

STATE-OF-THE-ART

A practical guide to neonatal volume guarantee ventilation

C Klingenberg^{1,2,3}, KI Wheeler^{2,4,5}, PG Davis^{2,4,6} and CJ Morley^{2,4,6}

¹Department of Paediatrics, University Hospital of North Norway, Tromsø, Norway; ²Department of Newborn Research, Royal Women's Hospital, Melbourne, Australia; ³Department of Paediatrics, Faculty of Health Science, University of Tromsø, Tromsø, Norway; ⁴Murdoch Childrens Research Institute, Melbourne, Victoria, Australia; ⁵The Ritchie Centre, Monash Institute for Medical Research, Monash University, Melbourne, Victoria, Australia and ⁶Department of Obstetrics & Gynaecology, University of Melbourne, Melbourne, Victoria, Australia

A recent systematic review and meta-analysis shows that volume-targeted ventilation (VTV) compared with pressure-limited ventilation (PLV) reduce death and bronchopulmonary dysplasia, pneumothorax, hypocarbia and severe cranial ultrasound abnormalities. In this paper, we present published research and our experience with volume guarantee (VG) ventilation, a VTV mode available on the Dräger Babylog 8000plus and VN500 ventilators. The VG algorithm measures the expired tidal volume (V_T) for each inflation and adjusts the peak inflating pressure for the next inflation to deliver a V_T set by the clinician. The advantage of controlling expired V_T is that this is less influenced by endotracheal tube leak than inspired V_T . VG ventilation can be used with an endotracheal tube leak up to ~50%. Initial set V_T for infants with respiratory distress syndrome should be 4.0 to 5.0 ml kg⁻¹. The set V_T should be adjusted to maintain normocapnoea. Setting the peak inflating pressure limit well above the working pressure is important to enable the ventilator to deliver the set V_T , and to avoid frequent alarms. This paper provides a practical guide on how to use VG ventilation.

Journal of Perinatology (2011) **31**, 575–585; doi:10.1038/jp.2011.98; published online 14 July 2011

Keywords: infant; newborn; volume-targeted ventilation; tidal volume; mechanical ventilation

Introduction

Mechanical ventilation is required to manage neonates with severe respiratory failure. Pressure-limited ventilation (PLV), delivering a fixed-peak inflating pressure (PIP), has traditionally been used to control the arterial carbon dioxide (PaCO₂). During PLV the tidal volume (V_T) fluctuates widely due to the baby's breathing, changes in lung mechanics and variable endotracheal tube (ETT) leak.^{1,2} As high V_T (volutrauma), and not pressure *per se*, causes lung injury, controlling V_T rather than PIP is a logical strategy for ventilating preterm infants.^{3–5}

Modern microprocessor-controlled ventilators allow volume-targeted ventilation (VTV) even in very preterm infants. VTV modes vary in how they measure and control V_T delivery.^{6,7} Measurements are only accurate with the flow sensor placed at the Y-piece.^{8,9} The flow-sensors measure inspired and expired V_T , and ETT leak is calculated. The advantage of targeting inspired V_T is that the ventilator controls the V_T as it is delivered. The major disadvantage is that variable ETT leak alters the delivered V_T . The advantage of using the expired V_T is that this most accurately reflects the V_T that entered the infant's lung, and is less influenced by ETT leaks unless they are very large.

Volume guarantee (VG) ventilation is a VTV-mode controlling the expired V_T . In Australasia and the Nordic countries, 50% of level 3 neonatal units routinely use VTV modes, and 80% of these used VG.¹⁰ In contrast, a recent cross-sectional study in Europe revealed that only 11% of ventilated infants received VTV modes.¹¹ The current paper presents practical guidance about using VG ventilation drawing upon research and our experience with the Dräger Babylog 8000plus and our understanding about the Dräger Babylog VN500.

Why we have written this paper?

We recently completed a systematic review and meta-analysis on randomized controlled trials of neonatal VTV versus PLV.^{12,13} The review found that VTV significantly reduces rates of death and bronchopulmonary dysplasia, pneumothorax, hypocarbia and severe cranial ultrasound abnormalities. Lack of experience or knowledge of how to use VTV may explain why it is infrequently used in many countries.^{10,11}

This paper gives neonatologists practical guidance on the use of one type of VTV; VG ventilation with the Dräger Babylog 8000plus ventilator and the new Dräger Babylog VN500. Dräger Babylog 8000plus is the most commonly used neonatal ventilator in Europe.^{10,11} We have used VG ventilation for many years and reported different aspects on how this specific VTV mode works.^{14–20}

We believe it is more acceptable to the users, if such guidance is written by experienced clinicians without input from the manufacturer. We have checked details with the manufacturer's engineers but they had no part in commissioning or writing the manuscript.

Correspondence: Dr C Klingenberg, Department of Paediatrics, University Hospital of North Norway, Tromsø N-9038, Norway.

E-mail: claus.klingenberg@unn.no

Received 10 December 2010; revised 20 May 2011; accepted 14 June 2011; published online 14 July 2011

Why control tidal volume?

The purpose of mechanical ventilation is to ventilate the lungs with an appropriate tidal volume. VTV reduces the variability of V_T delivery compared with PLV.^{1,2} Avoiding a high V_T should reduce volutrauma.⁵ Decreasing V_T fluctuations, and reducing variations in minute volume, leads to a more stable PaCO_2 and less hypocarbia.^{1,21,22} This reduces fluctuations in cerebral blood flow and decreases the risk of brain injury.^{23,24} Avoiding a very low V_T may reduce risks of atelectotrauma and hypercarbia.^{21,25,26}

How does volume guarantee (VG) work?

The operator sets a target expired V_T (set V_T). The ventilator measures the expired V_T for each inflation and automatically adjusts the PIP for the next inflation of the same type, triggered or untriggered, aiming to deliver the V_T around the set level (Figure 1, Table 1).

How accurate is the control of expired tidal volume with volume guarantee?

The expired V_T may vary during VG ventilation but the ventilator algorithm makes automatic adjustments to the PIP for each inflation to keep the delivered V_T as close as possible to the set V_T .

Keszler and Abubakar¹ reported that when using VG ventilation >60% of breaths were within target range of set V_T . In another study of 6540 inflations from 10 preterm babies ventilated with VG, the mean expired V_T , as percentage of the set V_T , was 102% for triggered inflations and 98% for untriggered inflations.¹⁵ This study showed that VG maintains the average expired V_T accurately. Reasons for intermittently higher or lower V_T delivery are discussed below.

