Controlled Mechanical Ventilation in Equine Anaesthesia: Physiological Background and Basic Considerations (Part 1)

**Fernando Moreno-Martinez**

School of Veterinary and Life Sciences, Murdoch University, Perth, Western Australia, Australia

Phone: +61 0433842816

Email: fernando.morenomartinez@murdoch.edu.au

**Martina Mosing**

School of Veterinary and Life Sciences, Murdoch University, Perth, Western Australia, Australia

**Mark Senior**

Department of Equine Clinical Science, Institute of Veterinary Science, University of Liverpool, Neston, Cheshire, UK

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Abstract: Controlled mechanical ventilation (CMV) is routinely used in equine anaesthesia, with many different options available to mechanically deliver breaths. The complexity of respiratory pathophysiology in anaesthetised horses and the wide range of devices available is described in this scoping review.

The first part of the review outlines basic equine respiratory physiology and pathophysiology during anaesthesia to illustrate what makes horses prone to inefficient gas exchange and ventilation when they are recumbent. The difference between spontaneous ventilation and CMV is reviewed and basic considerations of CMV are explored in more detail.

# Physiology and pathophysiology of ventilation and its matching with perfusion

*Movement of gas*

In mammals, ventilation consists of the movement of gas in and out of the lungs. This gas movement allows the uptake of oxygen (O2) from the inspired gas to the blood, and the elimination of carbon dioxide (CO2). Ventilation is controlled by the respiratory centre in the medulla, assisted by peripheral and central receptors and, on some occasions, with input from the cortex (Hall, 2015). During inspiration intercostal muscles and diaphragm contract increasing the volume of the thoracic cavity and expanding the elastic fibres in the lung tissue creating a negative pressure of -1 to -2 cmH2O within the airways and alveoli (Figure 1A) (West, Luks, 2016a). This sub-atmospheric pressure drives the gas down the pressure gradient through the airways into the alveoli where it undergoes gas exchange. Inhalation is an active process. In conscious horses, expiration is divided into a first passive phase, and a second active phase when abdominal muscles contract to exhale actively (Koterba et al., 1988).

Ventilation ($\dot{V}$) is determined by the minute ventilation which equals respiratory rate (RR) times tidal volume (VT) -the volume of gas moved per breath- and therefore minute ventilation can be increased or decreased by changing RR or VT.

$\dot{V}= $RR x VT

Horses adapt their minute ventilation according to their metabolic requirements which directly influence the central respiratory control centres to meet O2 requirement and consumption, CO2 production and to keep blood pH stable. Under normal conditions, the arterial partial pressure of CO2 (PaCO2) will be the main driver of ventilation, whereas the arterial partial pressure of oxygen (PaO2) will only take over in cases of hypoxaemia (hypoxic drive) (Hall, 2015). However, in some situations like during strenuous exercise, a drop in PaO2 (< 80 mmHg), and acidaemia (pH < 6.9) may occur despite great increases in ventilation, while PaCO2 is maintained closed to resting level (40-45mmHg) (Hodgson et al., 1990). During general anaesthesia, O2 consumption and CO2 production is close to resting levels (Hall, 1971). Therefore resting $\dot{V}$ is sufficient to maintain adequate gas exchange during anaesthesia.

*Dead space*

The mammalian respiratory tract is not “well designed” regarding efficiency in gas exchange compared to the work of breathing required for gas exchange. A proportion of the inhaled gas never takes part in gas exchange as it does not reach the alveolar level and is therefore “wasted” ventilation. This volume represents dead space. The total dead space volume -meaning all the gas that is inhaled but does not take up any CO2 or give off any O2- is known as physiological dead-space (VDphys) which can also be expressed as a ratio between the dead-space volume and tidal volume (VD/VT).

Physiological dead-space can then be divided into:

1. Airway dead-space (VDaw): this includes the volume in the conducting airways from lips down to the interphase where gas molecules are not moving by bulk flow (convection) but by diffusion (West, Luks, 2016a). Thus, VDaw can change from breath to breath depending on where this interphase lies, which varies with flow and volume inhaled (Fletcher, 1981).
2. Alveolar dead-space (VDalv): this includes volume in alveoli that are ventilated but are non-perfused so gas exchange does not occur (West, Luks, 2016a). VDalv is negligible in the awake standing horse and the spontaneously breathing anaesthetised patient (Mosing et al., 2018).

