Mandatory Minute Ventilation: Background and Clinical Applications

J. Jane Pillow
Important note:

Medical knowledge is subject to constant change as a consequence of research and clinical experience. The author of this booklet has taken great care to make certain that the views, opinions and assertions included, particularly those concerning applications and effects, correspond with the current state of knowledge. However, this does not absolve readers from their obligation to take clinical measures on their own responsibility.

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Foreword

Improvements in technology, and the development of miniature sensors underpins many of the substantial improvements in conventional mechanical ventilation of for newborn and young infants over the last few decades. Key refinements in conventional ventilation include the incorporation of synchronisation with spontaneous breathing efforts, and the addition of volume targeted pressure limited ventilation. Synchronised ventilation improves patient comfort, decreases the risk of airleak, and reduces the risk and severity of diaphragmatic dysfunction. The most common synchronised contemporary ventilator modes used in newborns are pressure-controlled (PC), and include synchronised intermittent mandatory ventilation (SIMV), assist control (AC), pressure support ventilation (PSV). SIMV does not support spontaneous breaths above the mandatory ventilator respiratory rate (RR), imposing a high work of breathing on the infant breathing above the ventilator rate, as occurs during weaning. At the opposite end of the spectrum, AC and PSV support each and every spontaneous breath. More recently, the development of SIMV with pressure support (PS) provided an intermediate ventilator option, providing differential pressure support of mandatory and spontaneous breaths.

Volume targeting promotes more stable gas exchange, whilst reducing the risk of cyclic volutrauma and promoting more rapid reduction in ventilator pressures, compared to ventilation without volume-targeting. On Dräger neonatal ventilators, volume targeting is offered as Volume Guarantee (VG), and may be incorporated in PC-SIMV, PC-AC, and PC-PSV. Although VG facilitates automated reduction of peak inspiratory pressures during weaning in PC-SIMV, the reduction of the respiratory rate, and transition of the work of breathing from ventilator to patient is highly dependent on active changes of ventilator settings by the clinician.

Mandatory minute ventilation (MMV) builds on the advantages of these standard neonatal respiratory modes including synchronisation, Volume Guarantee and the differential pressure support of spontaneous and mandatory breaths offered in PC-SIMV/VG+PS. MMV offers the benefit of even more stable gas exchange, as the mandatory ventilator rate is continuously and automatically adjusted to “guarantee” a minimum level of minute ventilation (MV) – the key determinant of carbon dioxide removal from the lung. However, MMV also “closes the loop” in that weaning and transition of the work of breathing from ventilator to patient is a seamless process, operating continuously in real time.

This booklet aims to assist neonatal clinicians to become familiar with the principles and rationale for using MMV. The chapters that follow outline the theory, control,
mechanisms, strategies and complications of using MMV. Particular emphasis is placed on understanding the basis for clinical application of MMV to maximise the potential benefits of MMV and to ensure its safe application. There is a steep learning curve as clinicians transition to learning how to separately adjust ventilator support parameters for the mandatory and spontaneous breathing cycles. Neonatal teams considering use of MMV for the first time are advised to obtain comprehensive guidance from experienced users and preferably also practical experience using MMV in a unit where it is practiced routinely and successfully.

The theory and recommendations contained herein represent current knowledge and understanding of MMV theory and application and my experience evaluating the pitfalls and benefits of MMV over the last five years. Nonetheless, current clinical experience and manuscripts evaluating the application of MMV in the neonatal and small infant group are limited. It is inevitable that new knowledge and practical understanding of how to apply MMV in clinical practice will evolve further as the MMV mode is taken up in neonatal units. Consequently, the descriptions and recommendations contained herein will likely need revision over time.

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Contents

Foreword

1 Background of MMV ................................................................. 8
  1.1 Definition .................................................................................. 8
  1.2 History of MMV and evidence relating to use of MMV in neonates ... 8
  1.3 Understanding how MMV works ................................................... 10
    1.3.1 Open versus closed loop ventilation ..................................... 10
    1.3.2 Operating principle of PC-MMV ............................................. 13
    1.3.3 Similarity of MMV to other common used modes of mechanical
         ventilatory support in neonates .................................................... 15
  1.4 Potential theoretical benefits of MMV ........................................... 15
    1.4.1 Spontaneous (supported) ventilation ....................................... 16
    1.4.2 Smooth control of blood gases – avoidance of hypoventilation and
         preservation of lung volume .......................................................... 16
    1.4.3 Supporting automated weaning of mandatory ventilation .......... 17
    1.4.4 Seamless apnoea ventilation .................................................... 17
    1.4.5 Potential reduction in lung injury through combination of mandatory
         and spontaneous ventilatory support ............................................. 19
    1.4.6 Increased patient control over breathing pattern/rhythm .............. 20
  1.5 Risks of MMV ............................................................................ 20
    1.5.1 Risks associated with selection of mandatory ventilation settings ... 20
    1.5.2 Risks associated with settings for pressure support .................... 21

2 Clinical Application of PC-MMV/VG + PS in Neonates .................. 22
  2.1 Indications for MMV ................................................................. 22
  2.2 Defining the ventilator parameters .............................................. 23
    2.2.1 Setting the Mandatory MV ..................................................... 24
    2.2.2 Setting the pressure support for spontaneous breathing .............. 30
    2.2.3 Adjustment of mandatory and spontaneous ventilatory support ..... 33
  2.3 Use of Automatic Tube Compensation to assist weaning ............... 35
  2.4 Leakage compensation ............................................................... 36
  2.5 Monitoring .................................................................................. 38
    2.5.1 Ventilator screen set up .......................................................... 38
    2.5.2 Alarm limits ............................................................................ 39
  2.6 Additional considerations ............................................................ 39
  2.7 Measured variables ..................................................................... 40

3 Troubleshooting – Sample Screenshots ....................................... 42

4 Abbreviations ............................................................................. 45

5 References .................................................................................. 47
List of Tables
Table 1 Differentiating features between various neonatal ventilatory modalities .................................................................15
Table 2 Recommended settings for mandatory breaths during MMV in resting neonates .................................................................26
Table 3 Initial setting and adjustment of ΔPsupp .................................................................34
Table 4 Recommended monitoring variables ........................................................................40
Table 5 Suggested alarm limits for respiratory rate and minute volume during MMV .................................................................41

List of Figures
Figure 1 Schematic of open-loop ventilation .........................................................................11
Figure 2 Schematic of closed-loop targeted ventilation ..........................................................12
Figure 3 Seamless apnoea ventilation and weaning during PC-MMV ..................................14
Figure 4 Recommencement of mandatory ventilation during apnoea or hypopnoea.. .........................................................................................................................18
Figure 5 Recommencement of mandatory breaths after apnoea following a period of strong respiratory drive. .................................................................18
Figure 6 Selecting PC-MMV ..................................................................................................23
Figure 7 100 % mandatory breathing ..................................................................................27
Figure 8. Setting inspiratory time .........................................................................................29
Figure 9 Setting slope ..........................................................................................................30
Figure 10 100% spontaneous breathing .............................................................................33
Figure 11 Principles of automatic tube compensation (ATC) .................................................35
Figure 12 Effect of leak on inspiratory and expiratory flow and tidal volume. ..... 36
Figure 13 Leak compensation .............................................................................................37
Figure 14 Standard MMV display screen ...........................................................................39
Figure 15 A high mandatory minute volume inhibits spontaneous breathing. ..... 42
Figure 16 Inhibited spontaneous breathing from excessive TI. .......................... 42
Figure 17 Tachypnoea resulting from insufficient mandatory MV ..........................43
Figure 18 Tachypnoea resulting from insufficient pressure support during spontaneous breathing. .................................................................43
Figure 19 Excessive pressure support.. ............................................................................44

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I INFORMATION S SUMMARY T PRACTICAL TIPS
1 Background of MMV

1.1 Definition
Mandatory minute ventilation (MMV) promotes development of patient initiated breathing patterns, whilst guaranteeing a minimum level of minute ventilation. Pressure supported (PS) synchronised breaths initiated spontaneously by the patient are supplemented by pressure-limited, volume-guaranteed mandatory breaths when the minute volume generated by pressure supported breaths falls below the user set mandatory minute volume. Hence, MMV includes integrated apnoea ventilation.