The choice of ventilator modes

The Dräger Babylog 8000plus permits the use of VG only with triggered modes for example, synchronised intermittent mandatory ventilation, assist control (AC/SIPPV) or pressure support ventilation (PSV).²⁷ The new VN500 also offers the use of VG with non-triggered continuous mandatory ventilation. Breaths unsupported by an inflation during continuous mandatory ventilation + VG or synchronised intermittent mandatory ventilation + VG are not volume targeted. We prefer using VG combined with AC or PSV because these modes support all spontaneous breaths. AC + VG is associated with more stable expired V_T , better oxygenation and reduced tachypnoea when compared with synchronised intermittent mandatory ventilation + VG.²⁸ No trials have directly compared PSV with AC

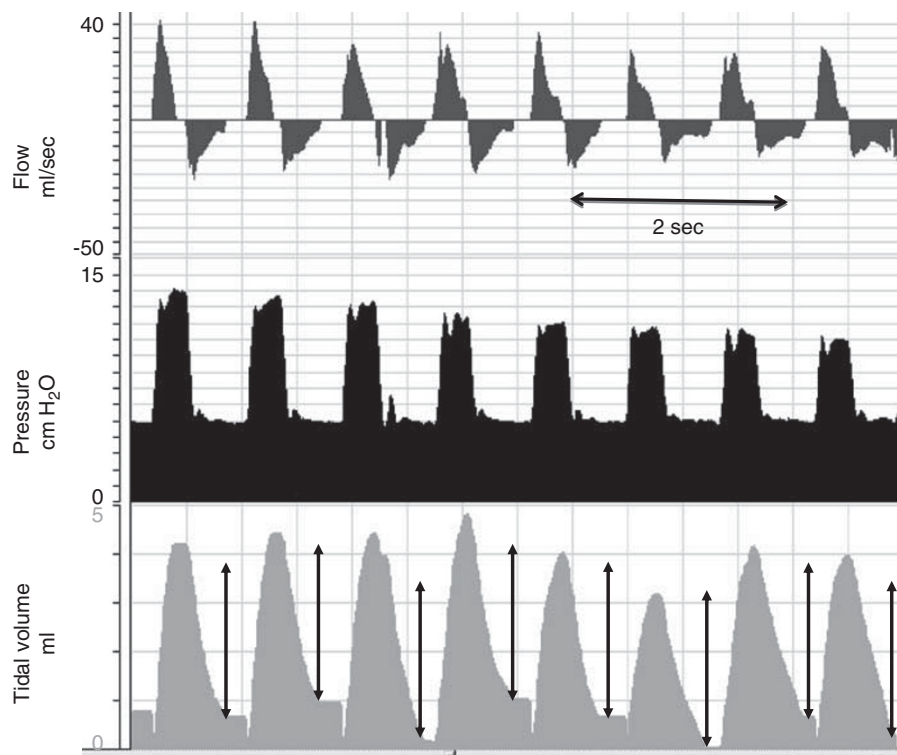


Figure 1 The volume guarantee (VG) software adjusts the peak inflating pressure (PIP) for the next inflation based on measurement of the expired V_T of the previous inflation. This figure shows nine triggered inflations from a 750-g baby ventilated with assist-control VG. The three waves are from top to bottom flow (ml sec^{-1}), pressure ($\text{cm H}_2\text{O}$) and V_T (ml). The set V_T of 3.2 ml is shown by the vertical arrows after each V_T . It shows the expired V_T is slightly larger than the set V_T for all inflations and so the PIP is reduced for each subsequent inflation.

Table 1 Selected characteristics of Dräger Babylog 8000plus and VN500 ventilators

<i>Flow sensor</i>	
Flow sensor; type	Hot wire anemometer
Flow sensor; dead space	0.9 ml
Flow sensor; accuracy of V_T measurement	± 0.5 ml (up to 5 ml) $\pm 10\%$ (above 5 ml)
Flow sensor; trigger sensitivity (combined flow and volume trigger)	With Babylog 8000plus this is an arbitrary scale from 1–10. 1 is the most sensitive setting; corresponds to a flow trigger at 0.21 min^{-1} , with no minimum volume required. With Babylog VN500, the trigger sensitivity is set in 1 min^{-1} and the most sensitive setting (0.21 min^{-1}) can be set directly
Flow sensor; trigger delay (at maximum sensitivity)	~ 30 ms; from the onset of inspiratory gas flow to the onset of inflation ¹⁵
<i>Safety features, circuit gas flow, alarms and expiratory triggering</i>	
Protection against excessive V_T delivery	The inflation stops and the expiration valve opens if inspired V_T (adjusted for ETT leak) exceeds 130% of the set V_T
Ventilator response to partial ETT obstruction and/or low V_T	Adjusts PIP, by up to 3 cm H ₂ O for each inflation, until set V_T delivered
Ventilator response to complete ETT obstruction	PIP is temporarily reduced to the midpoint of PIP and PEEP as a safety feature ¹⁷
Adjustments for ETT leak to provide accurate V_T delivery	PIP is automatically adjusted to deliver set V_T . It can be used with ETT leaks up to $\sim 50\%$
Circuit gas flow	Manually set; range $1\text{--}30 \text{ l min}^{-1}$. In practice often $6\text{--}8 \text{ l min}^{-1}$. VN500: optional automatically adjusted circuit gas flow
Low tidal volume alarm	If expired V_T is below 90% of set V_T
Alarm delay setting	Alarm delay should be set > 10 s. Low tidal volume alarm will only occur if the expired V_T is consistently below 90% of the set V_T for longer than 10 s
PSV mode	Expiration starts when inspiratory flow has fallen to 15% of the peak flow (trigger threshold is automatically adjusted for changes in ETT leak). Clinician needs to select an upper limit of the inflation time. We recommend $0.4\text{--}0.6$ s

Abbreviations: ETT, endotracheal tube; PEEP, positive end expiratory pressure; PIP, peak inflating pressure.

during VG ventilation. However, the difference between AC and PSV is probably small unless inflation times during PSV become very short.

Triggered and untriggered inflations

Ventilator inflations may be triggered by the infant or initiated by the ventilator in the absence of any effort from the infant ('untriggered inflations'). Babylog 8000plus and VN500 control the PIP for triggered and untriggered inflations separately, and adjust the PIP according to the expired V_T of the preceding inflation of the same type. Between adjacent inflations of the same type the change in PIP is usually well below 3 cm H₂O (Table 1).¹⁴ Between triggered and untriggered inflations, the PIP can vary much more than this as it depends on the PIP used for the previous inflation of that type. When an infant contributes to the V_T during a triggered inflation, the average PIP is 4 cm H₂O lower than during an untriggered inflation (Figure 2).¹⁴

Selecting target V_T for different clinical conditions

CO₂ exchange is determined by the alveolar minute ventilation ($\text{AMV} = (V_T - V_{\text{Deadspace}}) \times \text{rate}$). The anatomical dead space is ~ 2 to 2.5 ml kg^{-1} .^{29,30} A V_T around twice this is needed for

adequate ventilation.³⁰ Data on the 'appropriate' V_T to set for different conditions are limited.

Spontaneously breathing infants <32 weeks' gestation, receiving continuous positive airway pressure, had a mean (range) V_T of 4.4 (2.6 to 7.2) ml kg⁻¹.³¹ Vilstrup³² reported that preterm infants with respiratory distress syndrome (RDS) have a functional residual capacity of $\sim 11 \text{ ml kg}^{-1}$ and a total lung capacity of $\sim 19 \text{ ml kg}^{-1}$. A V_T of 4 to 6 ml kg⁻¹ is often considered appropriate for infants with RDS and experts suggest a $V_T > 8 \text{ ml kg}^{-1}$ may cause volutrauma.^{27,33} In infants <800 g, a V_T of $\sim 5 \text{ ml kg}$ was required to achieve normocapnoea in the first week of life.³⁴ The V_T per kg required for normocapnoea was inversely related to birthweight suggesting that the flow sensor contributes a modestly increased fixed dead space in the smallest infants.³⁵ Lista *et al.*²⁵ compared a set V_T of 5 ml kg^{-1} with 3 ml kg^{-1} in infants with RDS. The 3 ml kg^{-1} group showed higher levels of pro-inflammatory cytokines in tracheal aspirate and required a longer duration of ventilation.