VDphys = VDaw + VDalv

In the standing horse VD/VT is around 0.4 to 0.5 (Gallivan et al., 1989) which means that if a horse has a VT of 5L, 2.5L do not undergo gas exchange and is “wasted”. In contrast, VD/VT under anaesthesia in spontaneously breathing horses is around 0.3 to 0.4 (Mosing et al., 2018).

In anaesthesia VDaw can be increased by apparatus dead space (also known as equipment or mechanical dead space) which is the volume of gas extending the airway dead space distal to the lips (e.g. face mask or endotracheal tube in front of the lips) (Fletcher, 1981). Consequently, VDaw itself can be decreased using an endotracheal tube that ends at the level of the lips and bypasses the nasal cavity.

Another term used in the literature is anatomical dead space, that refers to the fixed volume within anatomical structures, where no gas exchange takes place (Bohr 1891). This space can only be measured by filling these anatomical structures with fluid after removal of the gas exchanging tissue -namely the alveoli (Bohr, 1891). As this is clinically not relevant it will not be further addressed in this review.

*Ventilation to perfusion matching*

To guarantee optimal gas exchange, ventilation needs to match the perfusion within one lung unit. A lung unit, which is functionally related to the perfusion of the lung, refers to all the structures perfused by one specific pulmonary artery branch whose obstruction or collapse would cause complete elimination of gas exchange in the named structures due to lack in perfusion (Hedenstierna et al., 2000). The size of a lung unit therefore varies between species.

Numerous studies have looked at the matching between ventilation and perfusion in both awake and anaesthetised horses (Hall et al., 1968; Gillespie et al., 1969; Amis et al., 1984; Dobson et al., 1985; Nyman, Hedenstierna, 1989; Nyman et al., 1990; Moens et al., 1995). In standing awake horses perfusion and ventilation are preferentially dorsocaudal (Staddon, Weaver, 1981; Dobson et al. 1985; Hlastala, 1996). Anatomical conformation of the pulmonary artery and its branches may favour a richer perfusion in dorsal regions, overcoming gravitational forces (Hlastala et al., 1996). Ventilation is greater in the dorsal region of the lung not only because ventilation is gravity dependent - air is less dense than blood and tissue structures - but also the diaphragm moves to a greater extend in the dorsal parts (Benson et al., 1982). Consequently, ventilation and perfusion match ($\dot{V}$*/*$\dot{Q}$) is maximised in the awake horse (Amis et al., 1984; Nyman, Hedenstierna, 1989) (Figure 2A). In contrast, anaesthesia, recumbency and mechanical ventilation will alter matching (Nyman, Hedenstierna, 1989) (Figure 2B and 2C).

*Ventilation to perfusion mismatching*

When ventilation does not match perfusion within one lung unit it is called $\dot{V}$*/*$\dot{Q}$ mismatch. There are two extreme states of mismatch (West, Luks, 2016b) (Figure 2):

1. No ventilation but good perfusion: $\dot{V}$*/*$\dot{Q}$ = 0/1 = 0; The **blood volume** passing through these lung units will not take part in gas exchange and is called SHUNT volume
2. Good ventilation but no perfusion: $\dot{V}$*/*$\dot{Q}$ = 1/0 = ∞; The **gas volume** moving in and out these lung units will not take part in gas exchange and is called ALVEOLAR DEAD SPACE volume.

Beside these two extremes there are millions of lung units where a mismatch occurs (Figure 2):

1. Low ventilation but good perfusion: low $\dot{V}$*/*$\dot{Q}$ ratio; The blood volume is not fully oxygenated while passing through these lung units. This unoxygenated **blood volume** PLUS the **shunt volume** is called VENOUS ADMIXTURE.
2. Good ventilation but low perfusion: high $\dot{V}$*/*$\dot{Q }$*ratio;* The gas in the alveoli cannot take up as much CO2 as normally perfused lung units and the gas contributes to the alveolar dead space volume.