1.2 History of MMV and evidence relating to use of MMV in neonates
MMV was first described by Hewlett and colleagues in 1977, who described its use as the first automated mode of weaning adults from mechanical ventilation. Modern MMV has replaced the mechanical adaptive systems typical of early MMV with electronic adaptive ventilation.

Despite the initial description of MMV in 1977, there are surprisingly few original studies in humans or animal models describing its use and application. Early studies of MMV in ventilated adults showed MMV effects more rapid weaning. A small RCT (n=40) showed similar weaning success between MMV (86 %) and IMV (89 %), but more rapid extubation was achieved with MMV: Mean (SD) time to extubation was 33 (21) h in IMV versus 4.8 (1.5) h in MMV.²

Twenty years passed after Hewlett’s original report before the first published study of targeted minute volume in neonates emerged. Claure and colleagues reported the application of “computer-controlled” minute ventilation (CCMV) in 1997 in 15 very low birthweight infants.³ This first custom-designed application of electronic adaptive minute ventilation calculated the total minute volume every five seconds according to the recorded expiratory flow over the previous 20 second interval. The automated changes in the ventilator rate were proportional to the difference between the measured and target minute volumes. The ventilator rate was also up-regulated or down-regulated according to any increasing or declining trends in measured minute volume. Tidal volume was not targeted and hence this mode differs slightly from contemporary MMV in which the clinician predefines the target tidal volume of mandatory breaths.

Target minute volume for the initial study of CCMV by Claure³ was set at only 100 mL/kg/min, as defined by observed tidal volumes in a similar population of very low birthweight infants on standard intermittent mandatory ventilation (IMV). The upper limit for respiratory rate was 60 breaths/min. Eligibility for the study included clinical stability with IMV settings of <30 breaths/min and a fractional inspired oxygen (FiO₂)
of ≤0.3. Exclusion criteria included evidence of congenital heart disease, muscle relaxation, or significant gas leak around the tracheal tube during expiration. In a simple cross-over trial, the babies were first studied on IMV then changed to CCMV: Observations were recorded over the ensuing 45-60 min. Other ventilator settings including peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), inspiratory time (Ti) and FiO₂ were not altered during the study. Claure and colleagues found that CCMV significantly reduced the number of mechanical breaths from a mean (SD) of 15 (2.8) breaths/min in IMV to 8.6 (2.8) breaths/min during CCMV, and hence also a significant reduction in the mechanical component of the total minute volume and lower mean airway pressure. Infants maintained the same level of total minute volume (~250 mL/kg/min) in both modes due to a concomitant increase in their spontaneous ventilation. The SpO₂, TcPO₂, and TcPCO₂ all remained stable throughout the period on CCMV and unchanged compared to baseline levels obtained during IMV. Of interest, 4/5 babies that had significant hypoxaemia during IMV, had a reduction in the duration of hypoxaemia during CCMV. CCMV is not a contemporary commercially available ventilator mode. MMV represents a further refinement of CCMV, as MMV also includes Volume Guarantee for mandatory breath cycles.

In 2005, a small (n=20) crossover study of MMV in moderately mature preterm neonates (>33 w gestation) was reported by Guthrie and colleagues. Synchronised intermittent mandatory ventilation (SIMV) was used as the comparison ventilatory mode. Infants were excluded if they had pre-existing lung disease, had sustained a neurologic insult or were receiving sufficient sedation to interfere with spontaneous respiratory drive. Infants were ventilated using the Dräger Evita 4 Ventilator (Drägerwerk AG & Co. KGaA ) which is a ventilator used across neonatal, paediatric and adult patient groups. The initial ventilator mode was randomised. Each study epoch was 2 hours in duration, with no change to ventilator settings other than ventilatory modality between epochs. Infants were normocapnoeic prior to study commencement with a minute volume of 150 - 250 mL/kg. A 15 minute equilibration period was allowed after changing to the second ventilator modality at the end of the first 2 hour period, prior to recommencement of recording. Tidal volume during SIMV and pressure support for spontaneous breaths (PS) for the MMV mode was targeted at 4-6 mL/kg. The study outcome supported the findings of Claure's CCMV study, showing that MMV was equally efficacious as SIMV for CO₂ removal, despite a decrease in the number of mechanical breaths and a decrease in the mean airway pressure. Together, the Claure and Guthrie crossover studies support a potential role for MMV to speed up the process of weaning newborns from mechanical ventilation. These findings need to be confirmed in an adequately powered randomised con-
trolled trial. The potential role of MMV in providing seamless apnoea ventilation and clinical stability after sudden changes in respiratory compliance, is further supported by a recent physiological study in juvenile rabbits by Clauere's group. They aimed to understand the independent and combined benefits of targeted tidal volume and targeted minute volume. Oxygenation and minute volume were compared between SIMV, SIMV+ targeted tidal volume, computer controlled minute ventilation (using just automated RR adjustment and constant peak inspiratory pressure), and computer controlled minute ventilation coupled with targeted tidal volume (similar to contemporary MMV). The four modalities were delivered by a customised Dräger Babylog 8000plus (Drägerwerk AG & Co. KGaA), with external computerised control of tidal volume, maximum and minimum peak inspiratory pressure, and mandatory respiratory rate. The decline in oxygenation associated with a propofol-induced apnoea was attenuated significantly when targeted MV was used, compared to SIMV alone. Further, when apnoea was combined with a substantial reduction in compliance (achieved with application of a restrictive chest band), only the combined modality of targeted minute ventilation and targeted tidal volume significantly damped the fall in oxygenation and increased hypercapnoea seen with either SIMV alone, or either of the two modalities targeting tidal volume or minute ventilation alone. Thus, MMV likely provides more physiological stability for ventilated preterm infants with periodic breathing or changes in respiratory mechanics.

1.3 Understanding how MMV works
1.3.1 Open versus closed loop ventilation
Chatburn defines targeted ventilatory modes as being based on closed-loop control systems. A basic understanding of open- and closed-loop ventilation, is helpful to understand MMV.

Historically, neonatal ventilation has centred on traditional open-loop mechanical ventilation, which is primarily dependent on clinician adjustment of mandatory ventilation settings to changes in clinical conditions. A basic diagram illustrating the key concepts of open-loop mechanical ventilation is shown below (see Figure 1). The clinician sets a number of ventilator parameters to define the desired waveform to be generated by the ventilator for delivery to the patient. The flow delivered to the patient may be influenced by various factors arising from the patient, circuit, or ventilator such that the actual output may vary from breath to breath according to respiratory mechanics. Importantly, an open loop system is unable to adjust to such disturbances or altered respiratory mechanics. Consequently, the clinical team are

1 MMV in the Dräger Evita 4 ventilator is a volume controlled mode with Autoflow, similar to Volume Guarantee in the Dräger Babylog VN500.
responsible for adjustment of the ventilatory pattern to meet the constantly changing needs of the infant. In reality, continuous adjustment of ventilatory settings by the clinical team is impractical, leaving the infant vulnerable to both over- and under-ventilation when ventilated with an open-loop ventilation modality.

In life, most mammals adapt their breathing pattern continuously in accordance with their physiological requirements, which change with exercise, sleep, and atmospheric conditions. This ability to adapt to changes in our environment (disturbances) is an essential component of maintaining health and wellbeing. The body has developed complex systems for feedback control of numerous physiological signals. Feedback control is integral to the structure of a closed-loop system.

Accordingly, the closed-loop ventilation of targeted ventilatory modes also includes a feedback loop. An example of a simple closed loop ventilation system is shown below in Figure 2. The additional features of a closed loop system include sensors, a feedback signal, and a comparator. Sensors define the characteristics of the delivered waveform and the feedback from these output signals are compared with the input ventilator settings defined by the clinician. The comparator determines how the

---

**Figure 1. Schematic of open-loop ventilation.** Adjustment of the ventilatory settings (input) to achieve changes in the delivered pressure, flow and volume (output) is dependent on the clinician operator.
Ventilator controller needs to change in order to reduce the difference between the input settings and the anticipated output (feedback). Ventilators with closed-loop control systems can respond to changes in internal and external conditions, resulting in more stable ventilation and physiology.