If the set V_T is below the spontaneous V_T , the VG mode lowers the PIP close to the positive end expiratory pressure (PEEP).²⁶ We have observed that with a set V_T of 3.5 ml kg^{-1} , many spontaneously breathing infants actually generate a V_T closer to 4 ml kg^{-1} .¹⁸

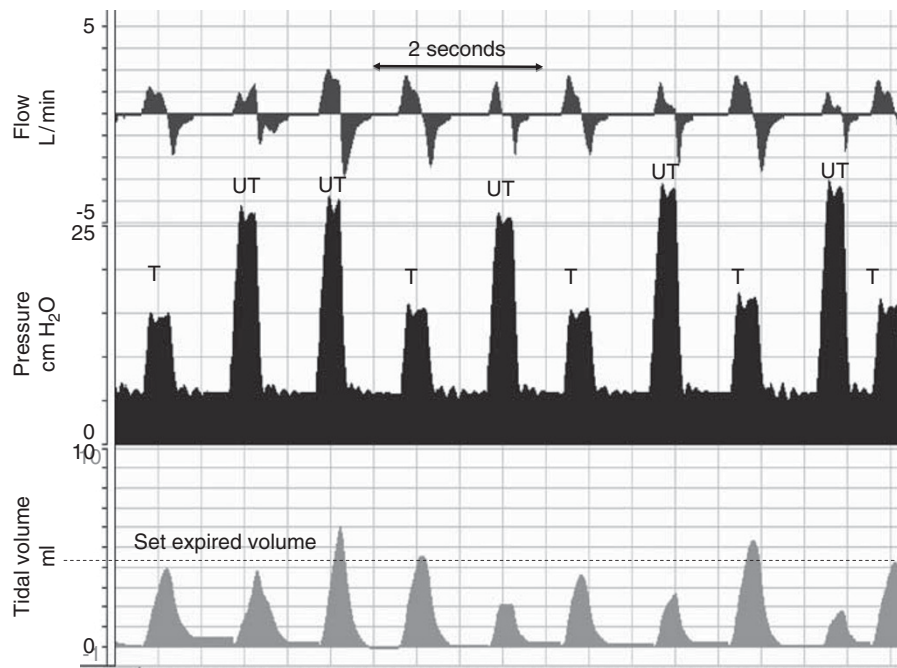


Figure 2 This figure shows a recording from an 850-g baby with ten inflations, illustrating the effect of triggered and untriggered inflations occurring close together because the back-up ventilator rate was too close to the baby's spontaneous rate. The three waves are from top to bottom flow (1 min^{-1}), pressure ($\text{cm H}_2\text{O}$) and tidal volume (ml). The triggered inflations and their V_T are indicated by T. The untriggered inflations are indicated by UT. The inflating pressure for each inflation depends on expired V_T of the preceding inflation of the same type. Note that although there is a large difference in the inflation pressures, there is relatively little difference in the delivered V_T .

For infants with RDS we recommend starting VG ventilation with set V_T of 4.5 to 5.0 ml kg^{-1} if birthweight $< 1000 \text{ g}$ and 4.0 to 4.5 ml kg^{-1} for infants $> 1000 \text{ g}$. Subsequent adjustments are made in increments of 0.5 ml kg^{-1} , usually within the range 4.0 to 6.0 ml kg^{-1} , to achieve acceptable PaCO_2 values.

Infants receiving prolonged mechanical ventilation can develop tracheal dilatation, increasing the dead space.³⁶ Ventilator-dependent infants > 2 to 3 weeks postnatal age may require a higher set V_T (5 to 8 ml kg^{-1}) to control their PaCO_2 .³⁴

Infants with congenital diaphragmatic hernia have pulmonary hypoplasia, but require the same minute ventilation as healthy infants to achieve normocapnoea.³⁷ The mean (s.d.) spontaneous V_T of infants with congenital diaphragmatic hernia immediately after birth was 3.8 (1.9) ml kg^{-1} .³⁸ We suggest using a set $V_T \sim 4 \text{ ml kg}^{-1}$ and high ventilator rates if necessary.

Setting the PIP limit (Pmax)

During VG the set PIP is not the same as the delivered PIP because the VG mode continuously alters the delivered PIP to achieve the set V_T . The set PIP limit needs to be high enough to allow fluctuations around the average or 'working' PIP.¹⁹ With Babylog 8000plus, the P_{insp} control knob is used to set the PIP limit. The VN500 has a specific Pmax setting. If Pmax is too close to the

working PIP, 'low tidal volume' alarms will occur frequently because the set V_T is often not achieved (Table 1). If the Pmax is much higher than the working PIP, there may not be an early warning of major changes in lung mechanics. However, the VG mode has safety features to prevent the delivery of excessive V_T , despite a high Pmax (Table 1).¹⁴ It should be noted that if the manual inflation button is pressed, the inflation is delivered with the Pmax because manual inflations are not volume targeted. Furthermore, closed endotracheal suction causes negative intratracheal pressure. Transiently higher PIP and V_T may follow a suction procedure.³⁹ This effect should be considered when setting the PIP limit during VG ventilation.

We recommend starting VG ventilation with a PIP limit (Pmax) of ~ 25 to $30 \text{ cm H}_2\text{O}$. This enables the ventilator to choose a PIP lower than this to deliver the set V_T . Thereafter, the Pmax can be adjusted to at least 5 to $10 \text{ cm H}_2\text{O}$ above the working PIP, allowing the ventilator flexibility to deliver the set V_T during variable ETT leaks and untriggered inflations.²⁷ The patient and ventilator should be assessed if the working PIP progressively increases, is persistently high (for example $> 30 \text{ cm H}_2\text{O}$), or if the ventilator frequently alarms 'low tidal volume'. The main causes are: increasing ETT leak, baby splinting its abdominal muscles against ventilator inflations, untriggered inflations, worsening lung mechanics, air leaks, the ETT slipping down the right main bronchus or ETT kinking.²⁷

Low tidal volume alarm

A 'low tidal volume' alarm occurs, if the expired V_T is $<90\%$ of the set V_T for the duration of the set alarm delay (Table 1). The number of these alarms may be reduced by increasing the P_{max} or by setting the alarm delay >10 s. Occasionally, the circuit gas flow may need to be increased in order to achieve the required PIP within the inflation time.

Setting the trigger sensitivity

The flow-sensor trigger threshold should be set at its greatest sensitivity (Table 1). If sensitivity is decreased, triggering is delayed and reduces synchrony between the baby's inspiration and ventilator inflation, and increases work of breathing. Movement of water within the circuit (rain out) is often misinterpreted by the flow sensor as the onset of a breath and inappropriately trigger inflations out of synchrony with the infant. The circuit must be kept free of condensed water. The flow sensor should be positioned with the plug pointing upwards to reduce condensation in the

sensor. It is inappropriate to reduce the humidity in the circuit to prevent rain out. The gas must be delivered to the airways at 37°C and 100% humidity to maintain ciliary and mucus function and prevent epithelial dehydration.⁴⁰ Water vapour permeable ventilator circuits should be used to prevent condensation.⁴¹

Setting the inflation time (T_i)

Sufficient T_i is required for the pressure to rise to the PIP selected by the ventilator and form a small plateau. If the T_i is too short, the PIP will not rise to a level sufficient to deliver the set V_T and a 'low tidal volume' alarm occurs. In an AC mode we recommend setting the $T_i \sim 0.3$ s for babies with RDS; similar to their spontaneous T_i .⁴²⁻⁴⁴ Infants with other lung pathologies may need a longer T_i . The appropriateness of the T_i can be evaluated by observing the ventilator graphics (Figure 3). If T_i is set too long, the pressure plateau is held after the inflation flow has stopped and there is no further increase in V_T . The PSV mode allows the infant to control and vary its T_i by triggering the onset of expiration (Table 1).