*Hypoxic pulmonary vasoconstriction*

Hypoxic pulmonary vasoconstriction (HPV) is an important physiologic reflex promoting contraction of vascular smooth muscle in the pulmonary circulation in response to low regional partial pressure of oxygen in the alveoli (PAO2) and / or low partial pressure of oxygen in the pulmonary blood (mixed venous Pv̄O2) (Lumb, 2015). The vasoconstriction redirects the blood away from the regions of poor to zero ventilation towards those with sufficient to good ventilation (Lumb, 2015). Horses are rated as a species with intermediate strength of HPV (Elliott et al., 1991; MacEachern et al., 2004). HPV may play role in $\dot{V}$*/*$\dot{Q}$ matching in horses during lung disease and anaesthesia in decreasing perfusion to regions with low $\dot{V}$*/*$\dot{Q}$ ratio and shunt and thereby reducing venous admixture (Figure 3).

# How do horses ventilate under general anaesthesia?

There are three main reasons why anaesthesia causes an impairment in gas exchange:

1. Influence of drugs used during anaesthesia on ventilation
2. Relaxation of respiratory muscles causing a decrease in functional residual capacity (FRC) and small airway collapse
3. Positioning

## Drugs

Sedative agents and those used for induction and maintenance of anaesthesia influence ventilation.

Alpha-2 agonists are routinely used for sedation of horses and premedication before induction. Although their cardiovascular impact may be better known by most clinicians, alpha-2 agonists also cause respiratory depression seen as an increase in PaCO2 (Lavoie et al., 1992; Ringer et al., 2013).

Although opioids are recognized as respiratory depressant in many species, opioids do not cause significant hypoventilation in horses (Nolan et al., 1991). Thus, their use cannot be contraindicated for this reason in equine practice.

Anaesthetic protocols that use injectable drugs for maintenance have, as a general rule, less impact on the cardiovascular system compared to inhalant agents. Respiratory depression may also be smaller when using injectables, but this assumption will greatly depend on the combination used. For example, a combination of midazolam, medetomidine and ketamine resulted in only mild respiratory depression, with PaCO2 around 50-55mmHg (Yamashita et al., 2007).

Volatile anaesthetic agents have a dose dependent effect on ventilation (Steffey, 2002). Besides the inhibitory effect on the respiratory centre, they also affect the $\dot{V}$*/*$\dot{Q} $match to a greater extent than injectables, causing an increase in venous admixture (Luna et al., 1996). This increase is due to the fact that volatile anaesthetics, halothane foremost, inhibit the HPV reflex while ketamine, opioids and propofol have no effect on HPV (Lohser, Ishikawa, 2011; Lumb, 2015). Common anaesthetic complications such as hypothermia and haemodilution also inhibit this important reflex (Lohser, Ishikawa, 2011). On the other hand, lidocaine and salbutamol, two drugs used during equine anaesthesia, potentiate HPV (Lohser, Ishikawa, 2011).

## Relaxation of respiratory muscles causing a decrease in FRC and small airway collapse

Muscle relaxation is a requirement of general anaesthesia especially in equine patients. However, complete relaxation of the respiratory muscles causes a decrease in functional residual capacity (FRC) which is the volume of gas in the lungs at the end of a passive tidal expiration. In conscious patients, when respiratory muscles are relaxed, the opposing forces of thoracic wall and elastic recoil of the lung tissue are in equilibrium at FRC, a volume that keeps the bronchioles open. A reduction in FRC as seen during anaesthesia leads to collapse of bronchioles. As the alveoli distal to these collapsed airways are not ventilated anymore, the reduction in FRC leads to lung regions that are aerated but unventilated (Sorenson, Robinson, 1980). This increases the number of lung units with low $\dot{V}$*/*$\dot{Q}$ (Nyman et al., 1990).