**Figure 2. Schematic of closed-loop targeted ventilation.** Adjustment of the ventilatory settings (input) to achieve changes in the delivered pressure, flow and volume (output) is automated by feedback provided by sensors of the ventilator output.

Chatburn defines different levels of closed-loop control in targeted ventilation modes. MMV is an example of adaptive closed-loop targeted ventilation as the MMV control algorithm considers the natural variability that occurs over time (e.g., in the rhythm and depth of spontaneous respiratory efforts).
1.3.2 Operating principle of PC-MMV

Clinicians familiar with PC-SIMV/VG know that the set tidal volume and set respiratory rate determine the minimum minute ventilation for their patient. The patient can take additional unsupported breaths in the end-expiratory pauses between the mandatory inflations.

In the PC-SIMV/VG + PS mode, these spontaneous patient breaths may be augmented with pressure support (PS) to overcome the resistance of the tracheal tube and the lower respiratory system resistance.

Whereas MMV is a volume-controlled mode in adults, MMV in neonates is a pressure-controlled mode. In neonates, the Dräger pressure-controlled Mandatory Minute Volume (PC-MMV) mode is based on conventional pressure-controlled synchronised intermittent mandatory ventilation with Volume Guarantee and pressure support (PC-SIMV/VG+PS). The set mandatory minute volume is defined as the product of the tidal volume and respiratory rate set by the clinician.

In PC-MMV, PC-SIMV/VG+PS has been enhanced further to provide endurance training during the weaning process and seamless apnoea ventilation. Volume Guarantee is a mandatory component of PC-MMV in neonates; mandatory breaths target a set tidal volume. The inspiratory pressure is regulated to apply the pressure that is necessary to achieve the set tidal volume, limiting the range to a user set maximum pressure Pmax. Like PC-SIMV/VG+PS, pressure support is available to provide assistance to the baby for any spontaneous breaths. The pressure support stays constant during all patient triggered breaths and is not regulated by the Volume Guarantee, unless manually adjusted by the clinician.

The difference between PC-SIMV/VG+PS and PC-MMV is the automatic reduction of the mandatory respiratory rate (RRmand) if the measured minute volume (MV) exceeds the set MV. PC-MMV provides the full range of ventilatory support: a passive patient (not initiating any breaths) will receive only PC-SIMV/VG whereas, at the other end of the spectrum, an active patient with strong respiratory drive may be ventilated purely with PS and receive no PC-SIMV/VG mandatory breaths.

The adaptive function controlling ventilation mode during MMV can be best understood as:

\[
MV_{\text{total}} = MV_{\text{mand}} + MV_{\text{spon}}
\]

where \(MV_{\text{total}}\) is the total minute volume, \(MV_{\text{mand}}\) is the minute volume arising from triggered or untriggered mandatory breaths, and \(MV_{\text{spon}}\) is the minute volume from pressure-supported spontaneous breaths. The spontaneous minute volume will vary according to respiratory drive and the tidal volume of each spontaneous breath. The ventilator software continuously compares the measured \(MV_{\text{total}}\) to the set minute volume to determine how many and when mandatory breaths should be delivered.
If MV includes zero percent spontaneous breaths, then the patient receives 100% mandatory breaths at the set RR and VT, to achieve the mandatory minute volume. At the other end of the scale, if the baby is breathing strongly and generating an MVspon that exceeds the set minute volume, then MVmand is reduced to zero, meaning that no mandatory breaths are delivered. In between these two extremes (i.e., when MVspon is more than zero but less than the set minute volume), the baby will receive a mixture of mandatory and spontaneous breaths. During PC-MMV, the ventilator continuously adapts the frequency of the mandatory breaths (and hence MVmand) as the MVspon changes, in addition to scaling the peak inspiratory pressure required to deliver the set tidal volume. This automated process of seamless apnoea ventilation, seamless transition of work between patient and ventilator and automated ventilator weaning is illustrated in Figure 3 below. The baby is protected from hypoventilation throughout, by the guarantee of a minimum minute volume.

![Figure 3. Seamless apnoea ventilation and weaning during PC-MMV](image)

The infant is transferred seamlessly from 100% mandatory ventilation to 100% spontaneous breathing during PC-MMV without clinician intervention to reduce mandatory rate.

Spontaneous breathing can also be supported by automatic tube compensation (ATC) to overcome the work of breathing imposed by narrow tracheal tubes in neonates (see also section 2.3 “Use of Automatic Tube Compensation to assist weaning”).
1.3.3 Similarity of MMV to other common used modes of mechanical ventilatory support in neonates

During MMV, the clinician retains control of the minute volume, unlike more complex closed-loop ventilation modes. A comparison of the key differentiating features between each modality is shown in Table 1 below.

Table 1: Differentiating features between various neonatal ventilatory modalities

<table>
<thead>
<tr>
<th>VENTILATORY MODE</th>
<th>IMV</th>
<th>SIMV</th>
<th>A/C</th>
<th>PSV</th>
<th>SIMV + PS</th>
<th>MMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory trigger</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Each breath assisted</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ventilator assisted RR</td>
<td>Fixed</td>
<td>Fixed</td>
<td>Variable</td>
<td>Variable</td>
<td>Fixed/Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Inspiratory time</td>
<td>Fixed</td>
<td>Fixed</td>
<td>Fixed</td>
<td>Variable</td>
<td>Fixed/Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Differential support of mandatory and spontaneous breaths</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Guaranteed minimum MV</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

1.4 Potential theoretical benefits of MMV

Definitive experimental evidence for benefits of MMV in neonates remains limited. However, MMV offers a number of theoretical benefits for the developing neonate, particularly the vulnerable preterm infant.

**BENEFITS OF MMV**

1. Wide range of ventilatory assistance to support an infant throughout its requirement for mechanical ventilation
2. More stable control of arterial blood gases resulting from more stable minute ventilation
3. Automated weaning of mandatory respiratory frequency and peak inspiratory pressures
4. Seamless apnoea ventilation within pre-set safety limits to avoid hypoventilation
5. Intrinsic benefits arising from biologically variable respiratory rhythms associated with increased patient control over breathing pattern
1.4.1 Spontaneous (supported) ventilation

PC-MMV supports spontaneous respiratory efforts through the provision of pressure support. Pressure support (PS) is applied above PEEP whenever a spontaneous breath is detected: the clinician sets the amount of additional PS supplied by adjusting ΔPsupp. ΔPsupp describes the pressure difference from PEEP level. The tidal volume of spontaneous respiratory efforts is influenced by the level of PS relative to the respiratory compliance. ΔPsupp may be increased or decreased as required to deliver acceptable tidal volumes that promote physiologically appropriate tidal volumes, respiratory rates and minute volumes. For example, ΔPsupp may need to be decreased as the lung compliance improves, or as efficiency of the muscle pump (respiratory muscles) increases.

Spontaneous respiratory efforts are vital to preserve diaphragm function and to avoid the development of ventilation induced diaphragmatic dysfunction.7,8 The preterm diaphragm has impaired structural and functional integrity at birth and hence the development of respiratory muscle endurance and fatigue resistance is essential for successful weaning and extubation to non-invasive respiratory support or independent respiration. Differential pressure support between the mandatory and spontaneous breaths promotes progressive and independent training of the respiratory muscles towards efficient independent ventilatory capacity.