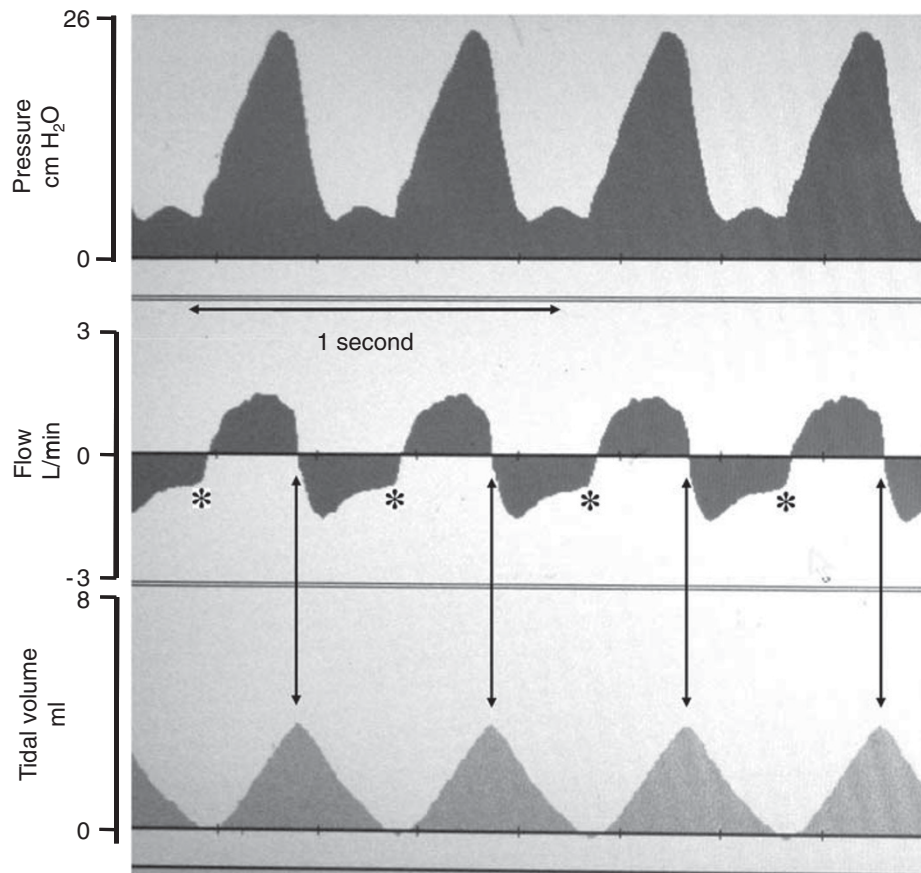


Figure 3 This figure shows a photo from the ventilator screen of five inflations. The three waves are from top to bottom pressure (cm H₂O), flow (l min⁻¹) and V_T (ml). It illustrates two main problems. First, the inflation time is too short therefore the flow wave ends abruptly at the end of inflation before reaching the baseline, and the tidal volume curve has a sharp peak. This is shown by the arrows. Second, the expired time is too short so the flow wave ends abruptly during expiration. This is shown by the asterisks.

Setting the ventilator rate

When using AC or PSV modes the clinician selects a ventilator back-up rate (BUR). The BUR delivers untriggered inflations if the infant's breathing rate falls below this rate. If the BUR is high, the baby has less opportunity to trigger inflations before the ventilator delivers untriggered inflations (Figure 2).¹⁴ In a study comparing BURs of 30, 40 and 50 per min in ventilated spontaneously breathing infants, there were most triggered inflations at a BUR of 30 per min.⁴⁵ It is important that infants trigger as many inflations as they need because their breathing contributes to the V_T , and therefore, the PIP required is lower. However, for infants with apnoea, or a poor respiratory drive, a BUR about 50 to 60 per min may be needed to maintain minute volume.

Setting the circuit gas flow

With the Babylog 8000plus, the clinician sets the circuit gas flow. This alters the slope of the pressure wave (Figure 4). The V_T will be limited if circuit gas flow is too low. An adequate flow is indicated by a short plateau of the pressure waveform during inflation. In contrast, a high circuit gas flow causes a rapid pressure upstroke, which may provoke active expiration/asynchrony and injure the lungs.^{46,47} We recommend a circuit gas flow of 6 to 8 l min⁻¹, which is usually enough for PIPs up to 30 cm H₂O if used with T_i 0.3 s. If there is no pressure plateau during inflation, the flow rate

or T_i should be increased and a reversible ETT leak is corrected. If the pressure wave has a plateau longer than the time needed to complete the inflation consider decreasing the circuit flow, or the T_i . During PSV, a high circuit gas flow shortens the T_i (Figure 4).⁴⁷ Thus, in the PSV mode the circuit gas flow may need to be reduced if T_i 's become very short (for example, <0.25 s). However, too low circuit flow (<4 to 6 l min⁻¹) may lead to difficulty in achieving the set V_T , particularly in the presence of ETT leak.²⁰

The new Babylog VN500 has two alternative modes of flow adjustment, which can be configured in the system setup. Manual adjustment of flow, is comparable with the Babylog 8000plus. Adjustment of a pressure-rise time means that the user directly sets a time after which the PIP plateau is reached. If this option is used, the Babylog VN500 selects the flow needed to reach a plateau within the rise time. A pressure-rise time between 80 to 150 ms is recommended.

Setting the positive end expiratory pressure (PEEP)

Adequate PEEP is vital to maintain functional residual capacity, prevent atelectasis and improve oxygenation.^{5,48,49} Most intubated infants require a PEEP \geq 5 cm H₂O due to underlying lung disease and the ETT bypassing the larynx.⁵⁰ Insufficient PEEP may contribute to heterogeneous ventilation, increasing the risk of regional lung injury from local volutrauma and shear stress.⁵¹

