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High-Frequency Oscillatory Ventilation: Theory and Practical Applications

Jane Pillow

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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.

1 Foreword

High-frequency ventilation (HFV) has progressed over the last thirty years from its initial status as a novel ventilatory tool, to become a routine ventilatory strategy. High-frequency ventilation comprises several different modalities including high-frequency positive pressure ventilation, high frequency flow interruption, high-frequency jet ventilation and high-frequency oscillatory ventilation (HFOV or HFO). This booklet concentrates on HFOV, the principal distinguishing feature of which is the inclusion of active inspiratory and expiratory phases.

A number of oscillatory devices are commercially available. They differ in technology, performance, versatility, user-friendliness, and cost. Where possible, recommendations in this booklet have been kept general in nature and apply across devices. References specific to the Dräger Babylog VN500[1] are largely contained within an appendix at the end of the booklet using software version 2.4n (Drägerwerk AG & Co. KGaA, Lübeck, Germany). It is important to note that other oscillators may function differently.

This booklet aims both to help less experienced clinicians become familiar with high-frequency oscillation, whilst also providing additional detail to enhance the understanding of more experienced HFOV users. The chapters that follow outline the theory, control mechanisms, strategies and complications of HFOV. Particular emphasis is placed on understanding the basis for practical application approaches that maximise the potential benefits and minimise the risk of adverse outcomes of HFOV therapy. It should be clear that there is a steep learning curve that needs to be climbed to ensure safe and effective ventilation with HFOV: neonatal teams considering use of HFOV for the first time are advised to obtain comprehensive guidance from experienced users and preferably also practical experience using HFOV in a unit where HFOV is practiced routinely and successfully.

Throughout the text, key points and more advanced concepts are highlighted in text boxes. The theory and recommendations contained herein represent current knowledge and understanding of HFOV theory and application and my experience evaluating the pitfalls and benefits of HFOV over a twenty year period. Nonetheless, as foreseen in the section on future directions of HFOV, rapid advances in medical technology and its miniaturisation to meet the challenges imposed by the neonatal patient will result in new HFOV knowledge and options. Consequently, the descriptions and recommendations contained herein will likely need revision over time.

Perth, September 2016
J. Jane Pillow

[1] Part of Infinity Acute Care System Workstation Neonatal Care.

2 Table of Contents

2 Table of Contents

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I DEFINITION

S SUMMARY

T PRACTICAL TIPS

3 High-frequency ventilation

3.1 Introduction

Many infants continue to require invasive ventilation, despite major advances in perinatal care including widespread use of antenatal steroid therapy, exogenous surfactant therapy and non-invasive respiratory support. Ventilation induced lung injury (VILI) is a complication of invasive ventilatory support that prolongs duration of supportive care. Ventilation induced lung injury in the developing lung has lifelong implications for respiratory well-being due to failure of alveolarisation and abnormal airspace development. The proportion of infants requiring mechanical ventilation increases at lower gestations: extremely preterm infants are additionally extremely vulnerable to injury. Consequently, ventilation research and device development over the past two to three decades has focused intensely on new therapies that facilitate life support with minimal risk of iatrogenic injury. Both extracorporeal membrane oxygenation (ECMO) and high-frequency ventilation offer opportunities for lung protective ventilation whilst minimising rheotrauma resulting from either excessive cyclic volume oscillations or repeated re-inflation of atelectatic air spaces.

High-frequency oscillation is a unique and the most well-known and used form of high-frequency ventilation. HFOV arose initially from observations by Henderson of patterns of smoke blown down a tube, and was subsequently described in more detail by Lunkenheimer in the early seventies (4, 28). HFOV has now emerged into a comprehensive ventilatory strategy applied throughout the world as both an a priori and rescue ventilatory modality.

3.2 Definition

Distinguishing characteristics of contemporary HFOV include:

1. a frequency range from 3-20 Hz (180 to 1200 breaths/minute);
2. active inspiratory and expiratory phases;
3. tidal volumes approximating anatomical dead space volume.

3.3 Devices and mechanisms for generating active expiratory flow

A range of technical principles are used to produce oscillatory ventilatory waveforms in different devices. The oscillations divert small volumes of gas to the patient at high frequency: the mechanically driven oscillations resulting in active inspiration and active expiration. Mean airway pressure is created through the pressure drop of the bias flow in combination with an expiratory resistance. True oscillators achieve roughly matching magnitude of the negative and positive pressure deflections when equal inspiratory and expiratory cycle durations are used. Matched

negative and positive pressure deflections can be achieved via several different mechanisms including a linear motor piston pump, an electromagnetically driven vibrating diaphragm (loudspeaker) or via a combination of servo controlled inspiratory valve and an expiratory venturi jet (which is generating sub-atmospheric pressures). Examples of contemporary oscillators include the Sensormedics SM3100A, SM3100B, Humming V, the Flowline Dragonfly, the Heinen and Löwenstein Leoni Plus, the Acutronics Fabian, the Stephan SHF3000, the SLE5000 and the Dräger Babylog 8000plus and Babylog VN500.

Although oscillators are traditionally classified according to the oscillatory flow generating mechanism, the function, capabilities and limitations of each device are of greater clinical relevance to practical application and potential physiological efficacy. A key differentiation is the frequency composition of the oscillatory waveform: oscillators generating sine waves with relatively “pure” fundamental frequency content contrast with those producing more complex and often square waveforms comprising multiple frequencies (1, 2). Although more complex waveforms may enhance gas mixing and regional ventilation homogeneity, the effect of the potential shear effects arising from more turbulent and inertive[2] oscillatory flow on airway wall properties is unknown (see Figure 3-1).

A second feature of clinical relevance is the practical ease of switching from conventional ventilation to HFOV, or even of combined conventional and HFO ventilation. The emergence of hybrid ventilators that can combine conventional and high frequency modalities will increase access to oscillatory ventilation and potentially encourage earlier a priori use of HFOV for lung protective respiratory support. A downside of this combination is that hybrid ventilators often have more limited power than standalone oscillators such as the SM3100 series. To a large extent, these limitations can be overcome by either switching to a lower oscillatory frequency, or changing from a 1:2 to a 1:1 inspiratory to expiratory ratio (I:E). Other features with practical implications for inter- and intra-hospital transport include minimum bias flow requirements and availability of inbuilt battery backup. The importance of incorporated tidal volume monitoring is recognised increasingly as clinical strategies are revised to include monitoring of volume and the diffusion coefficient to optimise ventilation and lung protection.

[2] Inertive flow refers to the variable flow occurring with sudden accelerations and decelerations accompanying reversal in flow direction at high frequencies.

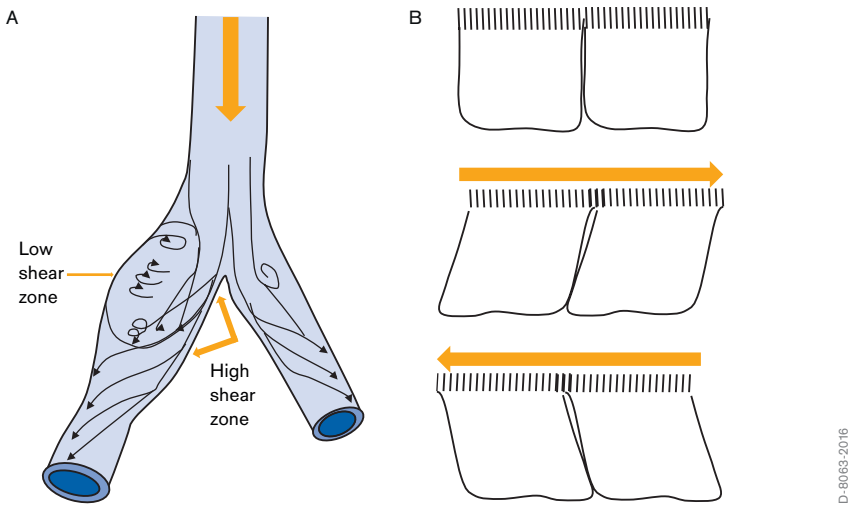

Figure 3-1: Reversing oscillatory flow at high frequencies may distort cells due to shear stress
A) Turbulent flows and formation of eddies creates high shear zones. B) Shear stress applied to the surface of an airway epithelial cell will promote deformation of the cell surface, whilst the base of the cell remains fixed. In HFOV, a reversing oscillating shear effect occurs due to shear effect in opposing directions during inspiration and expiration.

4 Gas mixing during high-frequency oscillations

High frequency oscillatory ventilation offers unique and highly efficient gas mixing, contributing to its success in both a priori and rescue treatment of patients with severe respiratory disease and impaired gas exchange. The gas mixing efficiency of HFOV over conventional ventilation is due to fundamental differences in the behaviour of gases in the airways and alveoli.

Gas mixing during conventional ventilation is primarily dependent on direct ventilation of the alveoli via bulk convective flow. To be effective, delivered tidal volumes need to be of sufficient size to fill the anatomical dead space of the airways as well as to distend and fill the volume of the alveolar compartment. Decreasing tidal volume to volumes at or below anatomical dead space volume, whilst delivering these volumes at conventional breathing frequencies, impedes clearance of the waste carbon dioxide from the alveolar compartment (dead space ventilation). Low tidal volume ventilation at conventional breathing frequency thus contributes to development of atelectasis and impaired oxygenation due to inadequate transmission of a distending pressure (reduction of mean airway pressure).

In sharp contrast to mechanical ventilation at conventional breathing frequencies, HFOV offers highly effective oxygenation and clearance of waste gas, despite use of tidal volumes at or below dead space volume. The efficiency of HFOV in ventilating the lung at very low tidal volumes is attributed to highly effective mixing of fresh and exhaled gases in the airways and alveolar compartment. The mechanisms contributing to this augmented gas mixing are multiple (3), and influenced by the ventilator waveform (sinusoidal or complex, multiple harmonic) and settings (eg frequency, mean airway pressure and oscillatory amplitude) as well as the respiratory mechanics (airway and parenchymal), homogeneity of ventilation and cardiac function.

4.1 Augmented longitudinal gas transport and enhanced dispersion

The concept of augmented longitudinal gas transport and potential penetration of the alveoli of gas delivered in volumes less than the anatomical dead space were foreseen by the early simple yet elegant studies by Henderson and colleagues in 1915 (4). Blowing tobacco smoke down a tube, they observe the formation of long thin spikes of smoke, and showed that importance of frequency with their conclusion that the “quicker the puff, the thinner and sharper the spike”. Because the velocity and concentration profiles of oxygen are not flat (with higher concentrations of oxygen at the core of the flow profile, fresh gas can penetrate the alveoli despite very low tidal volumes). Taylor showed that this flow profile contributes to longitudinal mixing of gas, which can be described as a process of diffusion that increases with average velocity and tube diameter, exceeding the molecular diffusion by many fold (5). Consequently, this mechanism of gas mixing appears particularly important in the large airways. At the same time as fresh gas is propelled forward, there is also lateral (radial) mixing of gas with movement of particles from the centre to the periphery of the gas flow, resulting in enhanced dispersion of gas. Finally, together with the accelerated projection of fresh gas into the lung, co-axial flow results in a slower moving peripheral expiratory gas flow, effectively pushed out of the lung by the force of the incoming gas.