1.4.2 Smooth control of blood gases – avoidance of hypoventilation and preservation of lung volume

PC-MMV offers constant ventilation regardless of changes in spontaneous respiratory rhythm, or mechanical factors that influence the delivery of tidal volume. Mandatory respiratory rate is up-regulated and down-regulated continuously, as required, to meet the minimum minute ventilation as defined by the clinician through tidal volume and respiratory rate settings. The guarantee of a minimum minute ventilation is advantageous as it avoids the fluctuations in carbon dioxide removal and oxygenation associated with hypoventilation that may occur as respiratory rate is decreased when using PC-SIMV/VG +/- PS.5

Aside from increased mandatory respiratory rate and ventilation during apnoea, the set tidal volume also has an important function to support pressure supported spontaneous breaths. Even in relative health, preterm infants display a “see saw” pattern to lung volume maintenance during spontaneous periodic breathing. Functional residual capacity decreases during a breathing pause, and “resets” after a sigh (normally defined as a breath volume of twice the average tidal volume).9 Thus, during PC-MMV, mandatory breaths delivered during a breathing pause in the midst of a predominantly spontaneous breathing pattern may serve the same function by
delivering a slightly higher breath volume to prevent derecruitment of the lung that otherwise occurs following prolonged low tidal volume ventilation. Such intermittent larger tidal volume breaths may also improve surfactant function and lung compliance.10

1.4.3 Supporting automated weaning of mandatory ventilation
A comparison of PC-SIMV/VG+PS versus PC-MMV will help the clinician to understand how PC-MMV supports automated weaning of mandatory ventilation. Weaning an infant on PC-SIMV/VG+PS requires the infant to increase the efficiency of its spontaneous breaths to account for a greater proportion of the minute volume with only a small amount of pressure support. As the infant’s breathing efforts become more efficient, the clinician can gradually reduce the rate delivered by the ventilator. However, this reduction in mandatory rate needs to be managed carefully as excessive reduction in the rate may result in desaturation and alveolar collapse if the infant has prolonged or multiple apnoeic intervals. Similarly, the clinician may also reduce the level of pressure support according to the infant’s respiratory drive and respiratory mechanics. When the level of pressure support becomes minimal, ventilatory support primarily acts to strengthen the respiratory muscle pump.
In contrast, PC-MMV facilitates a smooth transition of the work of breathing from the ventilator (100 % mandatory ventilation) to the patient (100 % spontaneous minute ventilation). Both rate and the peak inspiratory pressure of the mandatory breaths are automatically weaned in PC-MMV, rather than the manual weaning of mandatory breath frequency in PC-SIMV/VG modes. The automatic reduction in the peak inspiratory pressure of mandatory breaths is ensured by the use of Volume Guarantee. The automatic reduction of respiratory rate in PC-MMV occurs as the patient generates more spontaneous minute volume. Additionally, clinician guided, gradual reduction of pressure support for patients tolerating 100 % spontaneous ventilation promotes endurance of diaphragm contractile function.
In adults, weaning is achieved more rapidly with MMV than with SIMV dependent on clinician initiated weaning.2 No MMV trials with weaning from mechanical ventilation as an outcome are reported in infants to date.

1.4.4 Seamless apnoea ventilation
In the event of periodic breathing in the patient with 100 % spontaneous minute volume, mandatory breaths will commence as soon as the MV falls below the target MV.
Figure 4. Recommencement of mandatory ventilation during apnoea or hypopnoea. Mandatory breaths recommence if the MV falls below the mandatory MV.

If the respiratory pause occurs after a period of strong spontaneous ventilation with MVspon much higher than the mandatory MV set by the clinician, a maximum of 10 seconds after completion of the last spontaneous breath is allowed, before mandatory ventilation recommences.

Figure 5. Recommencement of mandatory breaths after apnoea following a period of strong respiratory drive. In the presence of a strong respiratory drive, it may take a while for the MV to fall below the mandatory MV. In this scenario, the Babylog VN500 will only allow a maximum of 10 seconds plus the set expiratory time (determined from the set RR and set inspiratory time) before delivering a mandatory breath. In this way, the infant is protected from clinical instability associated with a prolonged respiratory pause.
This seamless apnoea ventilation provides a safeguard for the patient; it reduces the frequency and severity of disturbance to oxygenation and cardiovascular stability, whilst providing the infant with opportunities to recommence breathing.

MMV ensures that ventilation is continued, delivering the mandatory minute volume until the infant recommences breathing. Once the infant starts breathing again, the frequency of mandatory breaths is again automatically reduced until the target MV is fully achieved with spontaneous pressure supported breaths. This prompt return to the biological variability inherent in a spontaneous breathing rhythm may be beneficial to lung function and ventilation distribution. Consequently, MMV offers an advantage over other modalities which either have a continuous stable mandated MV rate or which mandate a minimum 2 minutes of mandatory ventilation in the presence of apnoea (Apnea ventilation option). An overall reduction in mandatory breaths using a set inspiratory time, and increased spontaneous breathing with patient determined inspiratory time has potential to reduce risk of airleaks.

1.4.5 Potential reduction in lung injury through combination of mandatory and spontaneous ventilatory support

In the patient requiring mechanical respiratory support, the combination of mandatory time-cycled breaths and pressure supported spontaneous breaths offered in PC-MMV and PC-SIMV/VG+PS has potential advantages over the full, constant level of support offered by PC-AC and PC-PSV. The newborn infant is normally reliant on intermittent sigh breaths to maintain functional residual capacity. However, sighs are not a feature of ventilatory modes that use similar peak inspiratory pressures for each breath. During PC-SIMV/VG+PS, the intermittent time-cycled mandatory breath may provide sufficient inspiratory time and pressure to recruit atelectatic lung units. The spontaneous breath in turn promotes improved ventilation of dependent lung units.
1.4.6 Increased patient control over breathing pattern/rhythm

MMV promotes sustainable spontaneous breathing efforts by regulating the frequency of mandatory breaths according to the efficiency rather than just the rate of the spontaneous breathing pattern. Setting the minimum (mandatory) minute volume to target a mild hypercapnoea allows the infant to dictate their own respiratory breathing rhythm, rather than having that rhythm suppressed by an excessively high mandatory MV or high imposed respiratory rate in other neonatal ventilatory modes.\(^3\)

The inherent variability of tidal volume and respiratory rate of endogenous respiratory rhythms promotes:
- volume recruitment
- more homogeneous ventilation distribution
- increased compliance
- avoidance of actelectasis
- improved oxygenation with lower inspired oxygen requirement
- reduced inflammatory responses
- increased surfactant synthesis and secretion\(^{11,12}\)

Together, these features are likely to promote lung development, and potential avoidance of bronchopulmonary dysplasia.

1.5 Risks of MMV

1.5.1 Risks associated with selection of mandatory ventilation settings

Whilst MMV is a form of adaptive closed-loop ventilation, several factors remain dependent on clinician input and control. Setting the mandatory MV too low will result in cardiorespiratory instability and may promote hypercapnoea in the absence of adequate respiratory drive. Similarly, a low mandatory MV may result in respiratory muscle fatigue and/or excessive oxygen consumption in the infant with a strong respiratory drive but high intrinsic work load. In contrast, setting a high mandatory MV will depress respiratory drive, and limit opportunities for spontaneous breathing if the infant is unable to meet the mandatory MV with the pressure support provided. In setting the mandatory MV, the clinician needs to additionally consider appropriate combinations of set tidal volume and respiratory rate. The Volume Guarantee settings and respiratory rate should be appropriate for the nature and stage of the disease process and the patient’s respiratory drive. If the tidal volume is set too low, the patient will develop progressive loss of lung volume, particularly when there are no or inadequately supported accompanying spontaneous breaths. At the opposite extreme, setting the tidal volume too high will promote cyclic alveolar overdistension. Setting of other mandatory breath variables such as inspiratory time, Pmax and Slope follows the same principles as used in PC-SIMV/VG, and PC-AC.
1.5.2 Risks associated with settings for pressure support

Failure to remain vigilant in monitoring of spontaneous breathing patterns during PC-MMV as for PC-SIMV/VG+PS may result in failure to recognise inappropriately high or low levels of pressure support. Insufficient pressure support will result in inefficient (low-tidal volume, high dead space), rapid spontaneous breathing. Such rapid shallow breathing promotes atelectasis and respiratory muscle fatigue from increased work of breathing, and may increase oxygen consumption. The ultimate consequence of rapid shallow breathing is often the resumption of mandatory inflations and decreased frequency of spontaneous breathing. High respiratory rates may also increase the risk of developing inadvertent PEEP. Setting a high respiratory rate alarm (∼ 20 breaths above targeted respiratory rate) and high minute volume alarm will alert the carer to inadequate pressure support.

Excessive pressure support in the presence of a strong respiratory drive and effective respiratory muscle contractile activity may result in high tidal volumes from

---

**PRACTICAL TIP**

**Setting the mandatory MV too low**

**Can lead to**
- Cardiorespiratory instability
- Hypercapnoea in the absence of adequate respiratory drive
- Respiratory muscle fatigue
- Excessive oxygen consumption with a strong respiratory drive but high intrinsic work load
- Increased work of breathing

**Setting the mandatory MV too high**

**Can lead to**
- Depressed respiratory drive
- Unload respiratory muscles
- Increased risk of muscle atrophy
- Limited opportunities for spontaneous breathing if the infant is unable to meet the madatory MV with the pressure support provided
spontaneous breaths. High spontaneous tidal volumes will result in low spontaneous respiratory rates. Appropriate setting of high minute volume alarms provides partial protection against this event (see 2.5.2 Alarm limits).

