**Maintenance of equine anaesthesia over the last 50 years: Controlled inhalation of volatile anaesthetics and pulmonary ventilation**

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**Introduction**

In the first edition of this journal Barbara Weaver wrote a review titled ‘Equine Anaesthesia’ [1], stating, that, at that time it was quickly becoming accepted practice that many horses were being anaesthetised “by essentially similar procedures, i.e. premedication, induction and then maintenance by controlled inhalation.” Her review focussed upon the last procedure. Maintenance of anaesthesia through controlled inhalation implies that an anaesthetic agent can be suitably delivered via the respiratory system and that ventilation is sufficiently maintained to deliver that agent and maintain adequate gas exchange. In her review, Weaver [1] stated; “the introduction of Halothane has meant that deep anaesthesia may be employed to produce relaxation with reasonable safety, provided sufficient care is taken.” The remainder of her review discussed problems encountered with pulmonary ventilation in horses. Weaver [1] outlined that adequate pulmonary ventilation depends on an appropriate tidal volume, an even distribution of fresh gas throughout the alveoli, on adequate diffusion across the alveolar epithelium and capillary wall and finally on an adequate circulation to guarantee pulmonary capillary perfusion to take up O2 and give off CO2.

50 years later- nearly all equine anaesthetics, where anaesthesia is anticipated to last over 90 minutes (beyond the safe administration time limit on standard total intravenous anaesthetic protocols), will still be based on the delivery of a halogenated inhalation agent in a carrier gas and we still face challenges to maintain pulmonary ventilation and oxygenation during spontaneous and controlled mechanical ventilation.

So what has changed? In this ‘state-of-the-art’ review we aim to review the evidence that underpins current practice of maintenance of anaesthesia focussing initially on inhaled anaesthetic agents before discussing the physiology of pulmonary ventilation in horses and how this is altered by anaesthesia. Finally we will outline how we can control pulmonary ventilation in the anaesthetised horse.

**Part 1: Inhaled Anaesthetic Agents**

**Halothane**

During the 1960’s, chloroform, cyclopropane and halothane were listed as being used as inhalation maintenance agents at one centre, but, halothane was seen as superior over the alternatives for providing better relaxation, and by delivering it with oxygen, via a breathing system and endotracheal tube, it allowed for prolonged anaesthesia [2]. The ability to utilise halothane to maintain anaesthesia for longer periods without apparent penalty on fatalities or recovery times (compared to chloroform or cyclopropane) should not be underestimated in its impact on facilitating the development of modern equine surgical techniques. By the early 1990’s, when halothane was still the predominant inhalation agent used, the majority of anaesthesia times were >60mins with many lasting significantly longer than that [3].

However, even during its early utilisation or shortly afterwards, it was recognised that maintenance of anaesthesia with halothane in horses was not without problems. Large alveolar-arterial oxygen differences were shown to occur [4]. Halothane was shown to sensitise the equine myocardium to cathecholamines [5], as well as significantly reduce cardiac output [6] and, post-anaesthetic lameness (later to become known as post-anaesthetic myopathy) was being reported in the early 1970’s [7]. Over the years, halothane’s deleterious side-effects became well characterised: including, a reduction in cardiac output and arterial blood pressure as anaesthetic depth increases, an effect significantly exacerbated by positive pressure ventilation [8], hypoventilation [4], and significant biodegradation in the liver [9] leading to concerns of toxicity in patients and theatre personnel.

Halothane’s deleterious effects meant that the search for an alternative inhalation agent was constant. Enflurane and methoxyflurane, were rapidly dismissed for muscle twitching / convulsions [10] and prolonged recoveries [11] respectively. After early concerns surrounding possible carcinogenic properties proved to be wrong, isoflurane became available for clinical veterinary use in the mid-1980’s in the UK and USA [12; 13].

**Isoflurane**

Isoflurane received a great deal of attention as repeated laboratory and small-scale clinical studies provided evidence of many superior properties compared to halothane. It was less soluble in blood (the blood-gas partition co-efficient (λb/g)[[1]](#footnote-1) of isoflurane in horses is ~ 0.92 compared to ~ 1.66 for halothane)[14], meaning that changes in anaesthetic depth and more rapid recoveries could be achieved [11; 12; 15]. Under spontaneous ventilation, although isoflurane’s cardiovascular depressive effects were similar to halothane, the mechanism through which this occurred was mainly vasodilation [16; 17] (compared to the direct myocardial depression caused by halothane), and as a result, isoflurane was shown to have less severe cardiovascular depression relative to halothane when administered under higher doses (>1.5 x Minimal Alveolar Concentration (MAC)) and positive pressure ventilation [8; 18; 19]. Isoflurane was shown to protect the canine myocardium against cathecholamine induced arrhythmias [20], and to maintain better femoral perfusion/ muscle microcirculation compared to halothane [17; 18; 21; 22]. Isoflurane also maintained better circulatory function during prolonged hypoxaemia compared to halothane [23]. Isoflurane was shown to undergo minimal biodegradation, reducing toxicity concerns for patients and theatre personnel, and being a more stable molecule, not requiring a preservative eliminated the risk of preservative accumulation in vapourisers [13].