4.2 Asymmetric flow profiles

Gas mixing is further enhanced by differences in flow profiles between inspiration and expiration. Whereas the inspiratory flow profiles are sharp and pointed, expiratory flow profiles are more blunt in appearance.

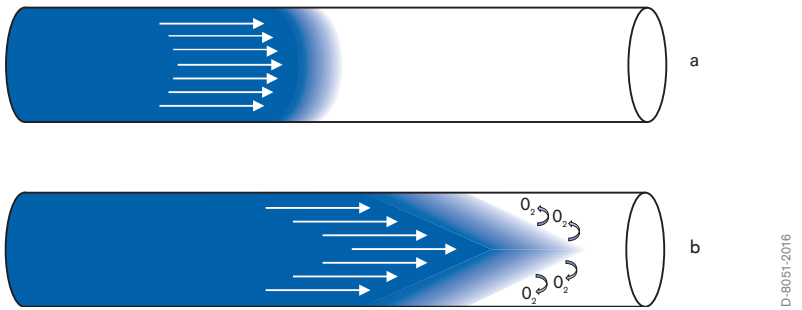

Figure 4-1: Augmented longitudinal flow and enhanced dispersion: boundary. Flow profile and boundary surface between two gases with different flows: a) low flow with flat profile; b) high flow with tapering, peaked flow profile. In high flow, fresh gas (O_2) diffuses radially (laterally) permitting gas exchange at the boundary surface.

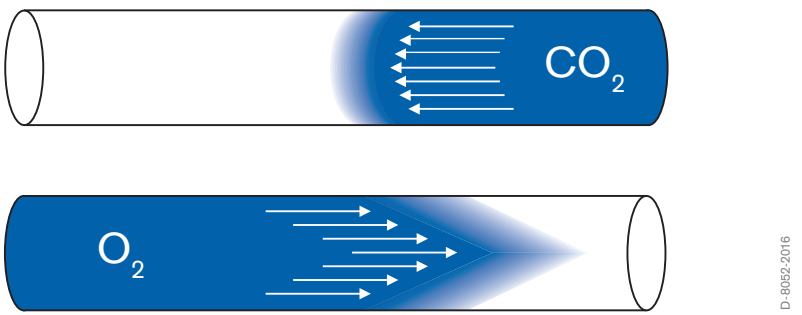

Figure 4-2: Asymmetric inspiratory and expiratory flow profiles. The peaked inspiratory flow profile penetrates the broader expiratory flow profile, permitting net movement of fresh gas distally, and expired CO_2 moves towards the airway opening via lateral pathways.

4.3 Branching angle asymmetries

Secondary gas movements occur at airway bends and bifurcations creating turbulent eddies that enhance radial gas mixing (movement of gas particles from the centre of flow to the stationary boundary layer along the wall) at the expense of longitudinal gas transport. Turbulences occurring at asymmetric airway branches induce pendelluft (see section 4.5), potentially further enhancing gas mixing.

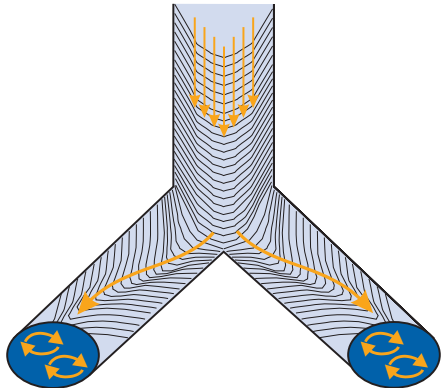

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Figure 4-3: Branching angle asymmetries. Gas flow profiles and boundary surfaces deform at airway bifurcations, together with generation of secondary eddying gas movements to enhance gas mixing.

4.4 Direct alveolar ventilation

Proximal alveoli (i.e. alveoli in close proximity to the central airways) continue to receive ventilation directly via bulk convective gas flow. Consideration of these airways is important in selecting frequency of ventilation, as lower frequencies require higher tidal volumes for effective gas exchange, which may be injurious to proximal alveoli.

4.5 Intra-alveolar pendelluft

Some degree of regional inhomogeneity is present even in the healthy lung. Intra- and inter-regional differences in compliance and resistance result in ventilation of neighbouring alveolar units out of phase: each alveolar or acinar compartment will fill and empty at different time constants. The resulting asynchronous behaviour results in intra-alveolar pendelluft – a form of mutual gas exchange in the peripheral gas exchanging compartments (6). Even small fresh-gas volumes are able to reach a large number of alveoli.

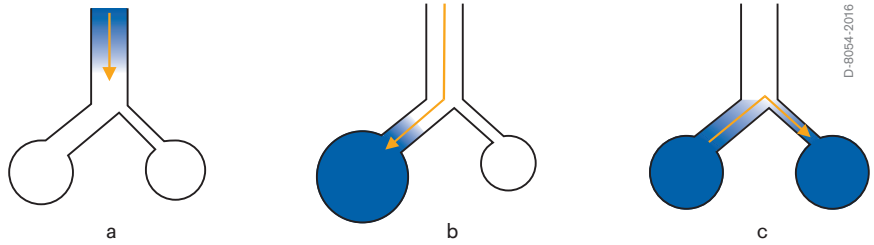

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Figure 4-4: Pendelluft. Gas mixing occurs through asynchronous filling and emptying of lung units with different time constants. Each phase lasts only a fraction of the full oscillatory cycle.

4.6 Cardiogenic mixing

Low-frequency cardiogenic mixing additionally augments gas mixing in the lung zones adjacent to the heart. Cardiogenic mixing may account for up to half of the oxygen uptake in the presence of totally apnoeic respiration (7).

4.7 Molecular diffusion

The same early observations by Henderson and colleagues in 1915 on the behaviour of tobacco smoke in a glass tube contributing to the concept of augmented longitudinal gas transport, also demonstrated the rapidity with which the boundary layer of a gas disappears when flow stops – a process referred to as molecular diffusion (see Figure 4-5: Henderson's Molecular Diffusion Experiment). Henderson and colleagues visualised the movement of gas in a glass tube using smoke. Their observations included that: a) centrally located particles were propelled further down the tube than expected from the volume of the smoke puff; b) slowing or cessation of flow resulted in instantaneous mixing or "diffusion" of the smoke particles (4). Molecular diffusion is especially important in the lung periphery where it occurs extremely rapidly and is enhanced further by the effects of cardiogenic mixing. Molecular diffusion and Taylor dispersion together account for almost all of the gas transport occurring during HFOV (8).

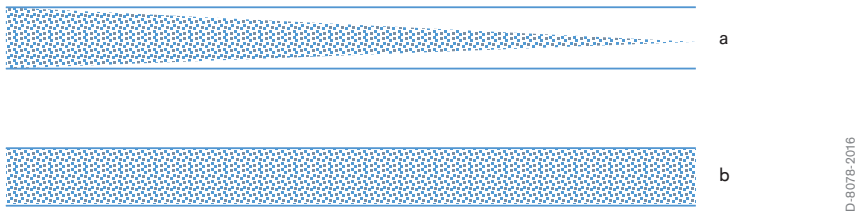

Figure 4-5: Henderson's Molecular Diffusion Experiment. Henderson and colleagues visualised the movement of gas in a glass tube using smoke. Their observations included that: a) centrally located particles are propelled further down the tube than expected from the volume of the smoke puff; and b) slowing or cessation of flow resulted in instantaneous mixing or "diffusion" of the smoke particles.

5 HFV ventilator parameters and control variables

Compared to conventional ventilation, control of HFOV is limited to four main ventilatory parameters (Figure 5-1):

1. the pressure waveform oscillates around a mean airway pressure;
2. the amplitude of the oscillatory pressure waveform defines the oscillatory volume delivered to the patient for any given set of mechanical conditions;
3. the oscillatory frequency defines the number of oscillatory cycles per second; and
4. the inspiratory to expiratory ratio (determined in some ventilators by a % inspiratory time setting) determines the relative duration of forward and reverse flow within each oscillatory cycle.

The strict definition of inspiratory and expiratory time is determined from the zero crossing points of the flow waveform when air starts to move in and out of the airway. Many ventilators determine the I:E time from the on/off time of the mechanism generating the oscillatory flow.

5.1 Mean airway pressure

Mean airway pressure in HFOV is ideally targeted to keep the lung inflated without over-distension. Mean airway pressures greater than the lower inflection point on the inflation limb of the pressure volume curve are required initially to inflate the collapsed lung. However, once open, the mean airway pressure is usually reduced substantially to achieve optimal distending volume at the lowest effective distending pressure. Mean airway pressure is the principle parameter used to control oxygenation and matching of ventilation-perfusion, avoiding unwanted intrapulmonary right-to-left shunting.

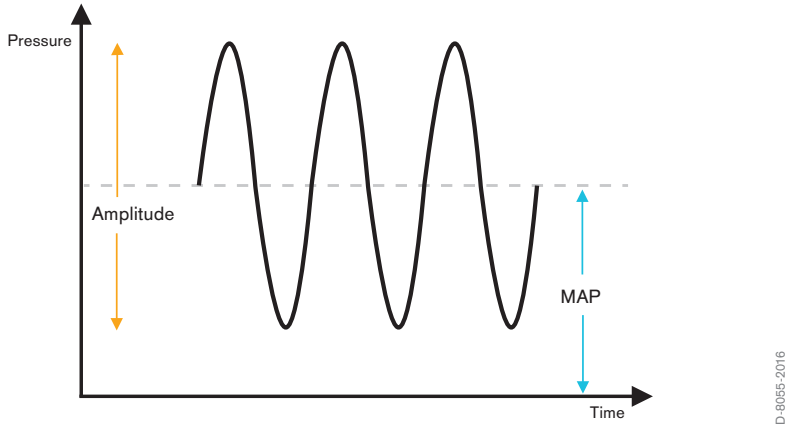

Figure 5-1: HFOV pressure waveform parameters. Amplitude is usually determined as the difference between peak and trough of the pressure waveform.

5.2 Pressure amplitude – oscillatory volume

The clinician sets the pressure amplitude on the ventilator as the principle modifiable parameter controlling oscillatory volume – which is ultimately the key determinant of CO_2 removal. Above approximately 3-5 Hz, oscillatory volume influences CO_2 elimination exponentially (9, 10)[3].