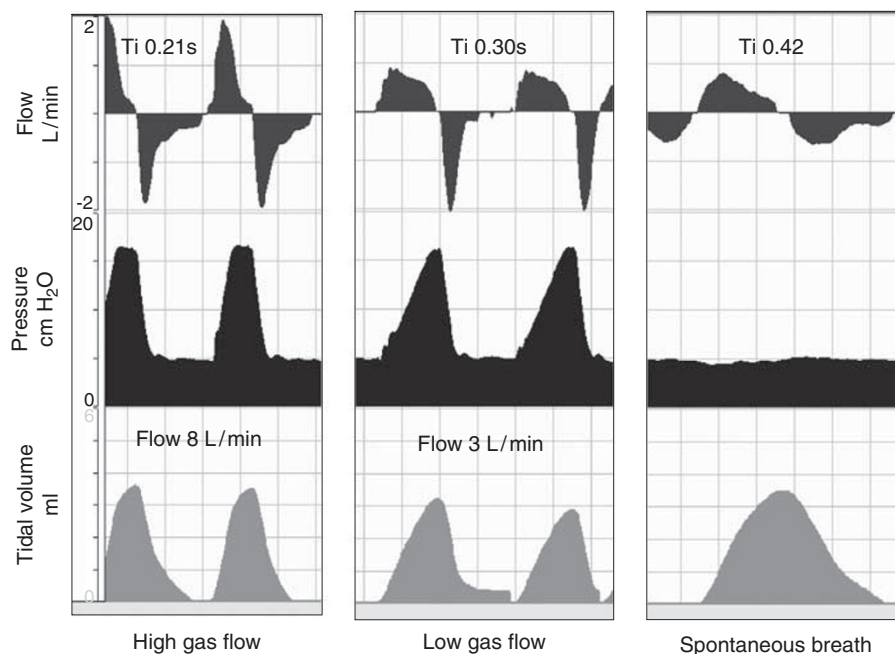


Figure 4 This is a recording of pressure support ventilation (PSV) + volume guarantee (VG) ventilation with the inflation time upper limit set at 0.6 s. It shows three panels. On the left is the effect of a high gas flow rate on the flow, pressure and tidal volume waves. It shows a rapid rise in flow, pressure and tidal volume with a very short inflation time (0.21 s). In the middle is the effect of a low gas flow. It shows a much slower rise in flow with a longer inflation time (0.30 s), a less steep rise in pressure and yet the same tidal volume. The third panel is for comparison and shows the pattern of flow, pressure and tidal volume with a spontaneous breath when the baby is breathing with continuous positive airway pressure (CPAP) only.

Weaning volume guarantee

VG ventilation automatically weans the PIP as an infant's lung function improves. In AC or PSV, the infant controls the ventilator rate. The only parameters that should be altered during weaning are the FiO_2 and the set V_T . Reducing the ventilator rate during AC or PSV has no effect on delivered rate unless respiratory effort is poor or the BUR is greater than the infant's breathing rate.

When the set V_T is below, the infant's spontaneously generated V_T the PIP will be reduced therefore the infant will be breathing on ETT continuous positive airway pressure, potentially increasing work of breathing and the risk of subsequent extubation failure due to fatigue. If this is observed for more than short periods, extubation should be considered. We do not recommend weaning V_T below 3.5 ml kg^{-1} .^{18,25,26} We consider extubation if the mean airway pressure is consistently <8 to $10 \text{ cm H}_2\text{O}$ with set V_T 3.5 to 4.5 ml kg^{-1} and blood gases are satisfactory. Readiness for extubation can be assessed using the spontaneous breathing test.⁵²

Endotracheal tube leak

Gas leak around an uncuffed neonatal ETT varies with its diameter, the applied airway pressure and the duration of ventilation.⁵³ It is largest during inflation. If there is an ETT leak,

some of the gas volume passing down the ETT will be lost before entering the lungs. Compared with inspired V_T , the advantage of targeting expired V_T is that it more closely reflects the actual V_T that entered the infant's lungs. However, as ETT leak increases, expired V_T becomes less accurate, because there is a leak during expiration, and the ventilator increasingly underestimates the delivered V_T . In general, VG ventilation can be used with ETT leaks up to $\sim 50\%$ ²⁷ because the ventilator automatically adjusts the PIP to deliver the set V_T (Table 1). An increasing ETT leak with a concomitant rise in PIP may be misinterpreted as worsening lung disease.²⁷ A very large leak may lead to hypocarbia due to underestimation of the delivered V_T .

In a ventilated infant who is breathing well and has adequate blood gases despite having a large ETT leak, extubation may be appropriate. Otherwise, if an infant has a large ETT leak it is usually technically easy to place a larger ETT. We recommend re-intubating with an appropriately sized ETT rather than turning off VG and leaving V_T delivery uncontrolled.

Large tidal volumes

During periods of crying, breathing hard or gasping, the spontaneous V_T may exceed the set V_T .¹⁴ VG permits infants to take large breaths but does not augment these inflations due to inbuilt safety features (Figure 5, Table 1).

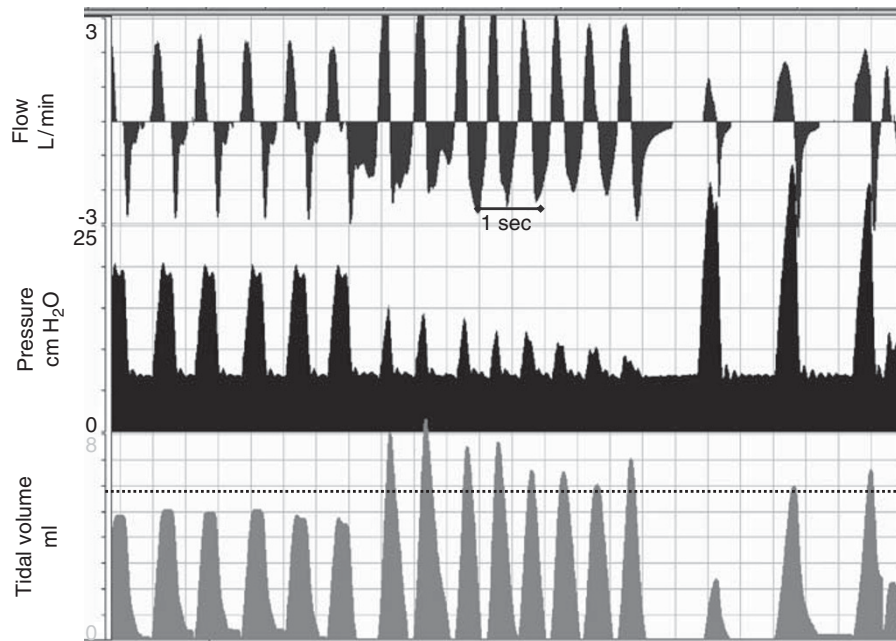


Figure 5 This recording of assist control (AC) + volume guarantee (VG) ventilation of a 1000-g baby illustrates the effect of the baby taking large spontaneous breaths. The three waves are from top to bottom flow (l min^{-1}), pressure ($\text{cm H}_2\text{O}$) and tidal volume (ml). During the first six inflations, the baby is breathing quietly and triggering inflations. During the next eight inflations the baby starts breathing hard. The inspired V_T then exceeds the set V_T , shown by the horizontal dotted line, by more than 130%. The inflating pressure is stopped early and therefore reduced for each successive inflation over 130% of the set V_T until the baby stops breathing. During the last three inflations, the baby is not breathing and three untriggered back-up inflations are delivered.