There were some properties of isoflurane that compared less favourably to halothane, it was shown to cause more severe respiratory depression in terms of respiratory rate [15] and apnoeic index (multiple of MAC of inhaled agent when apnoea occurs) [10], and to be less potent (MAC of ~1.3% c.f. ~0.9% for halothane), using more volume of isoflurane per hour of anaesthesia, which meant that it was significantly more expensive to use in the early days when the cost of isoflurane was initially far higher than halothane.

The burgeoning evidence of the many possible attributes of isoflurane led many equine anaesthetists to begin to use it instead of halothane for maintenance of anaesthesia, either completely, or in certain circumstances. After two large scale observational epidemiological studies into the causes and risk factors for peri-anaesthetic equine fatalities had identified ‘cardiac arrest or cardiovascular collapse’ as the most common cause of death of horses in the peri-anaesthetic period [22], a multi-centre prospective randomised controlled comparison study of over 8000 equine anaesthetics was designed to determine if isoflurane was ‘safer’ than halothane (CEPEF-3) [24]. Surprisingly, despite all the *a priori* evidence, this study did not demonstrate any difference in the mortality rate between halothane and isoflurane anaesthetised horses, although it did show a greater proportion of the deaths associated with halothane were due to cardiac causes (implying isoflurane was associated with more deaths caused by other means) [25].

Since CEPEF-3, isoflurane has remained the predominant inhalation agent utilised to maintain anaesthesia in horses, partly due to difficulties in some countries in obtaining/ maintaining supplies of halothane, partly because isoflurane became much less expensive as rival manufacturers were able to market it and partly because of the evidence of its many attributes as well as refinements to anaesthetic protocols/ techniques to minimise some of isoflurane’s deleterious side effects e.g. increased use of controlled mechanical ventilation to counter respiratory depression. During this time, two other halogenated inhalation agents have been studied as potential agents for use in horses, sevoflurane and desflurane.

**Sevoflurane and desflurane**

The first reports of sevoflurane and desflurane use in horses were in 1994 [24; 26] and 1995 [27] respectively. Both agents are similar in chemical structure to isoflurane. As such, both sevoflurane and desflurane possess many of the physical properties of isoflurane but there are some important differences. Like isoflurane, both sevoflurane and desflurane cause dose-related respiratory depression and a reduction in respiratory rate and have a low apnoeic index [16; 28-30]. Sevoflurane produces a similar dose-related reduction in cardiac output and systemic vascular resistance to isoflurane [15; 28], although it may produce slightly less profound effects on vasomotor tone [31]. Desflurane appears to have reduced dose-related cardiovascular depression effects [27; 29] compared to halothane, isoflurane and sevoflurane.

Both sevoflurane and desflurane have lower solubilities (λb/g sevoflurane in horses ~ 0.47, λb/g desflurane in man ~ 0.57)[14; 32] compared to isoflurane and should produce more rapid changes in depth and recovery from anaesthesia, with desflurane having a very low blood-gas partition coefficient near to that of nitrous oxide [33]. However, studies showing significant differences in recovery times when comparing between these agents or between these agents and isoflurane, are few (e.g. [16; 34; 35]), and others show no difference [36] or contradict the expectation of faster recoveries with the lower solubility agents [37], but desflurane has been consistently shown to produce ‘fast’ recoveries [26, 33].

Other ‘issues’ with sevoflurane and desflurane include: lower potency (higher MAC values: ~2.3% for sevoflurane and ~7.0-8.0% desflurane), which increase expense of use per hour of anaesthesia [31], neither are licensed for use in horses (UK), and in the case of desflurane may affect the concentration of oxygen deliverable to the patient. The high vapour pressure/ low boiling point (22.8oC) of desflurane means that it requires a vapouriser that requires a power supply to allow it to act like a kettle to deliver calibrated amounts of vapour. Sevoflurane reacts with dry soda lime to produce Compound A, a substance shown to have nephrotoxic effects in rats [38], but while serum fluoride levels have been shown to increase in horses anaesthetised with sevoflurane, the clinical effects, even after 10 hours of exposure, were judged minimal [39]. Currently, desflurane is not widely used in equine anaesthesia, at least partly due to the fact that many equine anaesthetists find the recoveries too ‘fast’, but sevoflurane has become popular with some anaesthetists [40].