Tidal volumes required for effective gas exchange depend on frequency, ranging from around 3.5 mL/kg at 5 Hz decreasing to 1.5-2 mL/kg at 15 Hz. The tidal volume delivered to the patient depends on the pressure amplitude, frequency, set I:E and compliance and resistance of the patient's respiratory system. Consequently, accumulation of secretions, changes in tracheal tube, and lung inflation all affect the oscillatory tidal volume delivered to the patient at any given pressure amplitude. The volume delivered by the ventilator is substantially greater than the tidal volume delivered to the patient. The volume delivered to the patient for any given oscillatory pressure amplitude is mainly dependent on the compliance of the patient circuit and humidifier chamber, as the ventilator has to fill the patient circuit with gas in order to build up the set pressure amplitude.

Pressure amplitude measured at the airway opening is dampened as it is transmitted down the airways to the alveolar compartment (see Chapter 6).

[3] Interestingly, the frequency at which this transition occurs depends on the ratio of the metabolic rate to dead space: consequently the transition frequency is lower in adults than for infants.

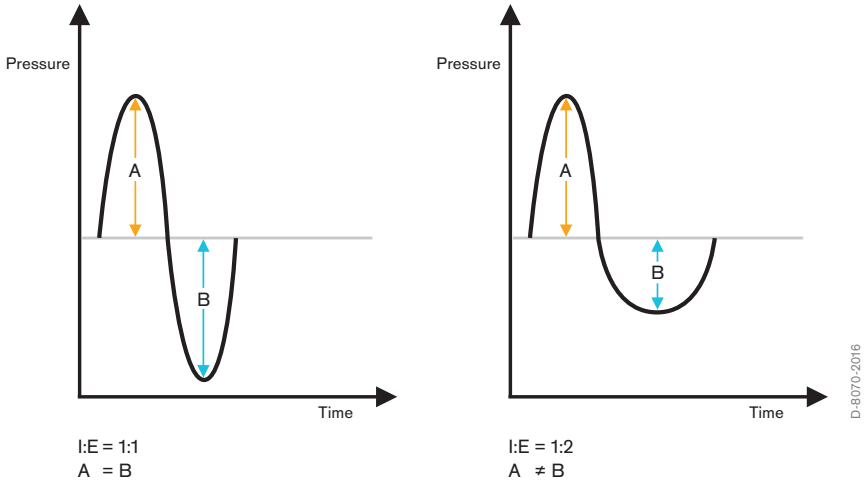

Figure 5-2: Influence of I:E ratio on symmetry of the oscillatory pressure waveform. At an I:E of 1:1, the peak and trough of the oscillatory pressure waveform are equidistant from the mean airway pressure. However, at I:E of 1:2, the trough of the pressure waveform is approximately half as far below the mean airway pressure as the peak of the pressure waveform is above the mean airway pressure. A larger inspiratory ΔP is required at I:E of 1:2 to achieve equivalent tidal volume delivery to an I:E of 1:1.

5.3 Oscillatory frequency

Oscillatory frequency (f) is a ventilator parameter measured in units of Hertz (Hz = 1/s). The frequency influences the oscillatory volume: as frequency increases, the available time for inflation and deflation decreases, limiting the delivered tidal volume for any given oscillatory amplitude and prevailing lung and circuit mechanics.

Frequency selection has important implications for the proportional transmission of pressure amplitude to the alveolar compartment (see Chapter 6), with smaller pressure amplitudes delivered as frequency increases. This fact is often not appreciated by clinicians, as the required amplitude (displayed by the ventilator) usually decreases as frequency is lowered.

Although amplification of alveolar pressure amplitudes may occur at frequencies close to the resonance frequency (11), amplification is rarely a problem in the over-damped neonatal lung.

Optimal oscillatory frequency needs to be adjusted according to the prevailing mechanical condition of the lung and associated disease characteristics. Frequency selection is covered in more detail in section 6.3 and section 7.1.2.

5.4 Inspiratory to expiratory ratio

The inspiratory to expiratory ratio (I:E) determines the proportion of time spent when oscillatory pressure is above (inspiratory) or below (expiratory) the mean airway pressure, resulting in similar fluctuations of positive and negative flow. The peak and trough of the oscillatory pressure waveform are similarly distant (in opposing directions) from the mean airway pressure when inspiratory and expiratory cycle durations are of equal value (I:E = 1:1). However, equidistance of the peak/trough from the mean does not apply when using I:E other than 1:1, to ensure that the area under the flow curve is the same during inflation and deflation and complete removal of any delivered volume. At I:E of 1:2 for example, the trough of the oscillatory pressure waveform will be approximately half the distance of the peak of the oscillatory pressure waveform away from the mean airway pressure, but the relative negative pressure will be maintained for twice as long (see Figure 5-2).

I:E of 1:2 were initially used in HFOV due to concerns about potential gas trapping at high-frequencies. However, gas trapping is not a relevant concern when active expiration is used. As the peripheral pressures are damped, the difference between inspiratory peak pressure and expiratory trough pressures is much smaller than seen at the airway opening, resulting in negligible differences between inspiratory and expiratory resistance. If mean airway pressures are high enough, the airways will be stented sufficiently to prevent collapse during expiration. Importantly, intra-thoracic expiratory pressures remain positive, despite potential for subatmospheric pressures at the airway opening (12). An exception occurs when extremely low mean airway pressures are set, creating opportunities for choke point formation with resultant airway collapse and gas trapping. I:E ratio may have implications for gas mixing efficiency and potential shear effects, however these have yet to be elucidated fully.

5.5 The coefficient of gas transport: DCO_2

Whilst not currently a controlled ventilator parameter, the gas transport/diffusion coefficient (DCO_2) is a vital, and often under-recognised variable in HFOV as a critical determinant of the efficiency of gas mixing and hence success of HFO ventilation.

Removal of carbon dioxide in conventional ventilation is determined by the product of alveolar tidal volume and respiratory rate, known as alveolar minute volume, or alveolar minute ventilation. As alveolar tidal volume is difficult to measure, the minute volume (determined by the product of tidal volume and respiratory rate) is used instead.

Several studies show that the relationship between carbon dioxide removal and the factors tidal volume and respiratory rate changes as respiratory frequency increases. Above 5 Hz in particular, there is a transition such that CO_2 elimination becomes approximately correlated to $f^* V_T^2$ (9, 10). The $f^* V_T^2$ product is commonly referred to as the CO_2 diffusion (gas transport) coefficient, DCO_2.

DCO_2 is generally measured and displayed by oscillatory ventilators using flow and tidal volume monitoring. An increase in DCO_2 decreases $PaCO_2$. As DCO_2 is only linearly related to frequency, but increases exponentially with increases in tidal volume, improved CO_2 removal is achieved most efficiently by increasing tidal volume. For example, a 10 % and 20 % increase in tidal volume increase DCO_2 by 21 % and 44 % respectively.

In contrast, changes in DCO_2 with changes in frequency are dependent on whether HFOV is used with or without Volume Guarantee: if HFOV is used without Volume Guarantee, increase in frequency may be offset by a decrease in tidal volume, resulting in a decrease in DCO_2 unless ΔP is increased simultaneously; however, in the setting of Volume Guarantee, an increase in frequency will increase DCO_2, as the set tidal volume will be maintained as long as the oscillatory pressure amplitude required to achieve that tidal volume is achieved.

It is important to recognise that DCO_2 is an absolute value dependent on the tidal volume. As tidal volume requirements increase with increasing size of the patient, DCO_2 will similarly increase, but in an exponential fashion. However, DCO_2 calculated relative to the square of an infant's body weight (i.e. $f * V_T^2/kg^2$) is a more reliable variable to predict the absolute DCO_2 required for any given patient (see section 9).

THE COEFFICIENT OF GAS TRANSPORT *S*

- DCO_2 is the critical determinant of the effciency of gas mixing.
- The removal of carbon dioxide in HFOV is approximately $f * V_T^2$.
- DCO_2 is an absolute value and depends on the tidal volume.
- CO_2 removal is most efficiently achieved by increasing the tidal volume.

6 Understanding transmission of pressure amplitude

6.1 Pressure damping

A key purported advantage of HFOV is the achievement of adequate gas exchange with small tidal volumes and low intrapulmonary pressure amplitudes. During HFOV, the amplitude of the pressure waveform is damped progressively from the airway opening to the alveoli (Figure 6-1). In contrast, the full inspiratory pressure is transmitted from the airway opening to the alveoli during conventional ventilation (provided a sufficiently long inspiratory time is allowed).

For many years, clinicians assumed that the intrathoracic damping of pressure amplitudes in HFOV occurred regardless of the patient's condition, and that the babies were therefore protected from barotrauma. However, systematic reviews of HFOV versus conventional rate ventilation show increased pulmonary air leak for infants (13). Although at first this result seems surprising, an understanding of how mechanical factors influence the extent to which the pressure waveform is damped will help the clinician to use HFOV without causing barotrauma.

Whereas tidal volumes are inevitably lower during HFOV than conventional ventilation, research has shown that these low tidal volumes are not always associated with similarly low oscillatory pressure amplitudes.

6.2 Pressure amplitude transmission and respiratory mechanics

Damping of the oscillatory pressure amplitude as it traverses the airways to the alveoli is determined by the impedance to flow of the intubated respiratory system.

IMPEDANCE *I*

Impedance is a general mechanical term that describes the mechanical barrier to flow. Impedance incorporates the volume dependent (elastic), flow-dependent (resistive) and acceleration dependent (inertive) properties of the respiratory system. In the clinical setting, elastance (E) is more commonly understood as compliance (C) of the lung where C = 1/E.

6.2.1 Lung compliance

Clinical understanding regarding marked damping of the oscillatory pressure waveform (illustrated in Figure 6-1A) arose out of studies in healthy compliant lung models. However, HFOV was developed and applied initially for the extremely non-compliant and immature lung of the preterm infant with respiratory distress syndrome (RDS). Low compliance increases impedance to flow. Consequently, in the presence of low compliance (Figure 6-1B), higher pressure amplitudes are required to generate the same tidal volume and achieve effective gas exchange.

Clinically, the importance of compliance to damping of the oscillatory pressure waveform was demonstrated clearly in animal models. Studies using alveolar capsules to measure alveolar oscillatory pressure swings in preterm lambs during lung volume recruitment showed the proportionally higher transmission of oscillatory pressure amplitude from the airway opening to the alveolus when compliance was low (14). Similarly, the oscillatory pressure ratio[4] is lowest at the point of maximal compliance during the inflation and deflation limbs of a pressure volume recruitment manoeuvre (29).

LOW LUNG COMPLIANCE AND HFO *S*

If HFO is applied to immature, low-compliant lungs:

- higher ventilator pressure amplitudes (compared to more compliant lungs) are required to generate the same tidal volume.
- the inspiratory and expiratory lung time constants are shorter with lower compliance.
- the percentage transmission of pressure amplitude from the airway opening to the alveoli is higher compared to normally compliant lungs.