Surfactant treatment

Surfactant administration often causes brief increases in airway resistance and ETT obstruction.¹⁶ To maintain the set V_T , the PIP limit should be set 10 cm H₂O or more above the pre-surfactant PIP to enable the set V_T to be delivered.¹⁶ Within 30 to 60 min, the working PIP automatically falls as lung mechanics improve.¹⁶

Forced expiration, 'splinting' and episodes with low tidal volume

Babies can actively expire and then tighten their abdominal muscles so hard such that they prevent gas entering the lungs during an inflation; often termed 'splinting'.⁵⁴ Forced expiration and splinting cause hypoxemic episodes due to low lung volume and low V_T delivery,⁵⁵ causing 'ETT obstructed' and 'low tidal volume' alarms (Figure 6). A higher Pmax setting (for example, 35 cm H₂O) may allow the ventilator to increase the PIP and overcome the obstruction more quickly. The use of a higher target V_T (6.0 ml kg⁻¹) only slightly reduced hypoxemic episodes in studies with other VTV modes.^{55,56}

Diaphragmatic braking

Diaphragmatic braking causes an early interruption in expiratory flow (Figure 7) and is sometimes associated with a small inspiration as the diaphragm contracts.^{15,54} If this occurs within

the 0.2 s refractory period of the ventilator an inflation is not triggered. However, the VG software underestimates the expired V_T by incorrectly interpreting the small initial expired V_T as the total expired V_T , and increases the PIP for the next inflation. Despite a higher PIP, the safety features help to prevent delivery of large V_T (Table 1). Periods with expiratory braking occur with <5% of inflations and less during triggered than untriggered inflations. These episodes are usually short lived and revert spontaneously to normal ventilation.

Effect of the flow-sensor dead space

The small dead space of the Babylog flow sensor (Table 1) has little effect on ventilation.³⁵ One reason for this is that with ETT leaks the dead space is continuously flushed with fresh gas. Also, during neonatal ventilation gas movement is more complicated than simple bulk flow, minimizing the effect of dead space.³⁵ In babies <1000 g, the extra dead space may slightly increase PaCO₂ levels.^{21,34} The advantages of using flow sensors for monitoring, volume targeting and flow triggering, outweigh the small effect on PaCO₂.

Troubleshooting VG

If, during VG ventilation, an infant becomes tachypnoeic with low oxygen saturations or has a persistently low PIP with suboptimal

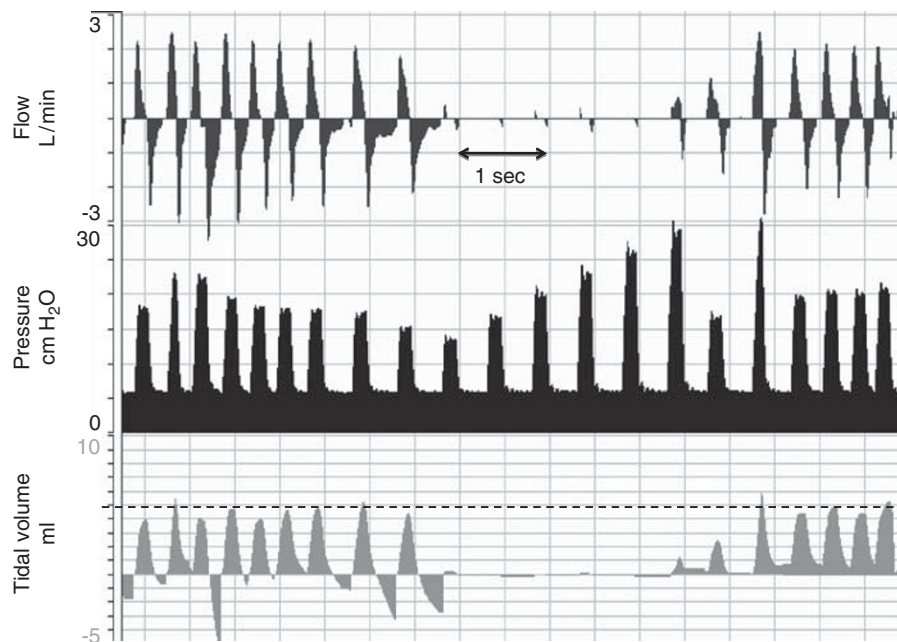


Figure 6 This is a recording from a 1000-g baby ventilated with assist control (AC) + volume guarantee (VG) ventilation at a rate of 50 per min, a set peak inflating pressure (PIP) of 40 cm H₂O, and a set V_T 5 ml. The three waves are from top to bottom flow (l min⁻¹), pressure (cm H₂O) and tidal volume (ml). It illustrates the effect on the inflating pressure when the baby tightens the abdominal muscles enough to temporarily stop inflation. This is preceded by active expiration. During the first ten inflations, the pressure is modulated to maintain the expired V_T . During inflations 7, 8 and 9 the expired V_T is larger than set V_T and so the pressure is reduced. At inflation 10 there is a very small V_T , and therefore the pressure is increased by 3 cm H₂O for each inflation for the next five untriggered inflations until a V_T is produced. This is then followed by triggered inflations at a similar inflating pressure to the start of this recording, with one untriggered inflation in between.

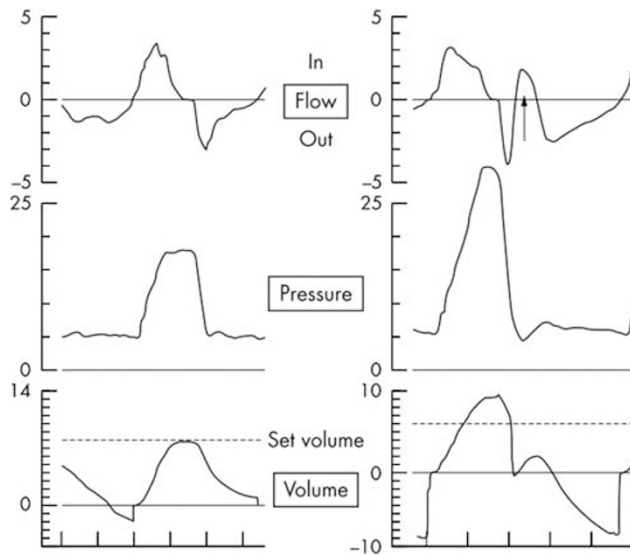


Figure 7 This illustrates the normal volume guarantee (VG) pattern (left) and the diaphragmatic braking pattern (right). The three waves are from top to bottom flow ($l\ min^{-1}$), pressure ($cm\ H_2O$) and tidal volume (ml). Diaphragmatic braking is characterised by an early interruption in expiratory flow, due to a small inspiration (arrow). This small inspiration starts shortly after the end of the inflation and separates the expiratory flow into two parts.

Box 1 Essentials of successful VG ventilation

Make sure:

- ETT leak is $<50\%$
- The PIP limit (P_{max}) is set well above the working PIP to allow fluctuations in PIP and to avoid frequent alarms
- The inspiratory pressure reaches a plateau before expiration
- The set V_T is high enough to support the infant's breathing effort
- The T_i during PSV is not too short, that is, $<0.20-0.25\ s$
- The circuit gas flow and PEEP are adequate for the infant's condition

blood gases, the condition of the infant and the ventilator must both be thoroughly assessed. Inadequate PEEP, very short T_i during PSV, a set V_T which is too low, or a large ETT leak need to be ruled out. Important points to consider for successful VG ventilation are listed in Box 1.