**Inhaled anaesthetic agents: problems for recovery?**

Whilst the number of anaesthetic-related fatalities attributed to ‘cardiac arrest/ cardiovascular collapse’ has reduced since isoflurane (and sevoflurane) largely replaced the use of halothane as inhalation anaesthetic agents, the overall mortality rate in the last 50 years has largely remained the same at around 1% [41], however, the most frequent cause of death has become catastrophic fractures during the recovery period [42]. The various risk factors for anaesthetic-related mortalities have been recently reviewed elsewhere [39; 40], but in terms of the influence of inhalation agent and the risk of catastrophic fractures in the recovery period, two points are worth noting. Firstly, total intravenous anaesthesia (TIVA) is associated with lower mortality rates when compared to inhalation anaesthesia [23; 43; 44] and whilst this finding may be confounded by other factors (e.g. shorter mean duration of anaesthesia for TIVA), it could be inferred that inhalation anaesthetic agents have a negative impact on the recovery period. Secondly, some reports noted that whilst recovery times were faster, subjective assessments of recovery quality indicated that isoflurane produced poorer quality recoveries compared to halothane [14; 15] and other agents [15; 32]. It should also be noted that sevoflurane [34] and desflurane [33] have produced equivocal recovery qualities in some studies. As a result, several studies have been published looking at the effect of sedation during the recovery period to improve quality of recovery after inhalation anaesthesia with some studies showing improved recovery quality [45] and others showing no effect on quality but increased recovery times [34; 46].

**Inhaled anaesthetic agents and partial intravenous anaesthesia (PIVA)**

Another current research focus on improving inhalation anaesthesia is the use of PIVA techniques. In horses, undergoing prolonged surgeries, PIVA is the use of volatile anaesthetics along with supplementary intravenous anaesthetics/analgesics, and in some cases, loco-regional anaesthetic techniques to produce balanced anaesthesia [47]. One motivation of the development of PIVA, apart from improving cardiovascular parameters during anaesthesia and providing multi-modal analgesia, is to reduce the amount of inhalation agent required and therefore improve recoveries [48-50]. The list of drugs, and combinations of drugs, utilised for PIVA techniques in horses is extensive, but consist mainly of α2-adrenoceptor agonists, ketamine, lidocaine, and opioids. The topic of PIVA in horses and appraisal of studies into PIVA has been comprehensively reviewed elsewhere [49; 50], and studies continue to be published (e.g. [51-53]). Attempting comparisons between the plethora of studies into PIVA is complicated by the usual factors associated with study design and limitations of small-scale clinical or laboratory studies. It is not surprising therefore that the evidence to support any one technique over another is equivocal at best, and whilst a case can be made for utilisation of PIVA techniques for each of α2-adrenoceptor agonists, ketamine, lidocaine and opioids, each drug choice is also associated with potential deleterious side-effects such as impairing cardiovascular function, ataxia/ excitement on recovery, or lack of anaesthetic-sparing effect on the inhalation agent respectively [49; 50]. It should also be remembered that, notwithstanding the evidence surrounding whether sedating for recovery or PIVA improves some aspects of inhalation anaesthesia, a prospective large scale multi-centre study demonstrating improved outcomes from sedating horses in recovery or from PIVA has yet to be published, and until data from such a study is available, broader conclusions of the likelihood of any approach improving mortality rates cannot be made.

**Part 2: Pulmonary ventilation and controlled ventilation**

Over the last 50 years we have gained many new insights into equine pulmonary pathophysiology during anaesthesia. This knowledge and the development of new ventilators has given us the opportunity to establish ventilatory techniques that reduce the deleterious effects of anaesthesia and mechanical ventilation itself on pulmonary function.

**Functional anatomy of the equine respiratory tract**

The first achievement helping with the understanding of specific effects of anaesthesia on equine pulmonary physiology, was made in the 1970’s and 1980’s with evaluation of species-specific anatomical and functional features of the equine respiratory tract. Anatomical factors like collateral ventilation, hypoxic pulmonary vasoconstriction (HPV) and functional residual capacity influence the ability to compensate for adverse anaesthetic effects.

*Collateral ventilation*

Collateral ventilation can be defined as the ventilation of alveolar structures through channels that bypass the normal airways and is determined by anatomical structures. Cattle and pigs have no collateral ventilation, while it is very distinct in small animals [54; 55]. Horse lungs have minor collateral ventilation, which is unable to maintain adequate gas exchange in the associated alveolar structures [56]. This reduced collateral ventilation may be because horses have no respiratory bronchioles, which normally connect functional lung units [57]. This means that every terminal bronchiole ends directly in an alveolar duct. A collapse of these terminal bronchioles leads to the loss of the whole lung unit for gas exchange.