[4] ratio of oscillatory pressure amplitude at the distal end of the tracheal tube to amplitude at the airway opening

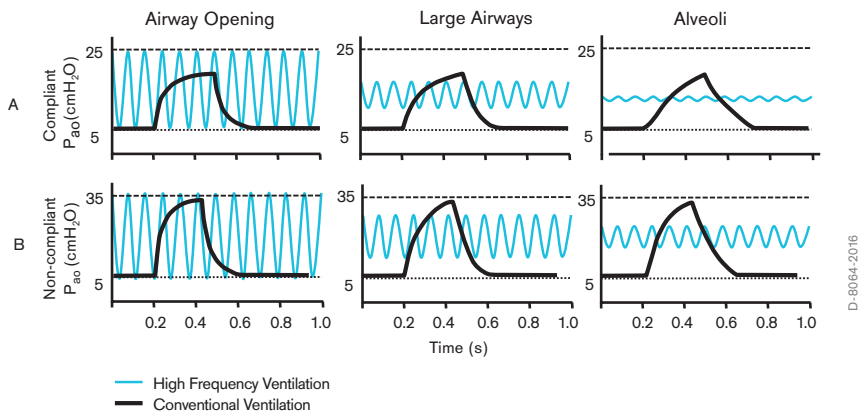

Figure 6-1: Pressure damping during HFOV. At physiological breathing rates (black line), there is sufficient time for the pressure waveform to be completely transmitted from the airway opening (patient wye) to the alveoli. In contrast, during HFOV (blue line), the very short inspiratory times are insufficient to fully transmit the complete pressure waveform. Instead, there is progressive damping of the pressure waveform as it travels from the airway opening to the alveolar compartment (Figure 6-1A). In the presence of low-compliance (Figure 6-1B), the inspiratory and expiratory time constants are shorter and higher peak inspiratory pressures (or ΔP) needs to be delivered to the airway opening to achieve the same tidal volume as is achieved in the compliant healthy lung using physiological breathing rates. For HFOV, not only are higher delta pressures required at the airway opening, but the extent of pressure damping is reduced. Consequently, in the poorly compliant lung, there is a higher percentage transmission of pressure from the airway opening to the alveolus.

6.2.2 Resistance

Peripheral Resistance

Increased peripheral resistance, associated with interstitial emphysema or collapsed peripheral airways also increases impedance to flow at the point of obstruction and beyond. Increasing peripheral resistance reduces the cyclic volume change in the alveolus accompanied by reduced alveolar oscillatory pressure amplitude. Consequently, higher ventilator oscillatory pressures are required to restore tidal volume to the same level as obtained prior to development of the increased peripheral resistance (14). The ventilation that is achieved however, is delivered at the cost of increased proportional transmission of oscillatory pressure amplitudes to the airways proximal to the site of increased peripheral resistance (14). Consequently, the use of HFOV in the patient with increased peripheral resistance presents a risk of barotrauma to the proximal airways.

Tracheal Tube and Large Airway Resistance

Resistance in the tracheal tube and the large airways is flow dependent, due to the turbulent nature of high flow through a tube of narrow diameter at high-frequencies. Consequently, as flow increases, the resistive contribution of the tracheal tube and large airways to overall respiratory system impedance also increases, necessitating increased pressure amplitudes to maintain flow delivery (and tidal volumes) (14).

RESISTANCE OF TRACHEAL TUBE *I*

Flow dependent resistance in the tracheal tube and large airways is calculated as:

$R_{TT} = k_1 + k_2\dot{V}$

where R_{TT} is the resistance of the tracheal tube, k_1 and k_2 are constants and $\dot{V}$ is the oscillatory flow.

HIGH PERIPHERAL RESISTANCE AND HFO *S*

If HFOV is applied to lungs with high peripheral resistance:

- higher pressure amplitudes (compared to lower resistive lungs) are required to generate the same tidal volume.
- the risk of barotrauma to proximal airways might be higher.
- the tidal volume is lower compared to normal resistive lungs.

6.2.3 Inertance

Complex (eg square wave) oscillatory pressure waveforms have higher inertive content than sinusoidal waveforms with more abrupt acceleration and decelerations in flow. Whether square waves are more beneficial or more harmful to the infant than sinusoidal oscillatory pressure waveforms remains unclear. The more abrupt changes in flow of square waveforms may enhance gas mixing efficiency, but also may exert more injurious shear effects on the airway wall and compromise airway wall stiffness. However, the complex waveform becomes more sinusoidal in morphology as it transverses the airways, hence most of the effect of different waveform morphologies (square versus sinusoidal) are likely to be effected in the large airways with minimal beneficial or adverse impacts on the distal lung parenchyma. Inertance per se does not impact the transmission of the oscillatory pressure amplitude from the airway opening to the alveolar compartment (14).

INERTANCE *I*

If a certain mass needs to be accelerated, a force is required to overcome the inertia. In mechanical ventilation, inertance is the pressure difference required to change flow (i.e. acceleration/ deceleration). Inertance has a negligible contribution to total impedance during tidal breathing at normal breathing frequencies, but contributes more substantially to the overall impedance during high-frequency ventilation. Inertance primarily arises from gas flow in the tracheal tube and major airways.

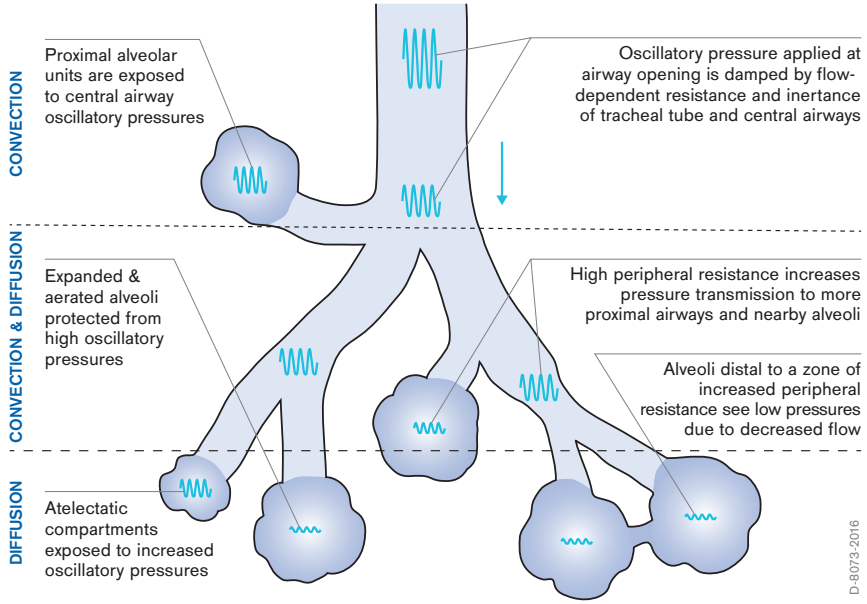

Figure 6-2: Factors influencing damping of the oscillatory pressure waveform amplitude. The extent to which the oscillatory pressure waveform is damped is influenced by the mechanical characteristics of the respiratory system. Atelectatic alveoli experience higher oscillatory pressure amplitudes than normally aerated alveoli, for the same unit change in cyclic volume. Increased peripheral resistance increases the oscillatory pressure transmitted to proximal airways and neighbouring alveolar units. Adapted from (3).

6.2.4 Inhomogeneous lung disease

High frequency oscillatory ventilation has cemented its place in the recruitment and ventilation of the homogeneously collapsed or atelectatic lung. However, the value of HFOV in the inhomogeneous lung is less certain.

As suggested by Figure 6-2, co-existence of high and low compliance alveolar compartments and areas of increased peripheral resistance may co-exist within the same lung. Areas with longer time constants will have reduced oscillatory pressure transmission whilst higher oscillatory pressures are transmitted to the short-time constant (eg low compliance) segments. Although increased oscillatory pressure transmission to low compliant lung zones increases risk of barotrauma in those areas, the increased oscillatory pressures may also promote recruitment of alveolar volume if the peak oscillatory pressures exceed the opening pressure of that lung region.

6.3 Pressure damping and frequency

As frequency increases, the proportion of the pressure waveform transmitted to the lung periphery decreases. What is not often appreciated by clinicians, is that whilst lowering frequency often results in a lower oscillatory pressure amplitude on the ventilator display the distal lung is exposed to at least the same pressure and likely higher oscillatory amplitudes (Figure 6-3): this effect occurs due not only to the higher proportional transmission of that oscillatory pressure to the lung periphery at low frequency. Higher volumes are required to maintain the same efficacy of CO_2 removal (ie DCO_2).

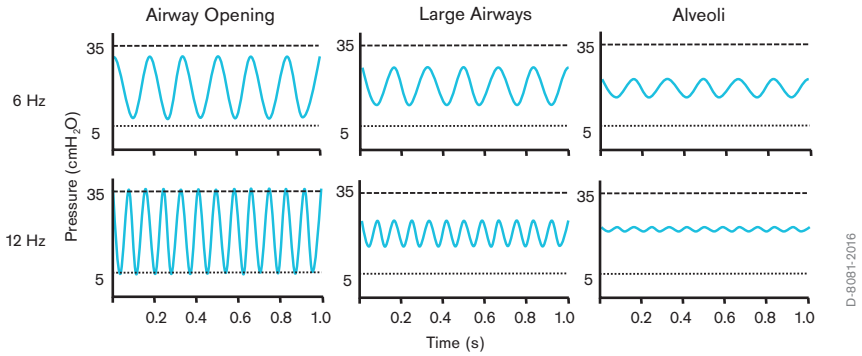

Figure 6-3: Effect of oscillatory frequency on transmission of oscillatory pressure. The proportion of the oscillatory pressure amplitude at the airway opening transmitted to the alveolus is higher at low frequency (eg top panel) than at higher frequencies (eg lower panel). Importantly, although the absolute oscillatory pressure displayed by the ventilator may be lower at the airway opening than that required for high frequencies, the absolute alveolar oscillatory pressure amplitude may actually be higher at lower frequencies, as a higher tidal volume is required to achieve equivalent CO_2 exchange (ie to maintain DCO_2).

6.4 Corner frequency and pressure cost of oscillatory flow

Impedance decreases rapidly with increasing frequency, reaching a minimum at the resonance frequency (f_0). However, in the neonatal lung, minimal additional damping of the oscillatory pressure is achieved above the corner frequency (f_C). Consequently, targeting oscillatory frequency to the corner frequency of the lung potentially achieves the minimum pressure cost per unit of oscillatory flow (15).

In more simple terms, using frequencies above the corner frequency may achieve small additional falls in the oscillatory pressure amplitude delivered to the alveolar compartment. However, this additional reduction in oscillatory pressure amplitude

is achieved at the expense of higher oscillatory pressure amplitude to the more proximal components of the respiratory system, such as the large airways.