2 Clinical Application of PC-MMV/VG +PS in Neonates*

2.1 Indications for MMV

MMV is normally considered as a weaning mode of mechanical ventilation. Babies will obtain greatest weaning benefit from MMV if they have at least some spontaneous breathing activity and are considered ready to wean. However, some babies who are ready to wean may not be taking their own breaths: the minute volume delivered by the ventilator may at least meet, or exceed the minute volume required to achieve normocarbia. Readiness for weaning may be ascertained by putting such babies onto MMV, and gradually reducing the mandatory MV until the baby shows spontaneous respiratory efforts.

However, as MMV has integrated Volume Guarantee and hence automated adjustment of peak inspiratory pressure to account for changes in respiratory mechanics, it may also be used in settings when full mechanical ventilation is required. MMV is delivered with all the documented advantages of Volume Guarantee ventilation. Use of MMV for full respiratory support is similar to ventilation with Volume Guarantee in other pressure control neonatal ventilatory modes such as PC-SIMV/VG.

MMV may also be indicated for improving ventilatory stability in babies who have an unstable or inefficient minute ventilation. Variable spontaneous minute volume may result from periodic breathing, or in the presence of an untrained or fatigued diaphragm.

*In the following section PC-MMV/VG+PS is shortened to MMV.
2.2 Defining the ventilator parameters

The ultimate goal of MMV is to drive the infant towards achieving normocarbia achieved with 100% spontaneous breathing with minimal pressure support at a physiologically appropriate respiratory frequency. This goal needs to be achieved in several steps.

We will first consider how to set the mandatory breath settings, followed by settings for the spontaneous breath support.

Figure 6. Selecting PC-MMV: After selecting the PC-MMV tab, the clinician sets VT to assign the level of Volume Guarantee, and then sets the RR to establish the desired absolute mandatory MV (VT x RR) based on the patient’s weight, deadspace fraction and target PaCO₂. The resulting MV is displayed at side. Pmax is set as the maximum peak inspiratory pressure for delivery of the guaranteed tidal volume during mandatory breaths. Other mandatory breath settings (FiO₂, Ti, Slope and PEEP) are set as for PC-AC and PC-SIMV. All settings must be confirmed by pushing the rotary knob, before changes are applied. ΔPsupp is selected initially to target a PIP just below the average PIP used for mandatory breaths, and then adjusted as required to target the desired VTspon.
2.2.1 Setting the Mandatory MV

Defining the mandatory minute volume requires consideration of the individual ventilatory needs and circumstances of each infant. Ideally, we would be able to measure the alveolar minute volume, which determines the removal of carbon dioxide from the blood and alveolar space. However, alveolar minute volume is not measured routinely during mechanical ventilation. Instead, we measure the minute volume as a proxy for alveolar minute volume.

The required minute volume may increase in the setting of
1) high carbohydrate intake (increased CO₂ production), or
2) inefficient carbon dioxide removal due either to a relative decrease in alveolar volume, or increased physiological deadspace.

Therefore, the mandatory minute volume target may vary from infant to infant according to diet, disease state, lung development (alveolar volume), airway distensibility and deadspace fraction. These factors need to be considered when setting the mandatory minute volume particularly in more immature babies: more immature babies have increased deadspace fraction in combinations with low volume alveolar spaces that are susceptible to overdistension.¹⁴

Different combinations of tidal volume and respiratory rate will work together to achieve normocapnoea. However, the actual delivered minute volume and ventilatory settings should not only achieve normocapnoea (or mild permissive hypercapnoea), but also allow the infant to optimise ventilatory efficiency whilst minimising work of breathing and avoiding cyclic volutrauma. Identifying this target minute volume may reduce consumption of energy (allowing calorie diversion to tissue growth), reduce oxygen consumption, and protect the respiratory muscles from fatigue imposed by high intrinsic workloads (these theoretical benefits need to be confirmed in a clinical study). Setting the MMV mandatory MV value too low may increase work of breathing by the patient. Conversely, setting the MMV mandatory MV value too high may completely unload the respiratory muscles, and increase risk of respiratory muscle atrophy and reduced spontaneous breathing efforts.

Currently, there are no reference equations for identifying minute volume that minimises the work of breathing in infants. However, the minute volume required to achieve permissive hypercapnoea in preterm infants is estimated at 200-300 mL/kg/min.¹⁵ Extreme preterm infants may have a MV that exceeds 400 mL/kg/min to achieve permissive hypercapnoea due to the increased deadspace fraction of the immature respiratory system.¹⁴ It follows that more mature term infants are likely to require an MMV mandatory MV setting around 200 mL/kg/min as their breathing
is more efficient due to more advanced alveolarisation and low deadspace fraction compared to preterm infants.

The set tidal volume and respiratory rate used to define the minimum mandatory minute volume are key to defining success and hence are considered separately below. The volume target should be defined first, as the mandatory respiratory rate is regulated by the ventilator in response to spontaneous breathing efficiency relative to the minimum MV.

**Volume Guarantee (VG)**

Set appropriately, Volume Guarantee provides increased protection for the infant against either volutrauma or atelectotrauma associated with pressure-controlled ventilation without volume targeting.\(^{13,16,17}\) During MMV, the infant is at particular risk of both of these complications during prolonged apnoeic intervals when the predominant ventilation is achieved with mandatory breaths. In contrast, inappropriately low tidal volumes may promote atelectasis and similar pro-inflammatory responses, and will necessitate a high mandatory respiratory rate during apnoeic intervals that may suppress spontaneous breathing activity.

Setting Volume Guarantee at 5-6 mL/kg, or at 6-7 mL/kg for infants after the initial weeks of life may provide a reasonable balance between avoiding volutrauma or atelectasis but retaining lung volume maintenance support. This may be particularly important for the infant breathing spontaneously with a periodic respiratory pattern and vulnerability to lung volume derecruitment.

**Rate**

Once tidal volume is set, the respiratory rate should be adjusted to target the minimum minute ventilation. The set respiratory rate should lie at the lower end of the physiologically appropriate range for the gestation, and size of the infant. If the required respiratory rate is outside this range it is likely that the tidal volume setting is incorrect. Recommended physiological ranges for different gestations are shown in Table 2.
Table 2. Recommended settings for mandatory breaths during MMV in resting neonates

<table>
<thead>
<tr>
<th></th>
<th>TERM 30-36° W GA</th>
<th>RDS &lt; 30 W GA</th>
<th>RDS</th>
<th>CLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target MV (mL/kg/min)</td>
<td>200-250</td>
<td>250-300</td>
<td>300-350</td>
<td>300-400</td>
</tr>
<tr>
<td>Set VT (mL/kg)</td>
<td>6-7</td>
<td>5.5-6.5</td>
<td>5-6</td>
<td>6-7</td>
</tr>
<tr>
<td>Set RR (breaths/min)</td>
<td>30-40</td>
<td>40-55</td>
<td>50-70</td>
<td>40-60</td>
</tr>
<tr>
<td>Inspiratory Time (s)</td>
<td>0.35-0.6</td>
<td>0.3-0.45</td>
<td>0.3-0.45</td>
<td>0.35-0.6</td>
</tr>
<tr>
<td>Slope (s)</td>
<td>0.17-0.3</td>
<td>0.15-0.22</td>
<td>0.15-0.22</td>
<td>0.17-0.22</td>
</tr>
</tbody>
</table>

The astute reader will notice that the recommended set RR during MMV listed in Table 2 are somewhat higher than those recommended to promote spontaneous breathing activity in PC-AC.

The rationale for this recommendation is that during MMV, the set RR is not a mandated minimum RR – rather it the set mandatory RR is only delivered when the baby is requiring 100 % mandatory ventilation. Setting a lower RR puts the baby at risk of hypoventilation, and high work of breathing (see 2.2.1 above). Setting a low RR would necessitate use of a substantially higher VG to achieve effective gas exchange, but this higher VG may be injurious in the event of protracted periods of mandatory ventilation. Therefore, the priority is given first to setting the tidal volume, and then adjusting the set RR to achieve the desired mandatory MV. If the patient does not commence spontaneous breathing after commencement of MMV, and there is not a justifiable reason for the apnoea (e.g., marked sepsis), then the clinician can gradually decrease the set RR until spontaneous respirations appear.