High concentration of oxygen (FiO2) is often used during anaesthesia in the inspiratory gas mixture. This is necessary to compensate for hypoventilation generally occurring due to the administration of the anaesthetic drugs (Mosing, Senior, 2018). However, this high FiO2 leads to *absorption atelectasis* behind closed airways; when the small airway collapses and no fresh gas gets into the alveoli, the gas trapped in these alveoli will get absorbed into the blood stream until a diffusion balance is reached between alveolus and blood (Hedenstierna, Rothen, 2000). If the gas is pure oxygen this balance will only be reached when all gas is absorbed and the alveolus collapses (atelectasis) (Hedenstierna, Edmark, 2010). Inspiratory gas mixtures with a high fraction of oxygen (FiO2) have been shown to enhance the formation of atelectasis in anaesthetised horses (Marntell et al., 2005).

## Positioning

As soon as a horse becomes recumbent, alterations in the $\dot{V}$*/*$\dot{Q}$relationship take place (Sorenson, Robinson, 1980; Dobson et al., 1985). Gas exchange impairment is larger in dorsally recumbent horses when compared to lateral recumbency (Day et al., 1995). The reason why recumbency has a great impact in ventilation lies in the dome-shaped diaphragm of the horse and the pressure exerted by abdominal viscera (Moens, 2013) which forces air out of lung units causing collapse and the formation of *compression atelectasis* (Hedenstierna, Edmark, 2010). An example of how compression of the lungs affects gas exchange is highlighted by comparing head up with head down position in anaesthetised horses in dorsal recumbency where a 7o head up position significantly lowered venous admixture compared to head down position (Binetti et al., 2018).

# What is the difference between spontaneous and mechanical ventilation and why do we need CMV?

During CMV, positive pressure is applied to the lungs and gas pushed into the airways to inflate the lung tissue (Figure 1B), which is the opposite of what drives the gas down the lungs during spontaneous ventilation (Corona, Aumann, 2011) (Figure 1A).

### Work of breathing

During conscious spontaneous breathing, respiratory muscles consume energy during inspiration and during the second active phase of expiration. The work required to overcome the elastic forces of the lungs and thoracic wall is called work of breathing (WOB). As aforementioned, both inspiration and second phase of expiration are active (Koterba, 1988). In contrast, expiration is passive in horses during anaesthesia.

Resistance to flow through nasal cavity, larynx and pharynx suppose between 50 to 70% of the total resistance of the conductive airways (Ewart, 2020). Thus, endotracheal intubation can decrease the WOB by bypassing the upper airway (Tomasic et al., 1997). However, using endotracheal tubes with too narrow internal diameters results in an increase in resistance and, thus, WOB (Tomasic et al., 1997). The WOB is increased in cases of airway obstruction e.g. equine asthma, as more elastic respiratory work is required during inspiration and expiration (Hoffman et al., 2007). During CMV the WOB is done by the ventilator thus favouring the use of CMV in horses suffering from equine asthma, pleural effusion or severe abdominal distension (Auckburally, Nyman, 2017).

Foals have an increased WOB compared to adult horses since foals’ chest wall is more compliant than adult horses’ (Koterba, 1994) -thus foals need to work harder to overcome elastic forces and expand the chest wall. Additionally, foals require higher $\dot{V}$ per kilogram of body weight than adult horses and have less metabolic reserves, making them prone to respiratory fatigue (Beech, 1985). Therefore, mechanical ventilation should be considered in foals especially if long surgeries are expected.

### Hypoventilation

Hypoventilation occurs when a reduced amount of gas is entering the alveoli (reduced alveolar minute ventilation) which results in hypercapnia and hypoxaemia. The drugs used to anaesthetise a horse will always cause a certain degree of hypoventilation (Hodgson et al., 1986; Day et al., 1995), becoming more severe with deeper levels of anaesthesia. To overcome the development of detrimental hypoxaemia due to hypoventilation, an oxygen enriched gas mixture is used during anaesthesia (Auckburally, Nyman, 2017).

Total intravenous anaesthesia (TIVA) or partial intravenous anaesthesia (PIVA) cause a lower degree of hypoventilation compared to inhalational anaesthesia (Luna et al., 1996; McMurphy et al., 2002).