RESONANCE FREQUENCY

The resonance frequency of a system is the frequency at which the response amplitude to a defined input is a relative maximum compared to the response at other frequencies. At resonance frequencies, small periodic driving forces may produce large amplitude oscillations due to storage of vibrational energy. Resonance frequency is calculated as $f_0=1(2\pi\sqrt{IC})$ where f_0 is the resonance frequency, C is the compliance and I is the inertance.

DAMPING

Damping refers to the reduction, restriction or prevention of oscillations within or upon that system. Damping in physical systems is a result of a process that dissipates the energy stored within the oscillation.
In an overdamped system the system returns (exponentially decays) to equilibrium without oscillating.

CORNER FREQUENCY

Corner frequency represents the point (boundary) within the frequency response of any system, at which the energy flowing through the system starts to be reduced rather than passing completely through. Corner frequency is related to the compliance and resistance (R) of the system, expressed as: $f_C=1/(2\pi RC)$. In the overdamped neonatal lung, f_C is usually below the resonance frequency (f_0).

A graphical representation of the relation between corner frequency and the time constant of the lung is shown below. As time constant increases, the corner frequency decreases.

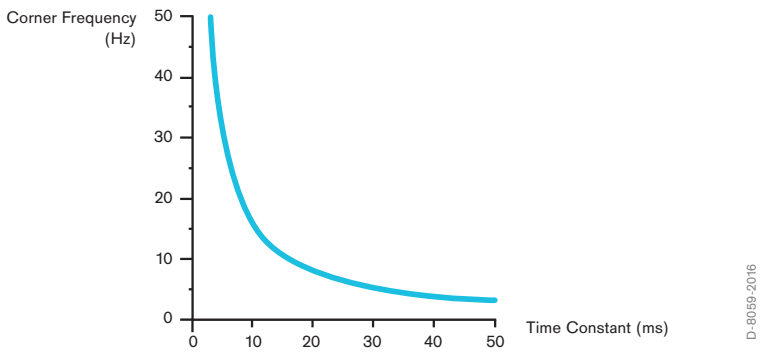

Figure 6-4: Effect of time constant on the corner frequency of the lung. The time constant (τ) is the product of resistance and compliance (τ = R x C). As the time constant shortens, the corner frequency of the respiratory system increases. A 600g preterm infant with a compliance of 0.1 mL/cmH_2O (severe HMD) and a resistance of 100 cmH_2O/L/s has a time constant of 10 ms and a corner frequency of 15.9 Hz.

6.4.1 Corner frequency in different clinical settings

Understanding the concept of corner frequency helps in the selection of frequency for different disease conditions. As time constant decreases, the corner frequency increases. Consequently, infants with RDS and non-compliant (short time-constant) atelectatic lungs have a higher corner frequency than infants with healthy, normally compliant lungs with relatively longer time constants. In contrast, infants with high airway resistance (long time-constant) will have an even lower corner frequency than the infant with healthy lungs.
The most important pressure for determining the potential for barotrauma during HFOV is the peak carinal pressure. Figure 6-5 illustrates the normal fall in peak carinal pressure with increasing frequency at a constant distending pressure of 10 cmH_2O for a normal newborn infant. The figure clearly shows the shift of the corner frequency to the right for the infant with low compliance, highlighting the benefits of higher frequency selection in the infant with acute atelectatic disease. Similarly, as the atelectatic lung is recruited and compliance normalises, then the optimum ventilation frequency shifts to the left and lower frequency selection is appropriate.

In contrast, there are penalties for incorrect frequency selection in the presence of increased airway resistance, with a more narrow frequency range across which peak carinal pressures are minimised. High airway resistance in the newborn most commonly occurs in the setting of pulmonary interstitial emphysema or acute meconium aspiration syndrome. Figure 6-5 also shows that similar penalties are evident for the patient who has high resistance as well as low compliance, such as might occur with heterogeneous chronic lung disease, or evolving meconium aspiration when chemical pneumonitis reduces alveolar volume and stiffens the lung parenchyma. High resistance combined with low compliance shifts the corner frequency to the right (ie to higher frequencies). What is evident, however, is that for both high resistance settings, the peak carinal pressure is relatively high compared to normal and low compliance lung.

THE CONCEPT OF CORNER FREQUENCY

High Frequency Oscillatory Ventilation undertaken at a frequency around the corner frequency will minimize pressure costs per unit of oscillatory flow.
As the time constant of the lung increases, the corner frequency decreases and vice versa.
The used frequency should be adjusted according to the underlying mechanical properties of the airways and the lung:

- Lower frequencies in high resistance and/or high compliant lungs.
- Higher frequencies in low compliant lungs with normal resistance.

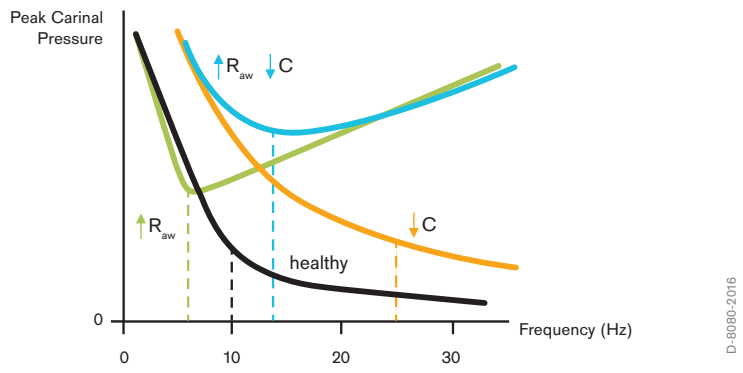

Figure 6-5: Effect of mechanical properties on the peak pressures transmitted to the carina. Adapted from (15). Corner frequency is shown by the dashed lines, representing the point at which most gain in minimising carinal peak pressures are achieved. Low compliance (C) shifts the optimal frequency to the right, whereas lower frequencies are more optimal for settings in which airway resistance (R_{aw}) is increased.

7 Understanding tidal volume delivery during HFOV

High-frequency oscillatory ventilation is widely understood to achieve effective ventilation using tidal volumes of less-than or equal to anatomical dead space (ie 2-3 mL/kg). However, as many oscillators used in the clinical setting did not measure or report delivered tidal volume, many HFOV users have an incomplete understanding of how tidal volume changes with changes in ventilatory settings and/or respiratory mechanics. The principles of volume delivery during HFOV are the same as in pressure-controlled/limited ventilation at more conventional physiological rates. Understanding the determinants of tidal volume helps us to understand how tidal volume in high-frequency ventilation changes with different ventilator settings. Taking the inspired tidal volume as an example, the inspiratory tidal volume waveform resulting from $V=(C\Delta P)(1-e^{-T_I/RC})$ shown in Figure 7-1: the plateau of this waveform is defined by the product of the compliance and the pressure amplitude; how quickly the maximum tidal volume is delivered is a function of the respiratory time constant (RC); the absolute volume delivered is determined by the elapsed inspiratory time (t_I), relative to the time constant.

CALCULATION OF TIDAL VOLUME *I*

Delivery of tidal volume follows the general formula of:
$V=(C\Delta P)(1 - e^{-T_I/RC})$ Equation where V_T is tidal volume, C is compliance, ΔP is ΔP (PIP-PEEP) and R is resistance. The product of R x C is the time constant (τ).

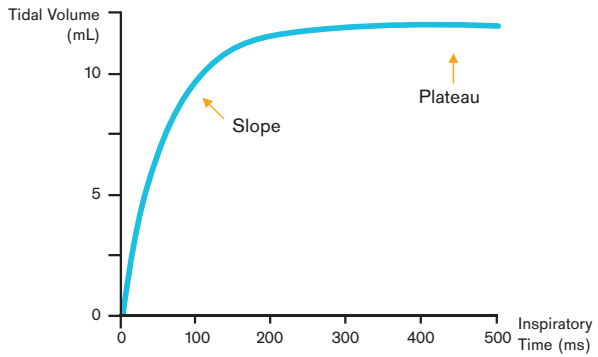

Figure 7-1: Waveform for inspired tidal volume pressure controlled conventional ventilation. The plateau (ie maximum tidal volume) delivered is determined by the product of compliance and ΔP (peak inspiratory pressure – positive end expiratory pressure). The rate at which the plateau tidal volume is achieved is determined by the time constant (τ = RC). How much tidal volume is actually delivered for any given combination of ventilatory pressure settings and respiratory mechanics is determined by the elapsed time (t).

7.1 Determinants of tidal volume

With this background understanding, it is possible to understand how changing HFOV settings such as amplitude, frequency and I:E ratio alter the delivery of tidal volume to the lung. We can also understand why tidal volume delivery varies as the mechanical properties of the lung change.

7.1.1 Oscillatory amplitude

During conventional ventilation, ΔP is the difference between the peak inspiratory pressure and the positive end expiratory pressure, with each parameter being set independently. During HFOV, oscillatory amplitude (ΔP) is set directly at the ventilator. As oscillatory amplitude increases, the maximum achievable tidal volume will also increase (see Figure 7-2).

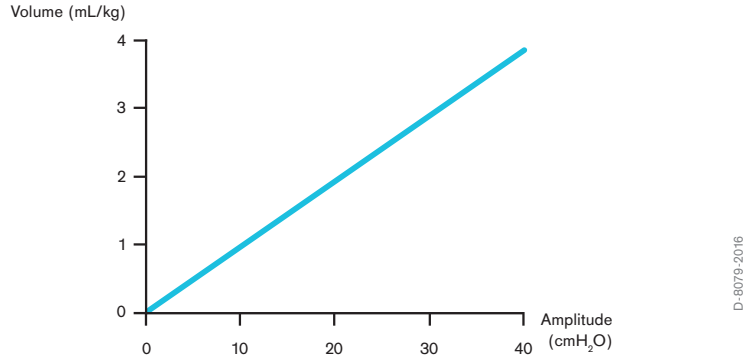

Figure 7-2: Effect of oscillatory amplitude on delivered tidal volume. For any given lung compliance, as amplitude increases, the delivered tidal volume also increases. Figure shows tidal volume/kg for a compliance of 0.1 mL/ cmH_2O, and resistance of 100 cmH_2O/L/s, and an inspiratory time of 33 ms (f=10 Hz, I:E 1:2) in a 1 kg infant.

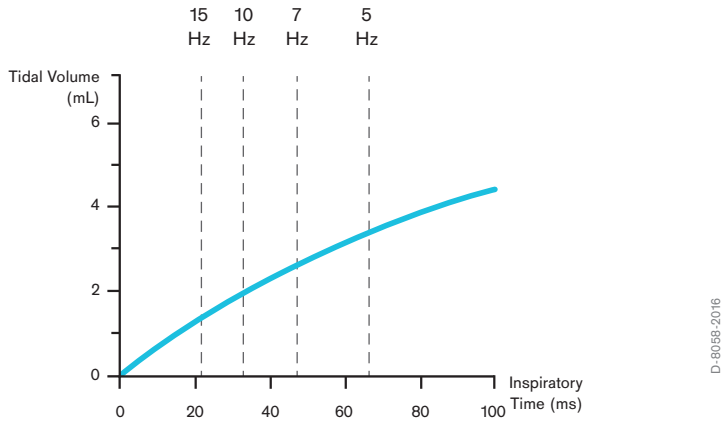

Figure 7-3: Decrease in absolute inspiratory time with increasing frequency. Graph shows inspiratory times with an I:E ratio of 1:2 (ie 33 % inspiratory time).