Conclusion

A Cochrane systematic review supports the use of VTV for ventilated preterm infants in need of mechanical ventilation.^{12,13} The VG mode controls the expired V_T and provides breath-by-breath adjustments of the PIP to achieve the set V_T . By controlling the expired V_T , this mode is less influenced by endotracheal tube leak and can be used with ETT leaks up to $\sim 50\%$. The initial set V_T for infants with RDS should be 4.0 to $5.0\ ml\ kg^{-1}$, but may need adjustments to maintain acceptable $PaCO_2$ values. Very high ($>8\ ml\ kg^{-1}$) and very low ($<3.5\ ml\ kg^{-1}$) set V_T may cause

Table 2 Examples of neonatal ventilators providing volume-targeted ventilation modes based on expired tidal volume

Manufacturer	Ventilator	VTV mode based on expired V_T
Dräger (Drägerwerk AG & Co, Lübeck, Germany)	Babylog 8000plus Babylog VN500	Volume guarantee
Stephan (F Stephan GmbH, Gackebach, Germany)	Stephanie ^a Sophie ^a	Volume limitation
Heinen & Lowenstein (Heinen & Lowenstein, Bad Ems, Germany)	Leoni Plus ^a	Volume guarantee
SLE (SLE Limited, South Croydon, UK)	SLE5000 (version 4.3) ^a	Targeted tidal volume plus

Abbreviation: VTV, volume-targeted ventilation.

^aWe have no experience with these ventilators and their specific VTV –modes, and there is no information available whether they have separate algorithms for triggered and untriggered inflations.

harm. Setting the PIP limit well above the working pressure is important to enable the ventilator alter the PIP to deliver the set V_T , and to avoid frequent low tidal volume alarms. We recommend combining VG with triggered modes supporting all inflations (AC or PSV modes). A ventilator BUR <40 per min permits the infant to trigger most inflations. VG automatically weans the PIP as the baby's lung compliance and respiratory effort improves.

This state-of-the-art review on VG ventilation is intended to be used with the Dräger Babylog 8000plus and VN500 ventilators, which have a similar VG mode. We have insufficient experience with other ventilators to make recommendations for their use. Some of the principles apply to other ventilators targeting expired V_T but caution should be applied, as these ventilators do not work exactly in the same way (Table 2). We urge the clinicians to report their experiences with all VTV modes and the manufacturers to describe the technical details of VTV modes in new neonatal ventilators.

Conflict of interest

Colin Morley has been a consultant to Dräger Medical. Dräger Medical has not contributed any financial support for this manuscript or had any part in the authorship, although they have checked the manuscript for errors of fact. Dräger Medical has assisted the authors with technical information involving different research projects some of which have been included in this manuscript.

Acknowledgments

Dr Wheeler is supported in part by a Monash University International Postgraduate Research Scholarship. Professor Davis is supported in part by an Australian National Health and Medical Research Council Practitioner Fellowship. The research has been supported by Australian NHMRC grants.

References

- 1 Keszler M, Abubakar K. Volume guarantee: stability of tidal volume and incidence of hypocarbia. *Pediatr Pulmonol* 2004; **38**: 240–245.
- 2 Swamy R, Gupta S, Singh J, Donn SM, Sinha SK. Tidal volume delivery and peak inspiratory pressure in babies receiving volume targeted or time cycled, pressure limited ventilation: a randomized controlled trial. *J Neonatal-Perinatal Med* 2008; **2**: 239–243.
- 3 Hernandez LA, Peevy KJ, Moise AA, Parker JC. Chest wall restriction limits high airway pressure-induced lung injury in young rabbits. *J Appl Physiol* 1989; **66**: 2364–2368.
- 4 Bjorklund LJ, Ingimarsson J, Curstedt T, John J, Robertson B, Werner O *et al*. Manual ventilation with a few large breaths at birth compromises the therapeutic effect of subsequent surfactant replacement in immature lambs. *Pediatr Res* 1997; **42**: 348–355.
- 5 Clark RH, Gerstmann DR, Jobe AH, Moffitt ST, Slutsky AS, Yoder BA. Lung injury in neonates: causes, strategies for prevention, and long-term consequences. *J Pediatr* 2001; **139**: 478–486.
- 6 Sharma A, Milner AD, Greenough A. Performance of neonatal ventilators in volume targeted ventilation mode. *Acta Paediatr* 2007; **96**: 176–180.
- 7 Jaecklin T, Morel DR, Rimensberger PC. Volume-targeted modes of modern neonatal ventilators: how stable is the delivered tidal volume? *Intensive Care Med* 2007; **33**: 326–335.
- 8 Cappa P, Sciuto SA, Silvestri S. Experimental evaluation of errors in the measurement of respiratory parameters of the newborn performed by a continuous flow neonatal ventilator. *J Med Eng Technol* 2006; **30**: 31–40.
- 9 Chow LC, Vanderhal A, Raber J, Sola A. Are tidal volume measurements in neonatal pressure-controlled ventilation accurate? *Pediatr Pulmonol* 2002; **34**: 196–202.
- 10 van Kaam AH, Rimensberger PC, Borenszajn D, De Jaegere AP. Ventilation practices in the neonatal intensive care unit: a cross-sectional study. *J Pediatr* 2010; **157**: 767–771.
- 11 Klingenberg C, Wheeler KI, Owen LS, Kaarensen PI, Davis PG. An international survey of volume-targeted neonatal ventilation. *Arch Dis Child Fetal Neonatal Ed* 2011; **96**: F146–F148.
- 12 Wheeler K, Klingenberg C, McCallion N, Morley CJ, Davis PG. Volume-targeted versus pressure-limited ventilation in the neonate. *Cochrane Database Syst Rev* 2010; **11**: CD003666.
- 13 Wheeler K, Klingenberg C, Morley CJ, Davis PG. Volume-targeted versus pressure-limited ventilation for preterm infants: a systematic review and meta-analysis. *Neonatology* 2011; **100**: 219–227.
- 14 McCallion N, Lau R, Morley CJ, Dargaville PA. Neonatal volume guarantee ventilation: effects of spontaneous breathing, triggered and untriggered inflations. *Arch Dis Child Fetal Neonatal Ed* 2008; **93**: F36–F39.
- 15 McCallion N, Lau R, Dargaville PA, Morley CJ. Volume guarantee ventilation, interrupted expiration, and expiratory braking. *Arch Dis Child* 2005; **90**: 865–870.
- 16 Wheeler KI, Davis PG, Kamlin CO, Morley CJ. Assist control volume guarantee ventilation during surfactant administration. *Arch Dis Child Fetal Neonatal Ed* 2009; **94**: F336–F338.
- 17 Wheeler KI, Morley CJ, Kamlin CO, Davis PG. Volume-guarantee ventilation: pressure may decrease during obstructed flow. *Arch Dis Child Fetal Neonatal Ed* 2009; **94**: F84–F86.
- 18 Wheeler KI, Wong C, Morley CJ, Davis PG. Volume guarantee ventilation: how low should we go? *J Paediatr Child Health* 2011; **47**(Suppl. 1): 60–116. Abstract nr.
- 19 Wheeler KI, Wong C, Morley CJ, Davis PG. Selecting the PIP limit for infants ventilated using assist control Volume Guarantee mode. *J Paediatr Child Health* 2011; **47**(Suppl. 1): 60–116. Abstract nr.
- 20 Wheeler KI, Wong C, Morley CJ, Davis PG. Selecting the circuit flow for infants ventilated using assist control Volume Guarantee. *J Paediatr Child Health* 2010; **46**(Suppl. 1): 7–55.
- 21 Cheema IU, Sinha AK, Kempley ST, Ahluwalia JS. Impact of volume guarantee ventilation on arterial carbon dioxide tension in newborn infants: a randomised controlled trial. *Early Hum Dev* 2007; **83**: 183–189.
- 22 Dawson C, Davies MW. Volume-targeted ventilation and arterial carbon dioxide in neonates. *J Paediatr Child Health* 2005; **41**: 518–521.
- 23 Erickson SJ, Grauaug A, Gurrin L, Swaminathan M. Hypocarbia in the ventilated preterm infant and its effect on intraventricular haemorrhage and bronchopulmonary dysplasia. *J Paediatr Child Health* 2002; **38**: 560–562.
- 24 Fritz KI, Delivoria-Papadopoulos M. Mechanisms of injury to the newborn brain. *Clin Perinatol* 2006; **33**: 573–591.
- 25 Lista G, Castoldi F, Fontana P, Reali R, Reggiani A, Bianchi S *et al*. Lung inflammation in preterm infants with respiratory distress syndrome: effects of ventilation with different tidal volumes. *Pediatr Pulmonol* 2006; **41**: 357–363.
- 26 Herrera CM, Gerhardt T, Claure N, Everett R, Musante G, Thomas C *et al*. Effects of volume-guaranteed synchronized intermittent mandatory ventilation in preterm infants recovering from respiratory failure. *Pediatrics* 2002; **110**: 529–533.
- 27 Keszler M, Abubakar KM. Volume guarantee ventilation. *Clin Perinatol* 2007; **34**: 107–116.
- 28 Abubakar K, Keszler M. Effect of volume guarantee combined with assist/control vs synchronized intermittent mandatory ventilation. *J Perinatol* 2005; **25**: 638–642.
- 29 Sandberg K, Sjoqvist BA, Hjalmarson O, Olsson T. Analysis of alveolar ventilation in the newborn. *Arch Dis Child* 1984; **59**: 542–547.
- 30 Milner AD, Vyas H, Hopkin IE. Efficacy of facemask resuscitation at birth. *Br Med J (Clin Res Ed)* 1984; **289**: 1563–1565.
- 31 te Pas AB, Davis PG, Kamlin CO, Dawson J, O'Donnell CP, Morley CJ. Spontaneous breathing patterns of very preterm infants treated with continuous positive airway pressure at birth. *Pediatr Res* 2008; **64**: 281–285.
- 32 Vilstrup CT, Bjorklund LJ, Werner O, Larsson A. Lung volumes and pressure-volume relations of the respiratory system in small ventilated neonates with severe respiratory distress syndrome. *Pediatr Res* 1996; **39**: 127–133.
- 33 van Kaam AH, Rimensberger PC. Lung-protective ventilation strategies in neonatology: what do we know—what do we need to know? *Crit Care Med* 2007; **35**: 925–931.
- 34 Keszler M, Nassabeh-Montazami S, Abubakar K. Evolution of tidal volume requirement during the first 3 weeks of life in infants <800 g ventilated with Volume Guarantee. *Arch Dis Child Fetal Neonatal Ed* 2009; **94**: F279–F282.
- 35 Nassabeh-Montazami S, Abubakar KM, Keszler M. The impact of instrumental dead-space in volume-targeted ventilation of the extremely low birth weight (ELBW) infant. *Pediatr Pulmonol* 2009; **44**: 128–133.
- 36 Bhutani VK, Ritchie WG, Shaffer TH. Acquired tracheomegaly in very preterm neonates. *Am J Dis Child* 1986; **140**: 449–452.
- 37 Sharma S, Abubakar K, Keszler M. *Tidal Volume in Infants with Congenital Diaphragmatic Hernia*. Pediatric Academic Society (PAS), Vancouver, Canada, 2010. Abstract 1466.146.
- 38 te Pas AB, Kamlin CO, Dawson JA, O'Donnell C, Sokol J, Stewart M *et al*. Ventilation and spontaneous breathing at birth of infants with congenital diaphragmatic hernia. *J Pediatr* 2009; **154**: 369–373.
- 39 Kiraly NJ, Tingay DG, Mills JF, Dargaville PA, Copnell B. Volume not guaranteed: closed endotracheal suction compromises ventilation in volume-targeted mode. *Neonatology* 2011; **99**: 78–82.
- 40 Schulze A. Respiratory gas conditioning and humidification. *Clin Perinatol* 2007; **34**: 19–33.
- 41 Deakins K, Di Fiore J. *Evaluation of Condensation in Three Commercially Available Heated Wire Ventilator Circuits*. American Association of Respiratory Care: San Antonio, Texas, USA, 2005. Abstract.
- 42 Beck J, Reilly M, Grasselli G, Mirabella L, Slutsky AS, Dunn MS *et al*. Patient-ventilator interaction during neurally adjusted ventilatory assist in low birth weight infants. *Pediatr Res* 2009; **65**: 663–668.
- 43 South M, Morley CJ. Respiratory timing in intubated neonates with respiratory distress syndrome. *Arch Dis Child* 1992; **67**: 446–448.