*Hypoxic pulmonary vasoconstriction*

To compensate for a lack of collateral ventilation, horses have a strong hypoxic vasoconstrictor response reducing the amount of blood flow in areas of low ventilation [58-60]. HPV is a reflex response in the pulmonary circulation to low partial pressure of oxygen (PO2) in the alveoli and mixed venous blood [61]. Unfortunately, all volatile anaesthetics inhibit HPV in a dose-dependent manner with halothane being the most efficacious inhibitor [59]. This results in an increase in perfusion of collapsed lung units and an increase in venous admixture.

*Functional residual capacity*

Functional residual capacity (FRC) is defined as the volume of air remaining in the lung after a normal tidal expiration and is an important index of lung function. In anaesthetised horses FRC is around 40 ml/kg in sternal recumbency [62; 63]. FRC is also the volume which is necessary to keep the small airways open. A drop in FRC below the closing capacity of a lung unit causes closure of small airways and happens particularly in dependent lung regions [60]. The alveolar structures behind the collapsed small airways do not participate in gas exchange and the gas content will be absorbed over time. This is especially true for horses where no or only minimal collateral ventilation is present.

**Effects of anaesthesia on lung function**

***Hypoventilation***

Also in the 1970’s and 1980’s new monitoring techniques, especially capnography, allowed the anaesthetist to evaluate the effects of anaesthetics on respiratory function. It was found that most drugs used during anaesthesia cause some degree of respiratory depression resulting in hypoventilation. Hypoventilation is defined as inadequate pulmonary minute ventilation resulting in hypercapnia [64]. Routine values for PaCO2 in anaesthetized horses are 5.3 – 8 kPa (40-60 mmHg) [65].

Hypoventilation and resulting hypercapnia have multiple effects on the body systems. The most important effect is hypoxaemia due to a fall in oxygen being delivered to the alveoli. During anaesthesia, the inspiratory fraction of oxygen is increased to help compensate for hypoventilation in an attempt to avoid hypoxemia.

Another important change with hypercapnia, which cannot be easily compensated for, can be seen in the nervous system. Hypercapnia causes an increase in intracerebral pressure through changes in cerebral blood flow in horses [66]. PaCO2 levels above 12.6 kPa (95 mmHg) are progressively narcotic and reduce halothane requirements in dogs [67].

An elevation in PaCO2 also increases the plasma levels of adrenaline and noradrenaline stimulating the sympathetic nervous system and increasing cardiac output and blood pressure in horses [19; 68]. However, interestingly hypercapnia has a biphasic cardiovascular response in horses [66]; a mild hypercapnia (PaCO2 = 55-65 mmHg) causes a fall in cardiac index (cardiac output normalized for body weight) and oxygen delivery despite the increase in blood pressure. Moderate (PaCO2 = 75 – 85 mmHg) to severe (PaCO2 > 95 mmHg) hypercapnia produced an increase in cardiac index and oxygen delivery, but also pulmonary artery pressure and venous admixture.

***Drop in functional residual capacity (FRC)***

Sorenson and Robinson [62] discovered in 1980 that the main reason for atelectasis formation during equine anaesthesia is the reduction in FRC below the closing capacity of lung units.

The reduction in FRC results predominately from changes in posture in horses, but also general anaesthesia itself [62; 69]. In lateral recumbency a marked fall in FRC occurs compared to sternal recumbency and the dependent lung is smaller, more compressed and receives less tidal volume then the non-dependent lung [62; 70-72]. In dorsal recumbency FRC drops further as the diaphragm and abdominal organs overlie a large part of the lungs and both lungs are compressed [70; 73; 74]. The FRC is further reduced during anaesthesia due to the loss of respiratory muscle tone of the diaphragm and changes in the distribution of ventilation throughout the lung area [75; 76].

***Mismatch of pulmonary ventilation and perfusion***

It was only demonstrated in the 1990’s that gravity has a minimal role in the determination of pulmonary blood flow distribution. In awake standing horses lung perfusion was detected preferentially in the central and dorso-caudal areas [77]. During anaesthesia blood flow distribution remains in the same areas as in the conscious standing horse [77-79].

In contrast, ventilation is mainly gravity dependent and is affected by the posture of the subject and changes to lung volumes and mechanics [71; 72; 74; 80; 81]. However, during spontaneous breathing, ventilation is also distributed against gravity to the dependent regions of the lungs. This is due to a greater movement of the diaphragm in the dorsal regions than in the ventral non-dependent parts in anaesthetized horses and humans in dorsal recumbency (Fig. 1). This dorsal diaphragmatic movement ‘pulls’ the gas into dependent parts [76; 82].

Another reason for lung collapse during general anaesthesia is the affect of volatile anaesthetics on surfactant, which is produced by alveolar type 2 cells [83]. Sevoflurane seems to have a less detrimental effect on surfactant than isoflurane [84]. The function of the surfactant is further decreased by a lack of intermittent deep breaths during anaesthesia [85], but forceful inflation of the lung to +40 cmH2O releases new surfactant in humans stabilizing the whole lung unit again [83].