7.1.2 Frequency

As frequency increases, the absolute oscillatory time for each volume delivery cycle decreases. If the inspiratory to expiratory ratio does not change, the absolute inspiratory time will decrease with increasing frequency. Because there is less time available, the tidal volume delivered will decrease with increasing frequency if all other ventilator settings and lung mechanical properties remain the same (see Figure 7-3).

7.1.3 I:E ratio

As I:E ratio increases from 1:2 to 1:1, the absolute inspiratory time also increases, allowing more time for volume to be delivered to the lung (see Figure 7-4). The effect that I:E ratio has on the absolute tidal volume delivered also depends on frequency and lung mechanics. As the steepest part of the change in tidal volume occurs early in the inspiratory phase, there is a larger percentage increase in tidal volume when I:E ratio is change from 1:2 to 1:1 at high frequencies than at low frequencies. Similarly, because the absolute time to reach maximum tidal volume increases as time constant of the lung increases, there is a larger percentage increase in tidal volume with an I:E ratio change from 1:2 to 1:1, as the time constant of the lung increases.

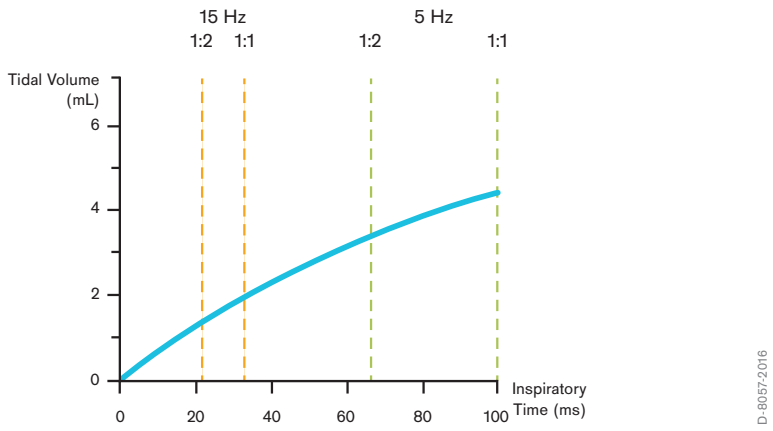

Figure 7-4: Change in absolute inspiratory time and delivered volume as I:E ratio changes. Graph illustrates changes at 5 Hz and 15 Hz frequencies.

7.1.4 Lung mechanics

As the inspiratory time during ventilation at conventional physiological rates usually exceeds 5 time constants, there is sufficient time for tidal volumes in the order of 4-6 mL/kg to be delivered to the lung.

However, during HFOV, the inspiratory times are much shorter than those used during conventional ventilation, and usually the inspiratory times during HFOV are well below the time taken for 3 to 5 time constants of the lung to elapse. Furthermore, the absolute inspiratory time usually changes with change in oscillatory frequency because the clinician sets the percent inspiratory time or defines an inspiratory/expiratory time ratio, rather than setting an absolute inspiratory time. Cycle length decreases as frequency increases: consequently, providing I:E is held constant, the absolute inspiratory time becomes shorter as frequency increases.

Figure 7-5 illustrates how limiting inspiratory time in HFOV results in the delivery of much smaller tidal volumes during HFOV than during conventional ventilation. Figure 7-5 also shows how the mechanical properties of the respiratory system markedly influence the tidal volume delivered during HFOV. The lung with very short time constant (ie low compliance), achieves the maximum tidal volume rapidly whereas the healthy and high resistance lungs may not reach their maximum potential tidal volumes before the inspiratory phase of the HFOV waveform is terminated.

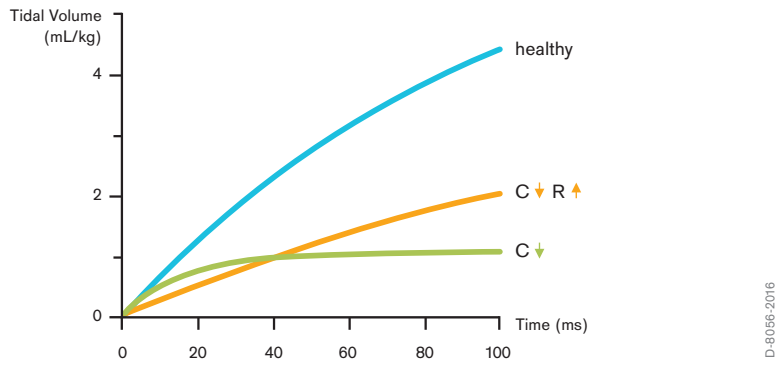

Figure 7-5: Effect of lung mechanics on inspiratory tidal volume during HFOV. Three lines are shown, representative of infants with healthy compliant (1.0 mL/cmH_2O) lungs (blue line), very low compliance (0.1 mL/cmH_2O) lungs (green line), or high resistance (250 cmH_2O/L/s), reduced compliance (0.6 mL/cmH_2O) lungs (eg BPD: orange line).

HFO VENTILATOR PARAMETERS AND TIDAL VOLUME *S*

CO_2 removal is mainly dependent on tidal volume and frequency (see chapter 5.5). The tidal volume is usually smaller or equal than anatomical dead space (i.e. 2-3 ml/kg).

Tidal volume is adjusted by changing the following control parameters:

- Amplitude
  - Higher amplitude leads to higher tidal volume.
- Frequency
  - Tidal volume delivered will decrease with increasing frequency (without Volume Guarantee).
  - Tidal volume is increased by decreasing the frequency (only if Volume Guarantee is not activated), at a cost of increased transmission (reduced damping) of the oscillatory pressure amplitude.
- Percent inspiratory time
  - Decreased percent inspiratory time (I:E = 1:2 or 1:3) will reduce tidal volume as less time is available to deliver flow.
  - Tidal volume increases with a higher percent inspiratory time (I:E = 1:1).
- I:E ratio
  - Tidal volume increases when changing from I:E ratio of 1:2 to 1:1 or 1:3 to 1:2.

8 Distending lung volume and mean airway pressure

Maintaining a well-recruited lung during HFOV that is neither overdistended or underinflated is essential to minimising injury to the lung and optimising arterial oxygenation. Lung recruitment is achieved primarily through the adjustment of mean airway pressure. Understanding the determinants of distending lung volume and how to achieve optimal distending lung volume during HFOV is essential to maximise the benefits and minimise harm when using this ventilatory modality.

8.1 Determinants of distending lung volume during HFOV

Distending lung volume is changed by altering the mean intrapulmonary pressure – ie the distending pressure within the lungs (P_L). However, as the intrapulmonary pressure is not easily measured, it is the mean airway opening pressure (P_{ao}) (the pressure measured at the airway opening or "patient wye") that is used by the clinician as a guide to the pressure in the lung. Understanding the determinants of both of these pressures is essential to understanding how to optimise lung volume under different clinical settings.

8.1.1 Control of mean airway pressure

Mean airway pressure during HFOV is usually adjusted directly by the clinician using a ventilator control. The ventilator achieves these increases or decreases in mean airway pressure settings by adjusting either the bias flow and/or the resistance to flow in the expiratory valve.

8.1.2 Determinants of mean intrapulmonary pressure

During conventional ventilation, the mean airway pressure at the airway opening is usually very similar to the mean intrapulmonary pressure (the pressure actually distending the lung). However, during HFOV, mean pressures in the lung may be either higher or lower than the mean pressure set or shown on the ventilator from recorded at the airway opening.

A mean intrapulmonary pressure higher than the mean airway opening pressure is usually a result of applying insufficient mean airway pressure and development of gas trapping. Increasing the mean airway pressure to splint the airways open will prevent the air from becoming trapped in the lung periphery.

More commonly, mean intrapulmonary pressure is lower than the pressure measured at the airway opening and displayed by the ventilator. As shown in Figure 8-1, this pressure loss (shown by a negative value for $P_L - P_{ao}$) is only present when an I:E ratio of 1:2 (or 1:3) is used and does not occur at an I:E ratio of 1:1. Furthermore, for the same tidal volume or pressure amplitude, the pressure drop from airway opening to the alveolar compartment in the lung increases with increasing frequency or decreasing tracheal tube size. This dependence of pressure drop on the I:E ratio is important to remember when changing from conventional ventilation to high-frequency oscillatory ventilation: the mean pressure set on the ventilator needs to be set higher when using a 1:2 ratio compared to 1:1 ratio to achieve the same mean intrapulmonary pressure.

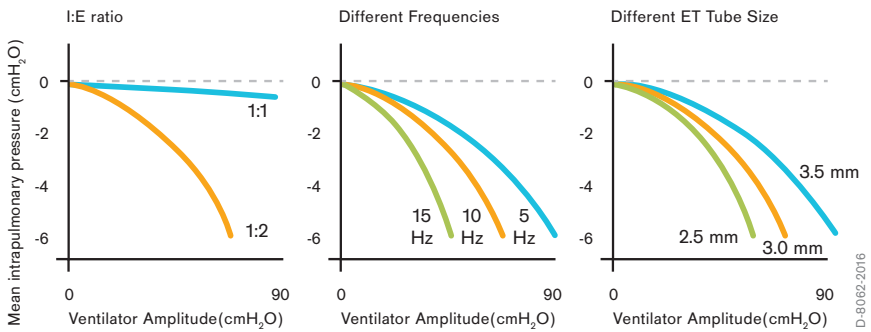

Figure 8-1: Effect of I:E ratio, frequency and tracheal tube size on fall in mean intrapulmonary pressure. Left panel: There is minimal difference in mean pressure between the airway and the alveolar compartment when I:E of 1:1 are used. However, at I:E of 1:2, there is a progressive fall in mean airway pressure as ventilator amplitude increases. Middle and right panel: At I:E of 1:2, the fall in pressure from airway opening to alveolar compartment becomes steeper as frequency increases, or as tracheal tube internal diameter decreases.

RESISTIVE PRESSURE DROP *I*

Resistive pressure drop during HFOV follows the general form of:

$P_{res} = k_1\dot{V} + k_2(\dot{V})^2$

Where P_{res} is the resistive pressure drop, k_1 and k_2 are constants and $\dot{V}$ is the flow in the tracheal tube. At I:E of 1:1, the inspiratory and expiratory P_{res} are approximately equal, and no net pressure drop results across the cycle. At I:E of 1:2, the inspiratory flow is higher than the expiratory flow, resulting in a greater pressure drop during inspiration than expiration. Mathematically, the magnitude of the pressure drop is proportional to the difference between the squared mean inspiratory and squared mean expiratory velocities (12).