Suggested approaches to adjusting the tidal volume and set RR for MMV during 100 % mandatory ventilation are shown in Figure 7.
Figure 7. 100 % mandatory breathing

(A) The goal is to target with the MV setting (set RR and set VT) the range of mild permissive hypercapnoea. The RR and VT shall be in the physiologic range of the patient (between dashed lines). If the patient is in the normocapnoeic range without spontaneous breathing, the set MV (defined by VT and RR) shall be decreased to trigger patient-initiated breathing activity. VT should be decreased if the set VT is above physiologic range (and RRmand is low). Alternatively, RR should be decreased if RRmand is above the physiological range and set VT is low.

(B) If the patient is in the hypocapnoeic range without spontaneous breathing, then MV shall be decreased with VT and RR targeting the physiologic ranges (dashed lines).

(C) If the patient is in the hypercapnoeic range without spontaneous breathing, the MV has to be increased in order to remove sufficient CO₂.
**Inspiratory Time**

Mandatory breaths are SIMV breaths and hence are delivered for a set inspiratory time. The inspiratory time setting should be adjusted to facilitate a brief end-inspiratory pause of 10% to 30% of the spontaneous inspiratory time. The adjustment can be refined based on the average Tispon, which is measured for the spontaneous breath, as well as by reviewing the inspiratory flow waveform. This approach provides flexibility to ensure that the target volume is achieved despite breath to breath changes in respiratory mechanics that influence the timing of volume delivery. Inadequate inspiratory time will necessitate higher peak inspiratory pressures to achieve the set tidal volume (and potentially contribute to shear injury as a result of rapid lung inflation), or result in low tidal volume alarms if the pressure limit is reached.

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**NEGATIVE CONSEQUENCES OF PROLONGED INSPIRATORY TIMES INCLUDE:**

Active expiration with resultant elevated work of breathing, asynchrony and increased risk of airleak may induce a Hering-Breuer reflex via activation of stretch receptors in the airways and lung. The Hering-Breuer reflex results in negative feedback of the central respiratory pattern generator to inhibit spontaneous respiratory drive, defeating the purpose of MMV.
Figure 8. Setting inspiratory time Screenshots from Dräger Babylog VN500 showing inspiratory times that are too short (1), appropriate (2) and too long (3). A short inspiratory time drives PIP higher as ventilator tries to deliver the guaranteed volume in a limited time period. The pressure and volume waveforms do not plateau, and the flow waveform is terminated before reaching zero flow. A long inspiratory time results in prolonged exposure of alveoli to high pressures, a long end inspiratory pause, associated with prolonged exposure of the alveoli to full inflation.

The Flow/Slope
The flow or slope (depending on the ventilator configuration) determines the rate of rise of the pressure during inspiration for any given respiratory time constant. A rapid pressure rise will promote higher inspiratory flows and more rapid change in lung volume. As the preterm newborn lung is relatively fragile, gentle ventilation is achieved through more gradual increases in lung volume during the inspiratory phase. A reasonable guideline to reduce shear forces associated with tidal volume delivery, is to adjust the flow (or slope) to achieve plateau pressure after at least 50 % of the spontaneous inspiratory time has elapsed.
2.2.2 Setting the pressure support for spontaneous breathing

Spontaneous respiratory activity during MMV improves homogeneity of ventilation distribution in the lung, and preserves and trains respiratory muscles to facilitate future weaning from the ventilator and independent respiration. The goal of pressure support during MMV is to support and stimulate the spontaneous respiratory drive, whilst minimising work of breathing and avoiding lung injury. Setting the level of pressure support thus becomes a very important component of the MMV strategy. In the Babylog VN500, pressure support (ΔPsupp) refers to the additional pressure superimposed on PEEP to augment the tidal volume generated by the infant during a flow-triggered inflation.

The level of pressure support will necessarily change as lung disease evolves: pressure support may need to increase as compliance decreases or resistance increases, whereas a decrease in pressure support may be appropriate as the infant’s clinical condition improves and the compliance increases or the resistance falls. Adequacy of pressure support thus needs continuous re-evaluation as the level of pressure support is defined by the clinician and is not under any automatic control. A wide combination of spontaneous tidal volumes and respiratory rates may achieve...
the target minute volume and hence target PaCO$_2$. Consequently, it is essential to monitor and adjust pressure support. Monitoring should ensure that minute volume is adequate to obtain the desired arterial PaCO$_2$, and also that physiologically appropriate tidal volume and respiratory rates are achieved. Excessive work of breathing may increase respiratory rate, increase energy consumption and increase oxygen consumption.

The clinician may initially set the pressure support to target tidal volumes that are 80% of the set tidal volume for mandatory breaths. It is important to assess the patient’s response to this pressure support setting (i.e., respiratory rate and effort) over the first 15-30 minutes after commencing MMV. The pressure support level should be altered as needed to target physiologically appropriate tidal volumes and respiratory rates for the infant and disease condition. If the patient is taking frequent, low volume spontaneous breaths, then increased pressure support should reduce the spontaneous breathing rate to a more appropriate lower respiratory frequency, and increase the efficiency of the spontaneous breaths. Conversely, if the spontaneous tidal volume is at least equal to or exceeds the set tidal volume, and the respiratory frequency is lower than the expected breathing rate, then the pressure support should be decreased.

A respiratory frequency that minimises work of breathing for the adult was determined by Otis in 1950. Similar minimal work of breathing studies have not been pursued in infants. Physiologically, we expect smaller subjects to breathe with lower tidal volumes but comparatively higher respiratory rates than larger subjects, as can easily be seen when comparing respiratory rates of adults, children, and newborns. Published reference values for respiratory rates in infants and young children can be used to identify physiologically appropriate respiratory rates in newborns. These reference values show that there is a non-linear decrease in respiratory rate with increasing postnatal age.

Healthy infants born at full term have a mean physiological respiratory rate of 40 breaths/min during sleep. The upper limit of a physiological breathing rate in premature infants can be estimated from published regression equations for the 95th centile of respiratory rates in these healthy infants, as shown in Table 2: allow for a further non-linear increase in respiratory rate to overcome the inefficient gas exchange of the low-volume preterm lung.

Once an infant on MMV has an established and consistent spontaneous respiratory pattern, the level of pressure support may be reduced gradually to promote increased efficiency. The rate at which pressure support is reduced is dependent on the infant and preceding clinical history. Infants ventilated for extended periods may benefit from more gradual reduction of pressure support to allow time for increased
efficiency of respiratory muscle contractile function. PEEP may need to be increased as ΔPsupp is decreased to maintain sufficient mean airway pressure for oxygenation. A review of the adequacy of tidal volume and respiratory rate should always precede any change in PEEP. Readiness for extubation, is indicated by maintenance of physiological respiratory rates and normal gas exchange despite a relatively low level of pressure support.

Suggested approaches to adjusting the tidal volume and set RR for MMV during 100 % spontaneous ventilation are shown in Figure 10. Priority of whether to change the set RR or the ΔPsupp will depend on whether the patient is hypercarbic or hypocarbic, and the relative balance between spontaneous tidal volume and spontaneous respiratory rate.