All the factors above result in high amounts of venous admixture to the arterial side and lead to a high incidence of hypoxaemia during equine anaesthesia [86].

**Effects of mechanical ventilation on vital functions**

Over the last 50 years positive airway pressure became the most accepted method to facilitate mechanical ventilation, treat hypoventilation and avoid atelectasis formation in anaesthetized horses. A lot of testimonials on how the lungs of anaesthetized horses have to be ventilated, if ventilated at all, appeared and disappeared again throughout recent decades. This is due to the fact that mechanical ventilation has several positive effects, but also possible detrimental side effects.

***Positive effects of mechanical ventilation***

Mechanical ventilation decreases work of breathing (WOB) and therefore oxygen consumption as the work needed for active inspiration is provided by the ventilator [87]. This is especially important in patients with decreased tissue elasticity of the lungs and pleura as seen during alveolar collapse and consolidation, lung oedema or pleural effusion. A decrease in elasticity of the chest wall (e.g. obesity) and abdominal content (e.g. colic) also increases the work of breathing. WOB also increases when resistance to gas flow increases during bronchoconstriction [64].

Mechanical ventilation can also be used to reduce the expected drop in FRC by keeping the airway pressure above ambient pressure throughout the breathing cycle. This can either be achieved by applying continuous positive airway pressure (CPAP) in spontaneously breathing patients or positive end-expiratory pressure (PEEP) during mechanical ventilation [88; 89]. Furthermore CMV can be used to open up collapsed alveoli by application of high peak inspiratory pressures and performing a recruitment manoeuver [90-93].

***Negative effects of mechanical ventilation***

However, excessive positive pressure can impair cardiovascular function and even pulmonary function itself.

Mechanical ventilation can cause ventilator-induced lung injury (VILI) even in healthy subjects as a consequence of an imbalance between lung stress and strain [94]. In humans low tidal volume ventilation and adequate PEEP levels have been shown to be important factors to prevent VILI during anaesthesia [95]. In horses CMV was associated with increases in several key proinflammatory cytokines, which have been associated with inflammatory lung diseases [96]. Highest changes in these biomarkers were seen after high airway pressures were applied during a recruitment manoeuver, while no differences were observed between awake horses and those breathing spontaneously during anaesthesia.

The positive pressure in the thorax during CMV compresses the vena cava and reduces venous return to the heart and therefore cardiac filling. This leads to a reduced stroke volume and cardiac output [18; 19; 76; 97]. Cardiac output directly influences blood pressure, which is important to maintain muscle perfusion and avoid post-anaesthetic myopathy [98]. The mean airway pressure (airway pressure over time) is the main determinant of the cardiovascular impact of CMV [99].

The decrease in cardiac output and over-expansion of alveoli due to applied positive pressure can cause narrowing or even collapse of pulmonary capillaries that interlace the alveoli. This increases the number of over-distended alveoli that are ventilated but not perfused. The volume of gas in these over-distended alveoli does not take part in gas exchange. This volume is called alveolar dead space. Positive pressure in the airways also increases the size of the conducting airways which increases airway dead space [100]. The increase in physiologic dead space (physiologic dead space = alveolar + airway dead space) causes an increase in ‘wasted’ ventilation when excessive airway pressures are used. In contrast, adequate tidal volumes and airway pressures which avoid perfusion impairment will keep the amount of physiologic dead space small [101].

**Aims of mechanical ventilation and anaesthetic management**

From what we learned over the last five decades the aims to maximize benefits and minimize adverse effects of mechanical ventilation should be:

1. Increase alveolar ventilation to facilitate elimination of CO2 from the lungs and avoid hypercapnia.
2. Increase FRC to keep airways and alveoli open, facilitate oxygenation and avoid hypoxaemia.
3. Reduce WOB.
4. Maintain pulmonary perfusion to the ventilated areas and maintain HPV to decrease perfusion to atelectatic parts.
5. Avoid impairment of cardiovascular function.
6. Avoid over-distension of alveoli and airways.

**Ventilatory support during anaesthesia**

***Spontaneous versus mechanical ventilation***

Before discussing ventilation strategies one has to decide if the desired effects of CMV overweigh the discussed complications arising from the positive pressure in the lungs. Since 1977, several papers have compared spontaneous with mechanical ventilation in horses, with conflicting results [18; 19; 76; 97; 102-107].

*Gas exchange*

Numerous studies have shown that mechanical ventilation improves gas exchange in anaesthetized horses [73; 102; 104; 107]. During CMV lower PaO2 values are observed in dorsal recumbency compared to lateral recumbency and CMV is more effective in preventing hypoxaemia and hypercapnia when initiated directly after induction of anaesthesia, while it fails to improve hypoxaemia in 20% of cases after an initial period of spontaneous ventilation [102; 107]. This shows that conventional CMV cannot open up already atelectatic lung areas, but can partially prevent the formation of atelectasis [73].