- 44 Hird M, Greenough A. Inflation time in mechanical ventilation of preterm neonates. *Eur J Pediatr* 1991; **150**: 440–443.
- 45 Wheeler KI, Morley CJ, Hooper SB, Davis PG. Lower back-up rates improve ventilator triggering during assist-control ventilation: a randomized crossover trial. *J Perinatol* 2 Jun 2011 (e-pub ahead of print).
- 46 Greenough A. The premature infant's respiratory response to mechanical ventilation. *Early Hum Dev* 1988; **17**: 1–5.
- 47 Bach KP, Kuschel CA, Oliver MH, Bloomfield FH. Ventilator gas flow rates affect inspiratory time and ventilator efficiency index in term lambs. *Neonatology* 2009; **96**: 259–264.
- 48 Monkman S, Kirpalani H. PEEP—a 'cheap' and effective lung protection. *Paediatr Respir Rev* 2003; **4**: 15–20.
- 49 Monkman SL, Andersen CC, Nahmias C, Ghaffer H, Bourgeois JM, Roberts RS *et al*. Positive end-expiratory pressure above lower inflection point minimizes influx of activated neutrophils into lung. *Crit Care Med* 2004; **32**: 2471–2475.
- 50 Keszler M. State of the art in conventional mechanical ventilation. *J Perinatol* 2009; **29**: 262–275.
- 51 Otto CM, Markstaller K, Kajikawa O, Karmrodt J, Syring RS, Pfeiffer B *et al*. Spatial and temporal heterogeneity of ventilator-associated lung injury after surfactant depletion. *J Appl Physiol* 2008; **104**: 1485–1494.
- 52 Kamlin CO, Davis PG, Morley CJ. Predicting successful extubation of very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed* 2006; **91**: F180–F183.
- 53 Greenough A, Milner AD. Pulmonary disease of the newborn: acute respiratory disease. In: Rennie JM (ed). *Robertson's Textbook of Neonatology*. 4th edn. London, England: Elsevier, 2005 pp 468–553.
- 54 te Pas AB, Wong C, Kamlin CO, Dawson JA, Morley CJ, Davis PG. Breathing patterns in preterm and term infants immediately after birth. *Pediatr Res* 2009; **65**: 352–356.
- 55 Hummler HD, Engelmann A, Pohlandt F, Franz AR. Volume-controlled intermittent mandatory ventilation in preterm infants with hypoxemic episodes. *Intensive Care Med* 2006; **32**: 577–584.
- 56 Polimeni V, Claire N, D'Ugard C, Bancalari E. Effects of volume-targeted synchronized intermittent mandatory ventilation on spontaneous episodes of hypoxemia in preterm infants. *Biol Neonate* 2006; **89**: 50–55.