A way to increase alveolar minute ventilation is to control minute ventilation $(\dot{V}$) by switching from spontaneous ventilation to CMV. Edner et al. (2005) maintained normocapnia (38-45mmHg for PaCO2) during CMV with a minute ventilation of about 44L/min and respiratory rate of around 6 breaths per minute in horses whose mean weight was 492kg. This would give a tidal volume of 15ml/kg.

However, one must consider that only a portion of the VT will reach the alveolar level and contribute to alveolar ventilation as 30-50% of the tidal volume is ‘wasted’ in the airways in awake and anaesthetised horses (Gallivan et al., 1989; Mosing et al., 2018). When tidal volumes below 10 mL/kg are used during CMV, the amount reaching the alveolar level may be insufficient to eliminate CO2 from the lungs even when using a high respiratory rate. Therefore, a sufficient VT is crucial to avoid hypoventilation (Bumbacher et al., 2017).

### Intrathoracic pressure and the effect on the cardiovascular system

As demonstrated in Figure 1A, gas flows into the lungs down a pressure gradient during spontaneous ventilation. The sub-atmospheric intrapleural pressure also supports the cardiovascular system by sucking blood into the thoracic cavity and therefore towards the heart, a phenomenon which is known as respiratory pump (Koterba et al., 1988). When CMV is applied (Figure 1B), the opposite effect occurs: the positive pressure applied to the lungs is transmitted to intrathoracic structures, including the relatively thin walled central veins, thereby reducing preload to the right atrium and, consequently, reducing cardiac output (Edner et al., 2005; Araos et al., 2020). During hypovolaemia, the effect of the mean positive thoracic pressure over time on venous return is enhanced compared to a patient with normal intravascular volume (Noel-Morgan, Muir, 2018; Araos et al., 2020). The positive pressure in the alveoli compresses the attached capillaries, which increases pulmonary vascular resistance (PVR) (Roos et al., 1961; Araos et al., 2020). This increase in afterload to the right heart further reduces cardiac output.

Many authors have previously evaluated the cardiorespiratory effects of CMV (Hodgson et al., 1986; Steffey et al., 1992; Edner et al., 2005; Raisis et al., 2005; Blissitt et al., 2008; Kalchofner et al., 2009), with conflicting results due to differences in study design. However, most studies show a negative impact of CMV on cardiac output with a drop of up to 25% (Edner et al., 2005) and therefore, even when the oxygenation of arterial blood may be better, the decrease in cardiac output might impact oxygen delivery to the peripheral tissues (Mosing et al. 2017). A certain drop in arterial blood pressure is therefore unavoidable when switching from spontaneous ventilation to CMV and, hence, hypotension should always be considered as a potential complication. Factors that magnify the effect of CMV on cardiac output include (Araos et al., 2020): the magnitude and time of the pressure applied, compliance of the lungs and thorax (how effectively the pressure is transmitted from the lungs to the great vessels) and volume status with hypovolaemic horses -e.g. colic- being at greater risk of hypotension if CMV is applied (Noel-Morgan, Muir, 2018). For these reasons, arterial blood pressure monitoring is warranted whenever CMV is used.

### Distribution of ventilation

As stated above, gas movement occurs primarily within the dorsal portion of the lung during spontaneous breathing as the contraction of the diaphragm is causing maximal movement in its dorsal parts. This directs the ventilation towards the more perfused regions of the dorso-caudal lung in the standing horse (Ambrisko et al., 2016) (Figure 2A) and in the anaesthetised spontaneously breathing horse in dorsal recumbency (Figure 2B) (Mosing et al., 2017). During CMV, the abolition of the natural movement of the diaphragm and passive caudal displacement of the diaphragm results in a shift of ventilation towards the non-dependent part of the lungs away from the perfusion (Ambrisko et al., 2017; Mosing et al., 2017; Auer et al., 2019) (Figure 2C).