*Distribution of ventilation*

As discussed above, gas is distributed towards the dependent well-perfused parts of the lung during spontaneous ventilation [76; 82]. During CMV the diaphragm is pushed caudally [106; 108] and makes gas distribution more gravity dependent and therefore ventilation moves into the non-dependent parts of the lungs and away from the perfusion as demonstrated in Figure 1 [72; 76]. Increasing tidal volumes will not redistribute ventilation towards the dependent lung, but will overinflate the non-dependent lung [72].

*Oxygen delivery, cardiac output and tissue perfusion*

Oxygen delivery to skeletal muscles is an important variable as one major reason for mortality is post-anaesthetic myopathy [23]. Oxygen delivery depends on CO and oxygen content of the arterial blood. However, CO determines perfusion of the skeletal muscles and if CO drops and the muscle is not perfused, adequate oxygen content does not guarantee sufficient oxygen delivery to the muscle. As discussed above, oxygen content increases with CMV as gas exchange improves and venous admixture decreases, but CO and blood pressure decrease [18; 97; 103; 104]. This results in a decrease in the muscle perfusion of the pelvic limbs during CMV especially of the lower limb in lateral recumbency [17; 102]. However, skeletal muscle microcirculation locally regulates tissue blood flow and local tissue oxygen diffusion. No published study has measured muscle microcirculation in anaesthetized horses comparing spontaneously ventilation to CMV. Therefore no statement can be made if the general cardiovascular effects of CMV are also forwarded to the muscular microcirculation.

***Continuous positive airway pressure (CPAP)***

A special ventilation strategy for spontaneously breathing subjects, which became available also for horses in the last decade, is CPAP. During CPAP, pressures above ambient are applied to the airways throughout inspiration and expiration. This improves oxygenation by maintaining FRC, preventing atelectasis formation and decreasing WOB [109].

A CPAP level of 8 cmH2O improves oxygenation and decreases venous admixture without compromising cardiac output in dorsally recumbent horses [110; 111]. The decrease in venous admixture can be explained by an improvement in matching of ventilation and perfusion as CPAP distributes ventilation towards well perfused dependent parts of the lungs without causing over-distension [112]. However, CPAP does not avoid hypoventilation [111].

Unfortunately, cheap freestanding CPAP devices as used in humans cannot be used in horses. In these systems a defined expiratory resistance (PEEP valve) is placed into the expiratory limb of the breathing system and the pressure within the system is kept above ambient pressure with high fresh gas flows and venturi devices meeting at least the peak inspiratory flow of the patient [113]. The high peak inspiratory flows in horses cannot be met by these systems causing drops of airway pressure below ambient. This drop causes closure of the airways resulting in atelectasis formation, alveolar hypoventilation and cardiovascular compromise with these systems and are therefore contraindicated in horses [114; 115]. The ability to apply CPAP to anaesthetised horses only became possible in 2008 with the adaption of a new piston-driven, computer-controlled ventilator (Tafonius, Vetronic Services Ltd and Hallowell EMC, Newton Abbot, Devon, UK). During CPAP the ventilator attempts to maintain airway pressure at a preset positive value chosen by the anaesthetist during the inspiratory and expiratory phases. However, airway pressures can drop below ambient in some horses in which individual adaptation of CPAP values > 8 cmH2O to avoid negative airway pressures is suggested [110]. CPAP levels up to 10 cmH2O have been used without compromises in clinically evaluated cardiovascular parameters [116].

*Which of the predefined aims for the perfect ventilation mode are fulfilled?*

CPAP meets all criteria of a perfect ventilation mode apart from the fact that it does not avoid unintended hypercapnia. This makes it the preferred ventilation mode for short procedures and for horses with sufficient ventilatory drive.

***Mechanical ventilation during anaesthesia***

**Terminology**

Positive airway pressure is delivered intermittently during mechanical ventilation. This is why historically this type of ventilation was called intermittent positive-pressure ventilation (IPPV). This implicates an apneic patient with the aid of neuromuscular blocking agents (NMBA) and the return of the airway pressure to atmospheric between breaths [117]. As NMBAs are seldom used in horses and the adjustable pressure limiting (APL) or pop-off valves will keep the airway pressure above atmospheric even during the expiratory pause the term IPPV should be avoided when a circle system is used. Nowadays the term controlled mechanical ventilation (CMV) should be used instead of IPPV.