<table>
<thead>
<tr>
<th>PRACTICAL TIP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Setting the ΔPsupp too low</strong></td>
</tr>
<tr>
<td>Can lead to</td>
</tr>
<tr>
<td>- Inefficient breathing (low VT, high dead-space)</td>
</tr>
<tr>
<td>- Rapid spontaneous breathing</td>
</tr>
<tr>
<td>- Atelectasis</td>
</tr>
<tr>
<td>- Respiratory muscle fatigue</td>
</tr>
<tr>
<td>- Increase of work of breathing</td>
</tr>
<tr>
<td>- Increase of oxygen consumption</td>
</tr>
<tr>
<td>- Increased risk of developing an inadvertent PEEP</td>
</tr>
</tbody>
</table>

| **Setting the ΔPsupp too high** |
| (in the presence of strong respiratory drive and effective muscle contractile activity): |
| Can lead to |
| - High tidal volumes |
| - Low spontaneous rates |
| - Increased ventilator dependency |
2.2.3 Adjustment of mandatory and spontaneous ventilatory support

Patients will spend periods of time receiving a mixed form of respiratory support from both mandatory and spontaneous breaths, during automated weaning from 100 % mandatory ventilation to 100 % spontaneous ventilation. In this mixed respiratory support mode, the clinician needs to consider carefully the primary problem to be overcome and outcome objective of adjustments to ventilator settings. The relative efficiency of the mandatory and spontaneous breaths contributions to ventilation should be evaluated separately relative to the desired physiological targets for VT, RR and PaCO₂. Suggestions for ventilator adjustment and troubleshooting ventilatory support during mixed mandatory and spontaneous ventilation are provided in section 3.
Starting of therapy

Set $\Delta P_{supp}$ to a level that achieves 80% of VT$_{set}$

wait for 15-30 minutes

Assess patient's response, re-adjust if necessary

- Frequent & low tidal volume breaths
  - RR$_{spon}$ > RR$_{set}$
  - VT$_{spon}$ < (80%) VT$_{set}$
  - Increase $\Delta P_{supp}$

- Few, large breaths
  - RR$_{spon}$ < RR$_{set}$
  - VT$_{spon}$ > (100%) VT$_{set}$
  - Decrease $\Delta P_{supp}$

Re-assess PEEP setting to sustain oxygenation and mean airway pressure

During therapy

Re-assess $\Delta P_{supp}$ setting regularly during therapy

- Decreased compliance
- Increased airway resistance
- Decreased respiratory muscle efficiency
- Frequent / low tidal volume breath
  - Increase $\Delta P_{supp}$

- Increased compliance
- Decreased airway resistance
- Increased respiratory muscle efficiency
- Fewer, large breath
  - Decrease $\Delta P_{supp}$

Extubation criteria:
- Physiological respiratory rate
- Normal gas exchange
- Low level of $\Delta P_{supp}$

Table 3. Initial setting and adjustment of $\Delta P_{supp}$. 
2.3 Use of Automatic Tube Compensation to assist weaning

Conventional PS used for spontaneous breaths only provides a fixed pressure, and hence often over-compensates or under-compensates for work of breathing during the inspiratory phase. Inclusion of automatic tube compensation (ATC) may overcome this mismatch in pressure support and facilitate this weaning process by compensating for the work of breathing through the tracheal tube. ATC may be especially important in the immature infant, as the resistance of the very small tracheal tubes is especially high.

During ATC, the pressure required to compensate the work of breathing (WOB) imposed by the tracheal tube is calculated continuously by the ventilator. The ventilator then provides the required level of pressure compensation to the circuit, in real-time. Thus, the patient is effectively only providing the work to overcome intrinsic work of breathing that would be present without the tracheal tube. Consequently, ATC is often referred to as “electronic extubation”.

ATC is a form of proportional support, as the pressure support given during ATC is proportional (non-linear) to the flow passing through the tube. Flow passing through the tracheal tube is a function of the tidal volume (influenced by patient effort during spontaneous breathing) and inspiratory time. As the adjustment to pressure support is continuous, the inclusion of ATC during weaning potentially also improves the synchrony between ventilator and patient.

![Figure 11. Principles of automatic tube compensation (ATC). Without ATC, the patient needs to use respiratory muscle effort to overcome the ΔP due to resistance across the tracheal tube, in addition to generating the pressure required to overcome the mechanical impedance of the lung. With ATC enabled, the pressure required to overcome the impedance of the tracheal tube is provided by the ventilator, and the patient only needs to overcome the impedance of the lung, providing relief and effective “electronic extubation”.

ATC is easily set up using the type of tube (tracheal or tracheostomy), the internal diameter (in mm) and the amount of compensation required (100 % compensation is complete compensation).
2.4 Leakage compensation

Leakage compensation provides a more accurate and reliable measure of the delivered tidal volume and minute ventilation. The ventilator calculates tidal volume and minute volume, which are corrected for the lost volumes through the ET-tube leak. The leakage compensated displayed values for VT and MV reflect the real volumes going to the lung. If leak compensation is active, Volume Guarantee will use the leak compensated VT. Use of leakage compensation is advisable to prevent inappropriate excessive down-regulation or up-regulation of the mandatory respiratory rate in the presence of a variable leak. The percentage of volume lost during inspiration is greater than the volume loss during expiration as the driving pressure during inspiration is higher. The leakage correction algorithm takes the inspiratory and expiratory flows into account. The measured volume and flow waveforms are also corrected by the leak compensation algorithm (see Figure 13).

Figure 12. Effect of leak on inspiratory and expiratory flow and tidal volume.

**DEFINITION LEAKAGE COMPENSATION**

Leakage Compensation is correcting the measured tidal and minute volume for the volume loss due to the ETT leakage. Additionally Leakage Compensation corrects the flow and volume waveforms. The leak compensated tidal volume (VT) is not an inspiratory or expiratory tidal volume, but the tidal volume, which is close to the true volume reaching the lungs. If Leak Compensation is activated, Volume Guarantee is using the leak compensated tidal volume (VT) for regulation of inspiration pressure.
Figure 13. Leak compensation. Illustration shows screenshots for PC-MMV+VG without leak (1), with an uncompensated leak (2) and with a volume-compensated leak (3). In the absence of leakage, the inspired and expired tidal volumes are very similar. When a leak occurs and leak compensation is not enabled, the inspired tidal volume is higher than the expired tidal volume. The ventilator increases pressure to try to match the expired tidal volume to the set VT. When a leak is present and leakage compensation is enabled, the delivered tidal volume is more closely approximated by an algorithm: the actual delivered tidal volume lies between the inspired and expired tidal volumes.
2.5 Monitoring

Appropriate monitoring and response to changes in respiratory status are vital to success in MMV. Monitoring includes awareness of target physiological variables (discussed above), setting up the ventilatory screen to display the essential measured variables that are needed to assess adequacy of ventilatory support for both the mandatory and the spontaneous inflations, and the use and attention to reasonable alarm limits to alert the carer to changes in physiology that may require adjustment to ventilatory settings. Routine peripheral oxyhaemoglobin monitoring is essential. Additionally, monitoring of transcutaneous carbon dioxide may help in assessment of adequacy of ventilation.

2.5.1 Ventilator screen set up

1. Waveforms:
   a. Flow is the most important waveform for display as presence of an appropriate flow waveform excludes significant obstruction or leak and is also useful for setting the inspiratory time. The pressure waveform helps the clinician to evaluate the rate of rise of the pressure waveform (slope) as a proportion of the inspiratory cycle. The volume waveform can be used to refine the slope and inspiratory time to achieve complete tidal volume delivery, whilst avoiding prolonged end-inspiratory hold.

2. Trends
   a. Trend screens are useful for bedside review of ventilation over a period of time or following a change in ventilator settings. Including both mandatory and spontaneous monitoring variables facilitates review of the spontaneous breathing activity and appropriateness of pressure support settings. Trends should be referred to whenever patient progress is being reviewed. Suggested variables to display in the trends include the following variables:
      - MV, MVspon, % MVspon
      - RR and RRspion
      - VT/kg BW, VTmand and VTspon
      - PIP
      - FiO₂, Pmean
   b. Incorporation of a trend in the VT/kg BW, RRspion and MVspon in the measured variables area on the main home screen assists rapid recognition of changes or trends in the PS breaths. Altered patterns may require clinical attention and a review of settings.
Figure 14. Standard MMV display screen. The standard monitoring includes ventilator waveforms, key ventilator and patient variables to allow adequate monitoring and comparison of mandatory and spontaneous ventilation. Display of short term (30 min) trend data allows more rapid recognition of a persistent change in mandatory and spontaneous breathing behaviour.

2.5.2 Alarm limits
Appropriate setting of alarm limits is essential to alert the clinician to changes in respiratory behaviour that may necessitate alteration to ventilatory settings (mandatory breaths or pressure support). Suggested settings for alarms are in table 5 below. Troubleshooting and ventilation adjustments relevant to each alarm are provided in Section 3.