MEAN INTRAPULMONARY PRESSURE AND I:E RATIO *S*

- The mean intrapulmonary pressure is the effective pressure distending the lungs. It cannot be measured directly.
- The mean intrapulmonary pressure is closest to the set mean airway pressure at an I:E ratio of 1:1.
- At I:E ratios of 1:2 or 1:3, the mean intrapulmonary pressure will be lower than the set mean airway pressure.

8.2 Achieving optimal lung volume

8.2.1 Approaches to recruiting and optimising lung volume during HFOV

There are several different methods for recruiting lung volume during HFOV. Most commonly, a stepwise incremental and then decremental change in mean airway pressure is used as this approach is the most effective in fully recruiting the lung and finding the optimal distending pressure on initiation of HFOV in the atelectatic lung. An example of how the stepwise approach is used to recruit the lung of an infant with atelectatic lung due to respiratory distress syndrome is outlined in Figure 8-2.

8.2.2 Avoiding volutrauma during lung volume recruitment

As the lung is recruited, the compliance of the lung will change: initially, the compliance increases as the lung volume increases on the steep part of the inflation limb (step 2 in Figure 8-2). As the opening pressure is achieved and the lung starts to become overdistended (step 3 in Figure 8-2), the compliance falls (step 3 in Figure 8-2). Then, as the pressure is reduced, the compliance will again increase, before falling again as the closing pressure is reached (step 4 in Figure 8-2).

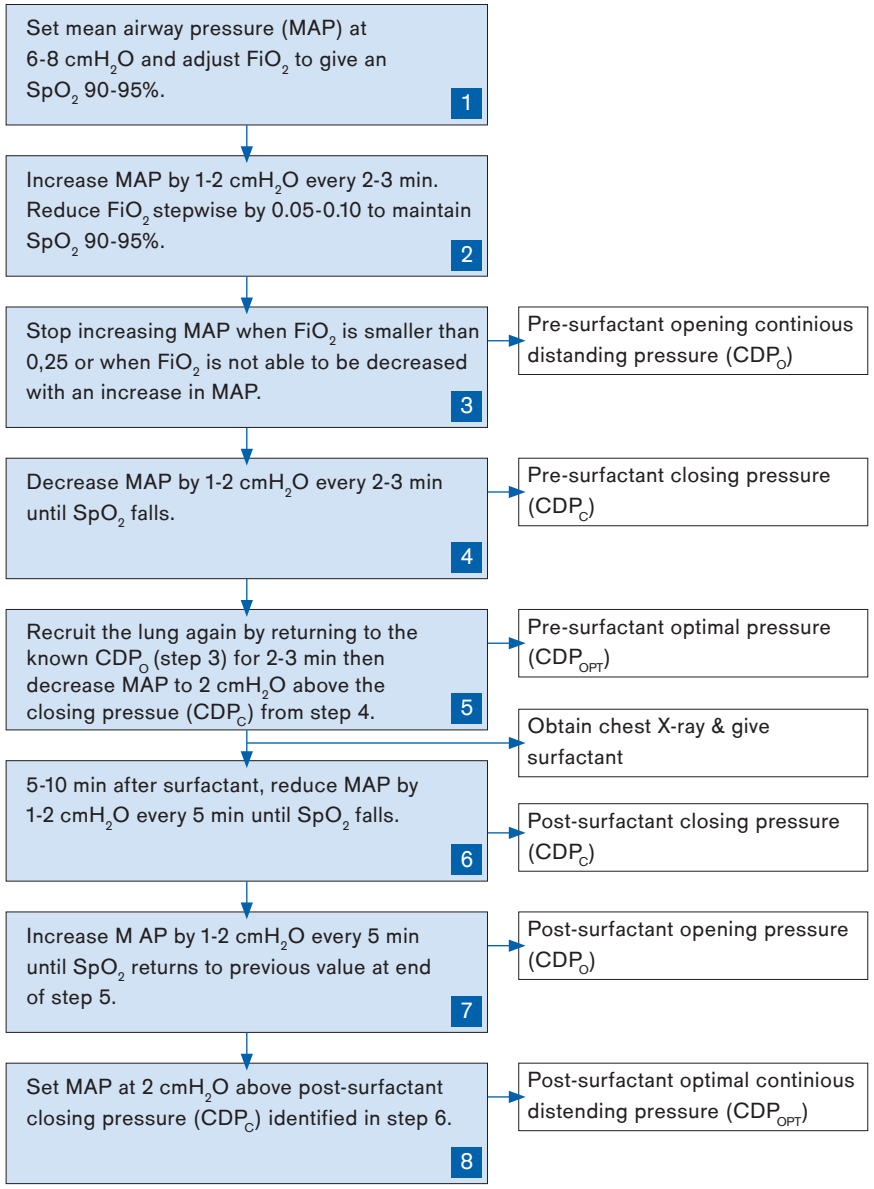

Figure 8-2: Algorithm for recruitment of the atelectatic lung during HFOV. Adapted from (16).

These changes in compliance have important consequences for tidal volume. Figure 8-3 shows that the tidal volume will change markedly during recruitment If Volume Guarantee is not being used, and the oscillatory amplitude remains the same throughout the recruitment procedure. Fluctuating tidal volumes may result in similar marked fluctuations in arterial partial pressure of carbon dioxide, and consequent unwanted fluctuations in cerebral blood flow. It is therefore very important to monitor carbon dioxide, tidal volume and the DCO_2 continuously during a recruitment procedure and to continuously adjust the oscillatory amplitude to avoid potentially adverse consequences of abrupt changes in cerebral blood flow or turn on Volume Guarantee.

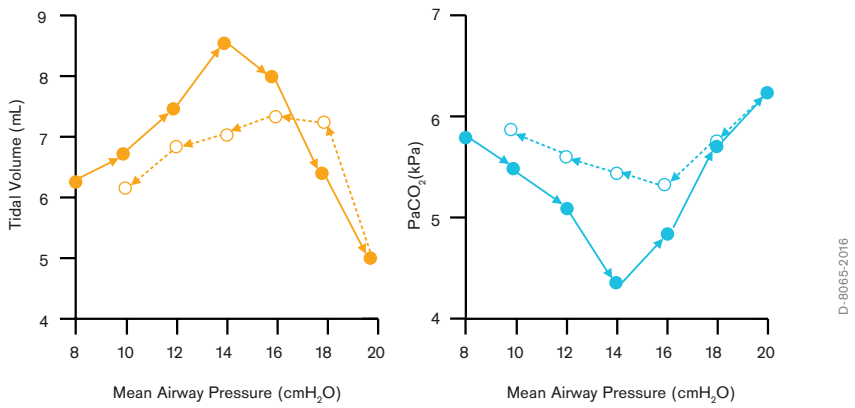

Figure 8-3: Change in tidal volume and $PaCO_2$ during lung recruitment. This figure illustrates changes observed if amplitude is held constant as mean pressure is first incremented (solid line/ filled circles), then decremented (broken lines, open circles) during a volume recruitment manoeuvre. Adapted from (17).

8.2.3 Maintaining optimal lung volume in HFOV

Once the lung is optimally recruited, it remains important to maintain the lung at this optimal volume to minimise the risk of ongoing iatrogenic lung injury. The optimal distending pressure will decrease as lung disease improves: consequently, mean airway pressure is reduced gradually until the patient is able to maintain gas exchange with mean airway pressure at approximately the same level as pressure used for continuous positive airway pressure (CPAP).

8.2.4 Avoiding atelectasis

Atelectatrauma is a consequence of ventilating the collapsed (atelectatic) lung. Atelectasis during HFOV may follow aspiration of secretions, overly enthusiastic weaning of mean airway pressure or consequent to prolonged HFOV with low tidal volumes in the absence of spontaneous breathing effort. Careful attention to maintaining appropriate humidification may reduce the risk of developing thick tenacious secretions that block small airways and promote collapse. Attention to prompt re-recruitment of the lung after suction is important to avoid unintended adverse lung collapse. Infrequent sigh breaths (approximately 1 per minute) with a moderate peak inspiratory pressure may facilitate maintenance of lung volume during prolonged HFOV with low tidal volumes.

8.3 Avoiding overdistension

Volutrauma during HFOV may result from both static overdistension as well as cyclic overdistension of the lung. The peak alveolar distension is the volume reached at the peak of inspiration and should not exceed 90% of the total lung capacity as shown in Figure 8-4 (15). As the lung is kept open at a level above functional residual capacity at high mean airway pressures, the MAP needs to be reduced if lung disease improves in order not to overdistend the more compliant lung.

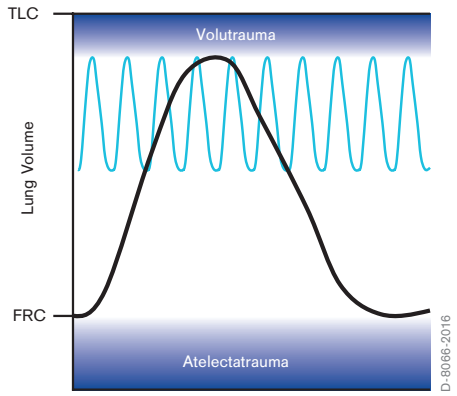

Figure 8-4: Difference in distending lung volume during HFO and conventional ventilation. The lung is maintained closer to total lung capacity (TLC) than functional residual capacity (FRC) during HFO compared to conventional ventilation.

9 Management of HFOV

9.1 Transition from conventional ventilation

Prior to commencing HFOV, it is important to consider the nature of the underlying disease and to have a clear plan for ventilation strategy as different diseases benefit from slightly different approaches to delivery of HFOV. The guidelines given below are appropriate for recruitment of the homogeneously derecruited lung such as occurs with RDS due to surfactant deficiency. Suggested approaches for other lung diseases are provided in section 12.

9.1.1 Prepare the patient and the monitoring environment

Ensure that appropriate monitoring is available and ready to facilitate informed adjustment and optimisation of HFOV ventilator settings after initiation of HFOV (see section 10). It is useful to note the current ΔP (PIP-PEEP) and mean airway pressure applied during conventional ventilation, as these variables guide initial selection of HFOV ventilator settings. Airway secretions present a major impediment to achieving adequate tidal volume during HFOV (much more so than during conventional ventilation) and pose a risk for increased oscillatory pressure transmission to proximal alveoli (see section 6.2.2). Consequently, it is advisable to also perform tracheal suction prior to commencement of HFOV to avoid clinical deterioration on commencement of HFOV.