### $\dot{V}$/$\dot{Q}$ mismatch

The change in $\dot{V}$*/*$\dot{Q}$matching after initiation of CMV has several consequences to consider:

* High airway pressures during CMV cause overdistension of the airways and non-dependent lung units (Moens et al., 1998). The overdistension causes a collapse of the adjacent capillaries causing non-perfused but ventilated lung units which increases “true” **alveolar dead space** (Moens, 1989) (Figure 2C). These non-perfused alveoli do not take up any CO2 from the blood causing a very low partial pressure of CO2 in the gas exhaled from these lung units and a decrease in the volume of CO2 being exhaled per breath (Tusman et al., 2012). However, it is important to note that the blood that gets redirected to well ventilated lung units can still take up oxygen, but cannot offload more CO2 as these well perfused alveoli are already fully “loaded” with CO2. The elimination of the CO2 from these alveoli depends on ventilation (West, Luks, 2016a) (Figure 4).
* Partial collapse of alveoli in the dependent parts of the lungs which remain normally perfused will generate units with a **low** $\dot{V}$***/***$\dot{Q}$(Figure 2B and C). The blood flowing through these lung units can give off CO2, but cannot fully oxygenate as not enough O2 is available in the reduced gas volume of the small alveolus. This leads to partially oxygenated blood reaching the left side of the heart and systemic circulation (venous admixture) and in the worst case leading to hypoxaemia (West, Luks, 2016b) (Figure 5). CMV can improve oxygenation in the presence of large lung regions with **low** $\dot{V}$***/***$\dot{Q}$by fully inflating the partially collapsed lung units and therefore increasing $\dot{V}$*/*$\dot{Q}$ ratio of these lung regions (Steffey et al., 1977; Day et al., 1995).
* In the dependent lung, alveoli will collapse due to gravitational factors and the reduction in FRC during anaesthesia. The blood flowing through these collapsed lung units will generate **shunt volume** which contributes to venous admixture. Routine ventilator settings during CMV will not be able to open up collapsed alveoli and, hence, CMV will not improve oxygenation (Hall et al., 1968; Gillespie et al., 1969; Weaver, Walley, 1975; Nyman, Hedenstierna, 1988). Peak airway pressures up to 50 cmH2O are needed to ‘recruit’ these alveoli (Schürmann et al., 2008; Ambrisko et al., 2017). This means switching from SB to CMV in lung states of large amount of atelectasis will not improve the oxygenation without special ventilatory interventions like a recruitment manoeuvre (Auckburally, Nyman, 2017).

### Volatile anaesthetic agent uptake

During spontaneous breathing, depth and rate of the breaths (and hence minute ventilation) varies causing an unpredictable uptake of the volatile anaesthetic agent (Moens, 2013). CMV aims to provide a constant minute ventilation with adequate alveolar ventilation, therefore speeding up the uptake of volatile anaesthetic during the transition from induction to maintenance. However, one also must be aware that this might deepen anaesthesia when switching from spontaneous ventilation to CMV during anaesthesia (Eger, 1974).

### Ventilator-induced lung injury (VILI)

There are multiple mechanisms through which CMV may damage the lung. Beitler et al. (2016) describe these mechanisms as volutrauma, barotrauma, biotrauma and atelectrauma. Volutrauma is caused by overdistension of the alveoli, not necessarily associated with high pressures. Barotrauma is caused by high transpulmonary pressures, not necessarily associated with high volumes. Biotrauma is caused by associated inflammation that develops in the mechanically damaged alveoli. Atelectrauma is caused by stress and shear on lung units that collapse during expiration and are recruited during inspiration - known tidal recruitment . It has been shown in human medicine that not only the mechanical stress itself but also the frequency at which this is applied plays a role in the development of VILI (Amato et al., 2015).

In horses, there is only one study looking at markers of VILI during different ventilation strategies, finding that proinflammatory biomarkers were higher when recruitment manoeuvres were applied, but not significantly different between spontaneous ventilation and regular CMV with no positive end-expiratory pressure (PEEP) (Hopster et al., 2016). However, these results should be interpreted cautiously as the most deleterious effects of CMV on the lungs in other species are observed in already diseased lungs or in long-term ventilation (Beitler et al., 2016).