**Controlled mechanical ventilation (CMV)**

Over the last five decades CMV became the most common type of ventilatory support used during anaesthesia in horses [118]. During CMV the ventilator is set to deliver a certain volume or peak pressure at a preset frequency independent of the patient’s spontaneous efforts. CMV can be applied to the lungs by a large animal ventilator, by manually squeezing the breathing bag or by using a demand valve (fig.2). However, manual ventilation and the use of a demand valve are cumbersome and not as reliable or consistent in providing appropriate minute ventilation [118]. In the following section we will only discuss mechanical ventilation delivered by a ventilator.

*Influence of drugs on conventional controlled mechanical ventilation*

The anaesthetic agents used have a major influence on the physiological effects of CMV but they also influence the requirements for CMV. All volatile anaesthetics cause dose dependent respiratory depression and CMV is often required to treat hypoventilation [18; 19; 29; 30]. CMV is more often required under isoflurane than halothane anaesthesia [18].

*Routine settings for CMV*

Routine settings are still made more on empirical observations than on scientifically evaluated data.

*Tidal volume* (VT) is the amount of gas delivered to the lungs during one breath. The normal VT used in anaesthetised horses is 10 ml/kg but can go up to 15 ml/kg [118].

*Respiratory rate* is normally set to 6-8 bpm.

The *peak inspiratory pressure* (PIP) is the peak airway pressure within one breathing cycle and is directly related to the delivered VT. Normal PIP values for a healthy horse are around 20 cmH2O, but can go up to 35 cmH2O.

The *inspiratory flow rate* is the volume of gas per unit time that enters the chamber / cylinder containing the bag or bellows and therefore determines the rate (ml/sec) that gas goes from the bellow into the lungs of the horse.

The *inspiratory time* is the period between the beginning and end of the flow of inspiratory gases. Normally the inspiratory time is adjusted to deliver the VT during 2- to 3-seconds.

The *inspiratory:expiratory ratio* (I:E) allows the operator to control the relative time of inspiration and expiration. A long inspiratory time allows recruitment of alveoli, but also causes more impact on the cardiovascular system as the mean airway pressure increases. The I:E ratio should be 1:2 to 1:3.

*Which of the predefined aims for the perfect ventilation mode are fulfilled?*

Conventional CMV facilitates elimination of CO2 and reduces the work of breathing. However, basic intermittent insufflation of the lungs can partially prevent atelectasis formation compared to spontaneous ventilation [73], but cannot reopen airways and associated alveolar structures, impairs cardiovascular function and bears the risk of moving ventilation away from perfusion.

**Special ventilator settings during CMV**

*CMV and positive end-expiratory pressure (PEEP)*

Positive end-expiratory pressure (PEEP) is the positive pressure within the breathing circuit and airways at the end of expiration during CMV and is set by the anaesthetist. Scientific equine data published in the early 1990’s already showed benefits on oxygenation with PEEP ventilation [72; 119; 120]. During this special ventilation mode the ventilator prevents the patient from exhaling to atmospheric pressure by either mechanisms incorporated in the ventilator itself or by a PEEP valve. Typical values of PEEP range from 5 - 10 cmH2O, but higher values up to 20 cmH2O have been used experimentally [72; 119; 120].

Positive end-expiratory pressure increases FRC and maintains it over the critical closing volume [120]. PEEP therefore helps preventing early airway closure and alveolar collapse at the end of expiration and increases oxygenation and decreases venous admixture in horses compared to atmospheric airway pressure [119; 120]. In laterally recumbent horses it can be used to shift the ventilation back towards the dependent lung, but high PEEP pressures are needed [72]. PEEP levels between 5- 30 cmH2O increase the mean airway pressure (pressure over time) and therefore will augment the impact of CMV on the cardiovascular system and the blood supply to vital organs [119-121]. Pharmacological support of the cardiovascular system is necessary, especially in physiologically compromised horses like colic cases [119]. It is important to note that clinically PEEP should be used to keep terminal bronchi and alveoli open and not primarily to re-open already collapsed lung units. This means that PEEP should be used at 5-10 cmH2O directly after induction of anaesthesia and not to improve oxygenation when hypoxaemia is already present. On the other hand, increasing PEEP pressures up to 30 cmH2O over a short time period can open up atelectasis [70; 119-121]. However, these stepwise interventions should preferably be called recruitment manoeuvre followed by PEEP ventilation.

*Which of the predefined aims for the perfect ventilation mode are fulfilled?*

Controlled mechanical ventilation in combination with PEEP has the same advantages and disadvantages as CMV alone. However, PEEP increases FRC and decreases venous admixture, but also increases cardiovascular impairment compared to basic CMV.

*CMV and recruitment manoeuvre (RM)*

The first report on the ‘open lung concept’ using a recruitment manoeuvre was published in 1992 in human medicine [122]. In 2006 the first paper in equine patients was published on this concept [90]. Since then the use of high peak inspiratory pressures to open up atelectatic lung areas has been extensively tested in horses [90-93; 123; 124].