2.6 Additional considerations
MMV works best in the presence of an active respiratory drive. Caffeine supplementation increases efficiency of diaphragmatic contraction and enhances respiratory rhythmicity in preterm infants, as well as reducing incidence and severity of BPD. Combination of MMV with other pro-weaning therapeutic options including anti-inflammatory therapies may facilitate more rapid weaning compared to a manual weaning modality and limit the duration of such additional pharmacotherapy. A further important factor to consider in optimising success of weaning includes appropriate nutrition targeted to increasing lean muscle mass (not fat), increasing the energy reserves and contractile force generated by the respiratory muscles.
Combination of MMV with other pro-weaning therapeutic options including anti-inflammatory therapies may facilitate more rapid weaning compared to a manual weaning modality and limit the duration of such additional pharmacotherapy.

2.7 Measured variables

The double column measured variable layout is suggested. Display of 2 variables per cell for paired/related variables (e.g., RR & RRsp and MV & %MVsp), will remind clinicians to consider the prevalent modality (MV or PSV) when interpreting the data, and will create additional room for display of recent trend data in some of the remaining cells. An example of a suggested default screen layout for MMV is shown above (see Figure 14).

Suggestions for monitoring of set parameters and measured variables are shown in Table 4 below. These settings and measurements provide data required for nursing observations, but also enhance appreciation by the clinician of the adequacy of the prevailing mode (mandatory, spontaneous or mixed mandatory and spontaneous breathing support).

Table 4. Recommended monitoring variables.

<table>
<thead>
<tr>
<th>GENERAL</th>
<th>SPONTANEOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO2</td>
<td></td>
</tr>
<tr>
<td>PIP</td>
<td></td>
</tr>
<tr>
<td>PEEP</td>
<td></td>
</tr>
<tr>
<td>Pmean</td>
<td></td>
</tr>
<tr>
<td>MV</td>
<td></td>
</tr>
<tr>
<td>VT, VT/kg BW</td>
<td>VTsp</td>
</tr>
<tr>
<td>RR</td>
<td>RRspon</td>
</tr>
<tr>
<td>% leak</td>
<td>Tispon</td>
</tr>
<tr>
<td>etCO₂*</td>
<td></td>
</tr>
</tbody>
</table>

*infants > 2 kg
Table 5. Suggested alarm limits for respiratory rate and minute volume during MMV.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>HIGH ALARM</th>
<th>LOW ALARM</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (breaths/min)</td>
<td>1.5-2.0 x target RR</td>
<td>target RR-10</td>
</tr>
<tr>
<td>MV</td>
<td>1.5-2.0 x set MV</td>
<td>0.75 x set MV</td>
</tr>
</tbody>
</table>
3 Troubleshooting – Sample Screenshots

1. Inhibited spontaneous breathing: Set MV too high

Figure 15. A high mandatory minute volume inhibits spontaneous breathing. The high MV is a function of the set VT and the set RR. Thus both set VT and set RR need to be reviewed if spontaneous breathing is not occurring to determine if one parameter or both parameters are set too high and be inhibiting a spontaneous breathing rhythm.

2. High set inspiratory time with prolonged end inspiratory hold

Figure 16. Inhibited spontaneous breathing from excessive Ti. A prolonged inspiratory time on mandatory breaths activates stretch receptors and inhibits spontaneous rhythm generation in the respiratory centre. This feedback inhibition results in loss of spontaneous breathing activity and increased dependence on the baseline mandatory ventilation.
3. Tachypnoea  
   a. MV set too low

   Figure 17. Tachypnoea resulting from insufficient mandatory MV. Setting the mandatory MV too low (either by a low VT or low RR) may result in hypercapnoea. The infant’s response to hypercapnoea is to increase respiratory rate to attempt to blow off the high level of carbon dioxide. Tachypnoea may not be seen if the infant has a low respiratory drive, as may occur in the presence of sepsis.

   b. Inadequate pressure support

   Figure 18. Tachypnoea resulting from insufficient pressure support during spontaneous breathing. Inadequate pressure support results in inefficient spontaneous breathing activity as the infant generates inadequate tidal volume with each spontaneous breath (see VT/kgBW on screen). The infant may develop hypercapnoea, and will respond to the inadequate pressure support with tachypnoea to increase CO₂ clearance, provided adequate respiratory drive is present. Increasing the ΔPsupp will increase VTspoons, reduce PaCO₂ and consequently result in a fall in the spontaneous RR to more physiological values.
4. High spontaneous tidal volumes/low respiratory rate.

Figure 19. Excessive pressure support. 
Excessive pressure support results in high spontaneous tidal volumes. The infant will reduce its respiratory rate to avoid developing hypocarbia. The high spontaneous tidal volumes may be injurious to the lung. The carer needs to monitor VTspon and compare it to the set VT to identify when spontaneous tidal volumes are high. The carer should review trend data: if excessive VTspon is a persistent rather than transient issue, then ΔPsupp should be decreased.
## 4 Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>$\Delta P_{\text{supp}}$</td>
<td>Pressure Support - Pressure difference from PEEP level</td>
</tr>
<tr>
<td>A/C</td>
<td>PC-AC; Pressure Control- Assist Control</td>
</tr>
<tr>
<td>ATC</td>
<td>Automatic Tube Compensation</td>
</tr>
<tr>
<td>CCMV</td>
<td>Computer-Controlled Minute Ventilation</td>
</tr>
<tr>
<td>CLD</td>
<td>Chronic Lung Disease</td>
</tr>
<tr>
<td>etCO$_2$</td>
<td>End-tidal CO$_2$</td>
</tr>
<tr>
<td>ET(T)</td>
<td>Endotracheal Tube</td>
</tr>
<tr>
<td>FiO$_2$</td>
<td>Fraction of inspiratory O$_2$ concentration</td>
</tr>
<tr>
<td>IMV</td>
<td>Intermittent mandatory ventilation</td>
</tr>
<tr>
<td>MMV</td>
<td>Mandatory Minute Ventilation</td>
</tr>
<tr>
<td>MV</td>
<td>Minute volume</td>
</tr>
<tr>
<td>MV$_{\text{mand}}$</td>
<td>Minute volume from mandatory breaths</td>
</tr>
<tr>
<td>MV$_{\text{spon}}$</td>
<td>Minute volume from pressure-supported spontaneous breaths</td>
</tr>
<tr>
<td>MV$_{\text{total}}$</td>
<td>Total minute volume</td>
</tr>
<tr>
<td>PaCO$_2$</td>
<td>Partial pressure of carbon dioxide in arterial blood</td>
</tr>
<tr>
<td>Paw</td>
<td>Airway pressure</td>
</tr>
<tr>
<td>PEEP</td>
<td>Positive end expiratory pressure</td>
</tr>
<tr>
<td>PIP</td>
<td>Peak inspiratory pressure</td>
</tr>
<tr>
<td>Pmax</td>
<td>Maximum applied pressure during Volume Guarantee</td>
</tr>
<tr>
<td>Pmean</td>
<td>Mean airway pressure</td>
</tr>
<tr>
<td>PS</td>
<td>Pressure Support</td>
</tr>
<tr>
<td>PSV</td>
<td>PC-PSV; Pressure Control- Pressure Support Ventilation</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>RDS</td>
<td>Respiratory Distress Syndrome</td>
</tr>
<tr>
<td>RR</td>
<td>Respiratory rate</td>
</tr>
<tr>
<td>RR$_{\text{mand}}$</td>
<td>Mandatory respiratory rate</td>
</tr>
<tr>
<td>RR$_{\text{spon}}$</td>
<td>Spontaneous respiratory rate</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SIMV</td>
<td>Synchronized intermittent mandatory ventilation</td>
</tr>
</tbody>
</table>
SpO₂  Saturation of peripheral oxyhaemoglobin
TcPO₂  Transcutaneous partial pressure of oxygen
TcPCO₂  Transcutaneous partial pressure of carbon dioxide
Te   Expiratory time
Ti   Inspiratory time
Tispon  Inspiratory time of spontaneous breath
VG   Volume Guarantee
VT   Tidal volume
VT/kg BW  Tidal volume per kilogram bodyweight
VTmand  Tidal volume of mandatory breaths
VTspon  Tidal volume of spontaneous breaths
w GA  Weeks gestational age
WOB  Work of breathing
5 References


