmHg (breathing room air), P:F < 300 (ALI/ARDS).

Hypercapnoic respiratory failure

PaCO₂ > 50 mmHg or PvCO₂ > 60 mmHg with hypoventilation, the physical examination of apnoea or weak ventilator efforts with minimal air movements.

Anaesthesia

Pre-oxygenation of the airways and rapid control of patent airways is essential. The induction of anaesthesia is dictated by the cardiovascular status of the patient. The patient is kept at a level of anaesthesia by means of total parenteral anaesthesia. Combinations of drugs are used including a benzodiazepam, propofol with an opioid. Long-term use of propofol can cause haemolytic anaemia in cats and hyperlipidaemia in general. Pentobarbital infusion is the main anaesthetic drugs for patients on ventilators long-term.

Modes of ventilation

The aim of ventilation (positive or negative) is to meet a target tidal volume (V_t) to create a normal PaO₂ and PaCO₂. This is achieved with PPV by the application of any pressure higher than atmospheric pressure to the airway. The physical factors in achieving PPV are volume, pressure, time and flow. The physical factor that will end the inspiration is used to classify the type of PPV which could be, volume-cycled (delivers a preset V_t) or pressure-cycled (delivers variable volume until a preset pressure is reached).

Pressure-cycled ventilators are not ideal for reduced lung compliance as the airway pressure can be reached with low V_t . Pressure support ventilation will relieve respiratory muscle work, it helps overcome the resistance of the tubing during weaning, it prevents respiratory muscle atrophy and improves patient comfort.

The ventilator has various modes of ventilation. Intermittent mandatory ventilation (IMV) is an outdated method of ventilating, it works independent of the patient's spontaneous breathing and will provide a set PPV at a set time interval. Synchronised IMV (SIMV) synchronises the patient's efforts (reduced patient-ventilator dyssynchrony) but once a breath is started it is ventilator driven. If the patient's breath rate is too little a default ventilator breath rate kicks in (mandatory breath). Assist control (A/C) either delivers a preset ventilator breath or allows the patient to trigger a breath and then is assisted by the ventilator.

A patient that has no respiratory drive would benefit from SIMV, a patient with normal respiratory drive but cannot achieve adequate V_t would benefit for A/C. However in a panting animal, A/C will lead to hypocapnoea and respiratory alkalosis.

Positive end-expiratory pressure (PEEP) increases end-expiratory pressure above atmospheric pressure, used to keep alveoli open (prevent shear force from opening and closing). The main indication is atelectasis. Traditionally PEEP is only used during PPV breaths, but can be applied continuously known as continuous positive airway pressure (CPAP), the pressure can be individually set for inspiration and expiration (bilevel PAP).

Ventilator settings³

Tidal volume must be calculated for the patient. Recommendations are low tidal volumes in the case of ventilating a patient with ARDS (6ml/kg) to 15-20 ml/kg in patients that are hypoventilating. The dead space in the pipes needs to be added to this.

PEEP can range from 0 cmH₂O to 15 cmH₂O but usually started at 3 cmH₂O.

Respiratory rate is adjusted according to the PaCO₂ ($RR \times PaCO_2 / \text{desired } PaCO_2$). For hypercapnoeic dogs the RR is higher, dogs with ARDS are put on settings for permissive hypercapnoea so RR are much lower. Target PvCO₂ at 40-60 mmHg (38-45 mmHg in patients with brain disease) or PaCO₂ at 35-55 mmHg (35-55 mmHg in dogs with brain disease). Hypercapnoea during ventilation could be caused by excessive dead space in tubing, kinked or obstructed tube or airway or possibly a pneumothorax.

FiO₂ is set at 1.0 as the starting point in order to prevent hypoxia being a complication of ventilator acclimatisation. The FiO₂ should not exceed 0.6 for prolonged periods.

Inspiratory time should be maintained at 1.5 to 2.5 seconds with an inspiratory to expiratory ratio of 1:1.5 to 1:3.

Most patients will ventilate better in sternal recumbency. Both sides of the thorax should be auscultated to ensure ventilation is diffuse.

Settings for hypoxaemic dogs

SIMV mode, FiO₂ of 1, V_t of 6 – 8 ml/kg, RR of 15 bpm (or lower), PEEP of 5 cmH₂O.

The inspiratory time can be prolonged up to 2.5 s.

Settings for hypercapnoeic dogs

SIMV mode, FiO₂ of 0.2-0.4, V_t of 15 ml/kg, RR of 12 bpm (increased based on PaCO₂), PEEP of 0 cmH₂O. Inspiratory time is maintained at 1 s.

Pathophysiological mechanisms of ventilator injury³

A retrospective case series examining ventilator associated diseases (n=41) showed a 56% of cases developed complications⁸. A total of 6 dogs (14.6%) developed ventilation induced pneumonia (VAP) with confirmed infiltrates on radiographs. Less common complications include corneal ulcers, gastric ulcers, muscle atrophy, limb compartment syndrome, pressure sores and machine failures. Some more common complications with potentially fatal outcome are discussed.