During RM peak inspiratory pressures up to 80 cmH2O and PEEP of 10 – 30 cmH2O are used to open up collapsed airways and adjacent alveolar structures. A stepwise approach by increasing and decreasing PEEP levels over a certain time period has a [93] better effect on oxygenation compared to a single sustained high-pressure manoeuver over 50 seconds [91; 123]. Furthermore the positive response is superior in dorsally recumbent horses compared to laterally recumbent ones [92; 123]. The augmentation in PaO2 after RM can be explained by a redistribution of the ventilation towards the dependent parts of the lungs improving V/Q matching [93]. Sufficient PEEP, which depends on the individual lung status and can be between 5- 30 cmH2O, has to be maintained after RM as otherwise the positive effect of RM on oxygenation and distribution of ventilation is only transient [93; 123].

The impact of RM on the cardiovascular system is conflicting. Some studies report acceptable impact on cardiovascular function based on clinical and advanced assessment, others found serious consequences with different anaesthetic protocols [90; 91; 93; 123]. Most importantly one has to be aware of the possible impact on cardiovascular system and has to abandon the RM when the cardiovascular status deteriorates. The high airway pressures applied during RM can cause lung tissue damage and inflammation [96]. Furthermore these pressures over-distend alveolar structures causing an increase in alveolar dead space during RM [125].

*Which of the predefined aims for the perfect ventilation mode are fulfilled?*

A recruitment manoeuver followed by PEEP can open up collapsed lung areas, decrease venous admixture and increase FRC. The downsides are cardiovascular compromises and possible over-distension of the lung tissue increasing alveolar dead space and causing inflammation.

**Weaning horses from CMV and pulmonary ventilation during and after recovery**

Weaning from mechanical ventilation is an essential element in the care of anaesthetized patients at the end of the anaesthetic. Only limited scientific data is available on weaning of horses and there is uncertainty about the best method for conducting this process, which makes weaning an important clinical issue. Most of the time, recovery of spontaneous breathing is performed by allowing PaCO2 to raise and stimulate the respiratory center. This permissive hypoventilation can induce hypoxaemia after discontinuation of inspiratory oxygen support during recovery [91; 126; 127]. Pressure support ventilation can be used to improve respiratory outcome [127].

In clinical practice, a demand valve is often used for oxygen administration and ventilatory support to avoid hypoxaemia and severe hypercapnia after disconnecting the horse from the ventilator [128].

Gas exchange returns to physiologic levels very quickly after the horses recover from anaesthesia [128]. This might be because they can auto-recruit their lungs after anaesthesia by inspiratory breath holding [129].

**Future work**

So what should we expect during the next 50 years for inhaled anaesthetic agents and ventilatory support in equine anaesthesia?

It is unlikely that any ‘new’ inhalation agents will appear on the horizon. Xenon continues to be studied in human anaesthesia but it is prohibitively expensive and not without side effects [130], thus it is unlikely to find a role in clinical equine anaesthesia. Therefore future work is likely to continue to try to identify the best combination of drugs / techniques to provide optimal maintenance and recovery from anaesthesia, and the strongest evidence should come from a prospective large scale multi-centre study demonstrating improved outcomes.

In contrast, new achievements on ventilatory support over the next decade are very likely. We still have not identified the ‘perfect’ ventilation mode, but our understanding of the pathophysiology of the lungs during anaesthesia has grown substantially and we can continue trying to adapt anaesthetic devices and ventilation modes to counteract these pathological processes.

One focus should be on the post-recovery effects of anaesthesia and CMV on lung function. We need to evaluate the long-term outcome of either allowing atelectasis to develop during anaesthesia and managing resulting hypoxaemia (spontaneous ventilation) or counteracting lung collapse with high airway pressures and dealing with the cardiovascular compromise (CMV, PEEP and RM). A high number of horses will be needed to come to a convincing conclusion regarding this question on long-term outcome and might therefore best be answered in a multi-centre study.

**Figure legend**

Figure 1:

Graphical illustration of the position of the diaphragm in a horse in dorsal recumbency during expiration and inspiration; A) awake horse (theoretical assumption) B) anaesthetised horse breathing spontaneously C) anaesthetised horse during controlled mechanical ventilation. Illustrations are based on Froese et al. (humans) [108], Benson et al. (anaesthetised horses) [105] and McDonell et al. (standing and anaesthetised horses) [69].

Figure 2:

Flow chart illustrating the different options for ventilatory support during equine anaesthesia. PEEP = positive end-expiratory pressure; RM = recruitment manoeuvre.

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1. *The blood-gas partition coefficient (λb/g) is defined as the ratio of the concentration of a given inhalation agent in blood to the concentration of the same agent in gas that is in contact with that blood, when the partial pressure in both compartments is equal* [↑](#footnote-ref-1)