# What should the clinician choose: spontaneous breathing or CMV?

The discussion above can be condensed to state that the anaesthetist’s aims when using CMV include:

1. **Control of hypoventilation**: CMV allows the clinician to provide a predetermined minute ventilation. This way, ventilation can be increased to eliminate CO2 from the lungs, avoiding hypercapnia, respiratory acidosis and its negative effects on homeostasis.
2. **Faster and more predictable inhalant anaesthetic uptake**: by ensuring a greater minute ventilation, more volatile anaesthetics gets into the alveoli and diffuses to the blood per unit of time. Therefore, the transition from induction with injectable anaesthetics to maintenance with volatile anaesthetics will be smoother and faster.
3. **Reduction of work of breathing (WOB)**: during CMV the patient does not have to spend energy for respiratory movements, which decreases oxygen consumption, which is especially important in horses that already have a high oxygen consumption (sepsis) or in horses that suffer from lung pathologies with already increased WOB when awake (pleural effusion, equine asthma).
4. **Maintain functional residual capacity (FRC)** and avoid formation of small airway collapse and atelectasis that would impair oxygenation of the blood by using PEEP.

However, the disadvantages of CMV also need to be appreciated:

1. **Reduction in cardiac output**: cardiac output will invariably decrease when CMV is used, being more pronounced in hypovolaemic patients.
2. **Overdistension of lung units creating alveolar dead space and shift in ventilation**: alveolar dead-space is negligible in spontaneously breathing horses, whereas some alveoli may get overstretched when using CMV, generating regions with high $\dot{V}$*/*$\dot{Q}$ ratio.
3. **Ventilator-induced lung injury**: important to consider in lung-diseased patients, but probably not as relevant as in other species to the fact that horses do not routinely receive long-term ventilation.

One important misconception should be discussed here, namely that switching from spontaneous to controlled mechanical ventilation does not necessarily improve oxygenation (Day et al., 1995; Bardell et al., 2019). Hypoxaemia can only be easily treated via ventilatory strategies when hypoventilation is the reason for the hypoxaemia (Auckburally, Nyman, 2017). Starting CMV also theoretically helps hypoxemic horses which have significant proportion of regions with low $\dot{V}$*/*$\dot{Q}$, in which increasing ventilation might result in better matching between ventilation and perfusion. However, if hypoxaemia is caused by collapsed lung units representing atelectasis, routinely used CMV settings will not open up these lung units and, thus, hypoxaemia may persist. In this case, performing alveolar recruitment manoeuvres (ARM) followed by PEEP may increase PaO2 (Hopster et al., 2011 and part 2 of this review).

In summary, there can be no definitive recommendation as to whether SB or CMV should be utilised in anaesthetised horses. The discrepancies in outcome between the studies comparing SB to CMV are due to different study populations, drug protocols, position, equipment, timing for interventions, and ventilator settings amongst others. Hence, the anaesthetist should decide on a *case-by-case basis* if CMV should be used and when it should be initiated.

# Preview of part two:

In the second part of this review we provide an overview over the existing technologies that are commercially and non-commercially available to apply CMV in horses. Furthermore, we describe how to set up and deliver CMV in horses.

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***Figure 1****. Simplified step-wise representation of inspiration during spontaneous (A) and mechanical (B) ventilation.* ***A****) 1. Contraction of the diaphragm and selected intercostal muscles increase the volume of the thorax. 2. This decreases the already negative intrapleural pressure in the mediastinal and pleural space further. 3. The alveolar pressure becomes negative. 4. As the pressure drops in the airways air starts to flow down the pressure gradient into the lungs. \*5. Vessels, especially veins due to their thin walls, both within and outside the lungs are exposed to the negative pressure, increasing venous return during inspiration (respiratory pump).* ***B****) 1. Air is ‘forced’ into the alveoli using positive pressure down the airways into the alveoli causing positive alveolar pressure. 2. This positive pressure is transmitted to the mediastinal and pleural space. 3. The lungs and the thorax expand ‘from inside’. \*4. Vessels both within and outside the lungs, especially the veins, are compressed by the positive pressure, reducing the diameter and decreasing venous return.*