Ventilator-induced lung injury (VILI) includes volutrauma which is caused by overexpansion of the alveoli secondary to high lung volume. Secondly, atelectrauma caused by shear stress with repetitive alveolar recruitment-derecruitment. This can be overcome by employing PEEP. Lastly biotrauma which is alveolar injury secondary to cytokine release in response to mechanical injury.

Barotrauma (or volutrauma depending on ventilator setting), lung damage due to changes in intrathoracic pressure with leakage of air to extra-alveolar space including pneumomediastinum, emphysema, pneumothorax and subcutaneous emphysema. In a study of dogs with LMN that were ventilated, those dogs that developed barotrauma did not survive⁶. Dogs are at risk of barotrauma when high airway pressures are used (> 30 cm H₂O). Thus for ARDS, a disease characterised by low compliance in order to avoid barotrauma, lower tidal volumes are indicated (6 ml/kg). Higher PEEP values could contribute to barotrauma due to higher peak airway pressures.

Ventilator induced pneumonia (VAP) is responsible for significant morbidity and mortality. This is primarily a nosocomial infection and thus steps to reduce the incidence include hand washing and gloving. Breaking the circuit for intermittent suctioning is a contributory factor.

The ventilator itself including the tubing with continual humidification is a source of infection. Changing the tubing regularly should be considered (every 24-48 hr). In humans, patient positioning can contribute and thus the standard position is elevating the head of the patient to reduce aspiration of gastric secretions. The selection of an inappropriate antibiotic is an independent risk factor for death in humans with VAP. Prior exposure to antibiotics at the time of diagnosis of VAP is associated with resistance. The biggest culprits are fluoroquinolones (2.5 fold increase). Up to 60% are gram positive organisms. Methicillin resistant *Staphylococcus aureus* accounts for 50-70% of gram positive organisms, with many now Vancomycin resistant. Shorter antibiotic courses are now indicated (8 days versus 15 days). Selective decontamination of the digestive tract (SDD) is a therapy that has shown promise in reducing both the incidence and mortality associated with VAP, by administering a non-absorbable, topical antibiotic orally. The use of SDD may be associated with resistance.

Oxygen-induced lung injury, due to the generation of free radicals resulting in cellular injury. The extent of damage is related to the duration of exposure and the concentration of oxygen. FiO_2 of 1.0 for 48 hours caused death in animal. This can be mitigated by reducing FiO_2 to less than 0.6 after 12 hours of ventilation.

Excessive drying of the mucous membranes can lead to large volumes of tenacious mucous leading to clogging of the endotracheal tube which could also lead to disproportionate ventilation of the lung.

High mean airway pressure, a function of RR, PIP, inspiratory time and PEEP. Decreased CO, due to compression of the pulmonary blood vessels by high mean airway pressure, leading to reduced venous return to the left heart and a decreased CO. This will be exacerbated by low circulatory volumes. This can compromise renal perfusion with reduced glomerular filtration rate.

PEEP, which increases FRC and stents smaller airways preventing alveoli collapsing and thus reduces shear force damage, will contribute significantly to increasing mean airway pressure. This will reduce venous return to the left heart, increased right ventricular afterload, increase pulmonary artery pressures and right ventricular end diastolic volume reducing right ventricular ejection fraction, shifting the interventricular septum to the left and further limiting left ventricular distensibility. Essentially PEEP will induce pulmonary hypertension.

Increased intracranial pressure due to impending venous return from the jugular veins.

Increased incidence of gastric ulceration and liver dysfunction, with reduced GFR, assumed to be as a result of reduced CO.

Ventilator induced increased secretion of anti-diuretic hormone (ADH) will cause a syndrome of inappropriate ADH secretion with decreased urine output. This will manifest in water retention and possible oedema formation.

Implementation of care bundles (check lists) reduced ventilation time and complications considerably in human ICU ventilator patients. These are checklists to ensure clinicians from different departments and ICU staff, do not miss straightforward treatment and monitoring.

Recommended precautions would be alteration of drug dosing based on liver and kidney dysfunction, judicious use of PEEP in intracranial disease, monitoring CO and perfusion of the kidneys by measuring urine output (indwelling urinary catheter) and in general by lactate concentration. Cardiovascular monitoring including blood pressure, ECG, pulse oximetry and capnography should be considered. Changing tubes and wearing sterile gloves can reduce nosocomial infections while oral disinfection (chlorhexidine oral rinse) can reduce infection rates. Frequent screening for corneal ulcers by fluorescein stains. Regular repositioning of monitoring equipment to prevent lingual pressure as well as deflating ET tube cuff and repositioning to avoid tracheal mucosal necrosis. Enteral nutrition and prokinetics (metoclopramide) must be started in any dog undergoing prolonged resuscitation (> 24 hr) with steps to avoid silent aspiration. Limbs should be padded and passive range of motion should be started to prevent muscle atrophy. High frequency ventilators deliver very small V_t at about 100-300 breaths/minute, require low PIP, thus will not reduce CO and can be used in hypovolaemic patients.

Failure of a patient to respond to ventilator therapy and has a $PaO_2/FiO_2 < 50$ mmHg is a candidate for extracorporeal membrane oxygenators. Essentially this is a lung bypass system employing an artificial membrane to oxygenate blood and carbon dioxide extraction.

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