***Figure 2****. Graphic illustration of a horse standing (A), in dorsal recumbency spontaneously breathing (B) and during controlled mechanical ventilation (C) showing the ventilation-perfusion matching over the lung field. Ventilation (*$\dot{V}$*) is illustrated in blue and perfusion (*$\dot{Q}$*) in red. Intensity of the shading (red or blue) represents regions of either increased perfusion (red) or ventilation (blue). Regions with maximal ventilation (*$\dot{V}$ *= 1) and zero perfusion (*$\dot{Q}$ *= 0) are defined as alveolar dead space. Regions with zero ventilation (*$\dot{V}$*= 0) and maximal perfusion (*$\dot{Q}$ *= 1) are defined as shunt. Adjacent regions to these two extremes have either a high or a low* $\dot{V}$*/*$\dot{Q }$ *ratio. Blood volume coming from regions with a low* $\dot{V}$*/*$\dot{Q }$*ratio and shunt regions is representing venous admixture. Arrows in C represent shifts in distribution of perfusion and ventilation when controlled mechanical ventilation is initiated.*

***Figure 3****: Graphical illustration of the effect of absence (A) or presence (B) of hypoxic pulmonary vasoconstriction (HPV). Venous admixture is reduced by redirecting the blood away from underventilated lung regions towards better ventilated regions.*

***Figure 4:*** *Graphical illustration on the effects of alveolar dead space on CO2; the graph shows the heart, the blood flow out of the right side of the heart (blue) through the lungs (change in colour from blue to red) and back to the left side of heart (red) and two lung units represented by two circles with conducting airways. The level of the CO2 partial pressure in each compartment is demonstrated by the size of the CO2 font.* ***A****) Under normal conditions, the partial pressure gradient between arterial and expired CO2 is minimal.* ***B****) During controlled mechanical ventilation some lung units might get overdistended which causes compression and collapse of alveolar capillaries. This leaves the lung unit unperfused preventing CO2 to diffuse into the alveolar gas. The CO2-free gas from the overdistended alveoli are mixing with the gas from well perfused lung units containing ‘normal’ CO2 and dilute the CO2 partial pressure measured at the end of expiration. This causes a large pressure gradient of CO2 between expired gases and arterial blood. The blood however is redirected towards well ventilated regions where it can take up oxygen depending on the partial pressure of oxygen in those alveoli. Therefore, an increase in alveolar dead space due to overdistension caused by controlled mechanical ventilation will not impair oxygenation, but the elimination of CO2 from the blood.*

***Figure 5:*** *Graphical illustration of the effects of atelectasis on blood oxygenation. PiO2, PAO2, PaO2, Pv̄O2, and Pc’O2: inspired, alveolar, arterial, mixed venous, and end-capillary partial pressure of oxygen, respectively; SaO2, Sv̄O2, Sc’O2: haemoglobin oxygen saturation in arterial, mixed venous, and end-capillary blood; FiO2: inspired oxygen fraction.* ***Graph A****) Under normal conditions when inhaling air with a FiO2 of 0.21 (21% of oxygen in room air) and a PiO2 of around 150 mmHg (at sea level – 21% of 760 mmHg atmospheric pressure), the PAO2 is 100mmHg. The mixed venous blood coming from the periphery reaching the lungs via the pulmonary artery has a Sv̄O2 of around 75% with a Pv̄O2 of 40- 45mmHg. While passing through the lungs the haemoglobin gets fully saturated, resulting in SaO2 of 100% with PaO2 of around 100mmHg.* ***Graphs B, C****) When atelectasis are present, despite inhaling air with a FiO2 of 0.21 (21% of oxygen in room air) and a PiO2 of around 150 mmHg (at sea level), only open alveoli will reach a PAO2 of 100mmHg; blood flowing through atelectatic lung regions cannot take up any oxygen. Thus, blood coming from the right side of the heart (mixed venous blood) and exiting the atelectatic lung unit have the same pressure of oxygen and haemoglobin oxygen saturation (Pv̄O2 = Pc’O2 = 45mmHg; Sv̄O2 = Sc’O2 = 75%). When mixing the poorly oxygenated blood from atelectatic lung units with the well-oxygenated blood from well-ventilated lung units, the PaO2 and SaO2 drop in a non-linear fashion (55mHg and 83%, respectively) due to the sigmoid shape of the oxygen haemoglobin dissociation curve. The blood volume flowing from the right to the left heart without getting oxygenated is called venous admixture.*