9.1.2 Setting the mean airway pressure

Mean airway pressure is the primary determinant of distending lung volume, and also influences pulmonary vascular resistance, and hence the flow of blood through the pulmonary capillaries. Consequently, mean airway pressure is the primary determinant of oxygen transfer from the alveolus to the pulmonary capillary. A strategy for identification of optimal mean distending pressure for first intention HFOV treatment in the setting of neonatal respiratory distress syndrome is shown in Figure 8-2. A similar approach can also be applied in the initial recruitment of the atelectatic lung when HFOV is used in the rescue setting. In the rescue setting, as useful guide for initial mean airway pressure approximately the same (I:E of 1:1) or 2-3 cmH_2O higher (I:E of 1:2) than the mean airway pressure used during conventional ventilation.

9.1.3 Setting oscillatory pressure amplitude (pressure controlled HFOV)

If commencing HFOV at 10 Hz, a ΔP on the HFOV ventilator approximately 1.5 times the ΔP (PIP-PEEP) used during conventional ventilation provides a reasonable conservative starting oscillatory pressure amplitude during HFOV. Higher initial

oscillatory pressure amplitudes need to be set on the ventilator at frequencies above 10 Hz, whereas lower amplitudes are required for frequencies below 10 Hz.
Immediately after commencing HFOV, adequacy of the oscillatory ΔP should be reassessed by the delivered tidal volume: as the tidal volume required varies according to frequency, the clinician is referred to the table below for approximate "target" tidal volumes for specific frequencies. In the absence of tidal volume monitoring in HFOV, visual confirmation of adequate chest wall vibration ("wiggle") is a useful alternative guide to adequacy of oscillatory amplitude. Regardless, close monitoring of arterial CO_2 via transcutaneous measurement of pCO_2 is essential to ensure amplitude is set such that changes in pCO_2 are gradual: rapid fluxes in pCO_2 may be accompanied by sudden and deleterious changes in cerebral blood flow.

INITIAL DCO_2 FOR DIFFERENT PATIENT WEIGHTS

Weight (kg)	5 Hz 3.46 mL/kg	7 Hz 2.93 mL/kg	10 Hz 2.45 mL/kg	15 Hz 2.00 mL/kg
0,5	15	15	15	15
1	60	60	60	60
2	240	240	240	240
3	540	540	540	540
4	960	960	960	960

Table 1: Different combinations of frequency and tidal volume to reach same DCO_2 for permissive hypercapnoea.

Inadequate or excessive chest wall motion should result in prompt readjustment of the ΔP to prevent hypocapnoea or hypercapnoea. If tidal volume monitoring is in place, adequacy of delivered tidal volumes and DCO_2 should be considered. In the event that HFOV is commenced in the setting of significant hypercapnoea, oscillatory ΔP should be adjusted to achieve a gradual fall in transcutaneous pCO_2 of about 2-3 mmHg/min (0.3-0.4 kPa/min) to avoid very rapid changes in cerebral blood volume that may result in intracerebral haemorrhage.

9.1.4 Setting oscillatory tidal volume (volume targeted, pressure limited HFOV)

Commencement of volume targeted pressure limited HFOV (HFOV+VG) focuses similarly on a controlled optimisation of pCO_2. Rather than selecting a starting oscillatory amplitude, the strategy is to set the volume target (Volume Guarantee) appropriate to the selected frequency for oscillation.
A DCO_2 of 40-60 $mL^2/kg^2/s$ will generally achieve $PaCO_2$ in the mild permissive hypercapnoeic range. Suggested tidal volumes to achieve mild permissive hypercapnoea during volume targeted HFOV are provided in Table 1 and illustrated in Figure 9-1. Importantly, larger tidal volumes are required at lower frequencies to achieve the same DCO_2 and consequently rate of CO_2 removal from the lung. Therefore, the decision to use a low frequency needs to be offset against the potential of increased risk of volutrauma to the alveolus because the higher tidal volumes required have potential to "overdistend" the immature alveolus.
Oscillators delivering volume targeted HFOV usually do so in a pressure-limited setting. For volume-targeted pressure-limited HFOV, setting the maximum oscillatory pressure amplitude (ΔP_{max}) is the equivalent of setting the maximum PIP during volume-target conventional ventilation. During HFOV, ΔP_{max} should be adjusted after the initial stabilisation period, to remain approximately 5 cmH_2O above the ΔP used to deliver the targeted volume required at the selected frequency that achieves the desired target $PaCO_2$. The 5 cmH_2O buffer in ΔP_{max} provides the ventilator with capacity to maintain ventilation in the event of brief, or sustained minor deterioration in oscillatory tidal volumes. It is important to avoid setting the ΔP_{max} more than 5 cmH_2O above the average ΔP, to avoid a significant deterioration in lung mechanics (and hence aeration of the lung) without notification to the clinician/nurse that the clinical status of the patient may have changed.

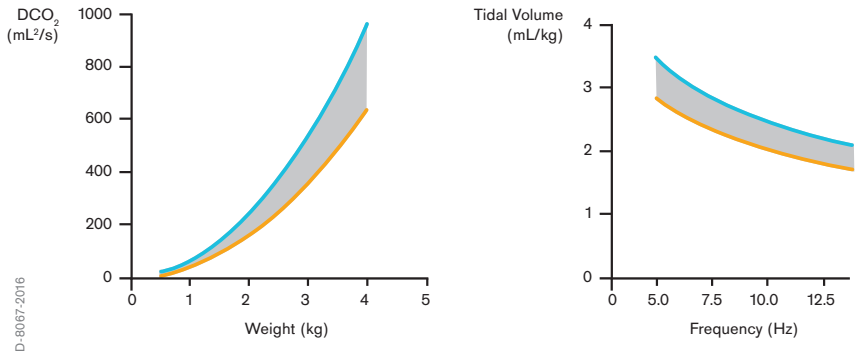

Figure 9-1: Target range for frequency and DCO_2 relative to frequency and patient weight.
Graph indicates estimated lower (orange) and upper (blue) targets for each variable.

9.2 Continuation of HFOV

Once HFOV is established, careful monitoring is required to maintain optimal patient condition. In particular, attention to lung distension and oxygenation inform on the need to adjust mean airway pressure; in contrast, fluctuations in transcutaneous carbon dioxide levels, high frequency tidal volume or chest wall vibration and perfusion may reflect more on the effectiveness of gas mixing and volume delivery.

New equilibriums in $PaCO_2$ with alterations in oscillatory amplitude are achieved rapidly (within minutes) due to the highly efficient gas mixing that occurs during HFOV. However, recruitment of lung volume resulting from changes in mean airway pressure occur more slowly, and after the initial recruitment period, effects of changes in mean airway pressure are best assessed after an interval of 15 minutes. Careful and informed interpretation of monitored variables during HFOV will inform required adjustments to HFOV parameters to appropriately manage the patient's condition.

9.2.1 Management of oxygenation

If oxygenation is satisfactory, the FiO_2 should be weaned to approximately 0.25 – 0.30 Vol.%. Subsequently, the mean airway pressure may be carefully, and gradually reduced (1 – 2 cmH_2O every 1 – 4 hours).

The cause of acute onset hypoxia will determine whether mean airway pressure needs to be increased again (eg atelectasis) or decreased (eg overinflated lung). When uncertain, it is often prudent to first decrease the mean airway pressure to avoid inadvertent progression towards overdistension. Increases in mean airway pressure, if necessary, may be achieved through a brief re-recruitment procedure, or through intermittent, sustained inflations using slightly higher airway pressures (ie increased pressure with minimal additional volume delivered to the lung). Avoidance of high mean airway pressures that impair systemic blood pressure, significantly increase central venous pressure and/or impede pulmonary blood flow is paramount. If overinflation develops and persists despite appropriate decreases in mean airway pressure, a decrease in the oscillatory frequency and use of 1:2 (or shorter) I:E ratios may permit more effective egress of air during exhalation phase (25).

9.2.2 Management of carbon dioxide

Hypercapnoea may occur secondary to airway obstruction with secretions, or as a result of changes in lung volume (either over- or under-distention). Airway obstruction needs to be dealt with promptly as it markedly impedes effectiveness of HFOV, and increases risk of injury due to excessive pressure transmission to proximal segments. Deflation of the lung during suction will result in subsequent respiratory deterioration, if post-suctioning recruitment measures are not used: effective post-suctioning recruitment is often achieved with brief small increases in mean airway pressure (2-4 cmH_2O) or transient (5 min) increases in sigh frequency (max 2-5 breaths/min) or application of 2-3 manual sustained inflations of 2-3 s each. The objective of any sigh is to raise mean pressure enough to reopen any collapsed alveoli, rather than delivery of significant tidal volumes. Consequently, the sigh may be best delivered with a long inspiratory time (ie 0.5 – 2.0 s), and a peak pressure as little as 5 cmH_2O above mean pressure.

Hypercapnoea/hypocapnoea is ultimately best managed through maintenance of the DCO_2 variable. Careful and constant monitoring of the delivered tidal volume (where volume monitoring is available) and/or chest wall vibration is essential in the absence of volume targeting as DCO_2 may change rapidly with any change in condition of the lung (improvement or deterioration) resulting in either hypocapnoea or hypercapnoea respectively.

Unless the nature of the lung condition changes, carbon dioxide elimination is optimally managed through increases in DCO_2. HFOV ventilators generally do not have a dedicated DCO_2 dial that can be adjusted on the ventilator; rather changes in DCO_2 are normally achieved through changes in tidal volume and frequency. Altering DCO_2 via changes in tidal volume is usually the preferred option, unless the nature of the lung disease changes. In the absence of volume targeting, tidal volume (and hence DCO_2) is altered by changing ΔP_{hf}. In volume targeted HFOV, DCO_2 is controlled directly by changing tidal volume, provided the maximum pressure amplitude remains at or above the oscillatory amplitude required to deliver that volume. As indicated above, using frequency to change carbon dioxide elimination may have unwanted effects. In the absence of volume targeting, decreasing frequency will increase the tidal volume for any given oscillatory amplitude – but also increases the iatrogenic cost of ventilation with increased pressure transmission to the distal airways a source of potential barotrauma. It is important to remember that the ventilator displayed oscillatory pressure amplitude is a poor and somewhat misleading indicator of pressure changes happening distally. Lower ventilator amplitudes at lower frequencies do not mean that the distal oscillatory pressure amplitudes within the airways and alveolar compartments have decreased! (see section 6). In contrast, in the presence of volume targeting, changing frequency has minimal, if any, effect on tidal volume delivery within the limits of the power of any given device. Consequently, a decrease in frequency in volume targeted HFOV will actually decrease DCO_2 and $PaCO_2$ will rise!

9.3 Humidification

Adequate heating and humidification (90% relative humidity) of the inspiratory gas is essential to avoid irreversible damage to the epithelial surfaces of the respiratory tract. In the absence of sufficient humidification, viscous secretions develop that obstruct the bronchi, promoting consolidation and collapse of the alveolar compartment and impaired gas exchange. The resultant reduced compliance also increases the risk of barotrauma as low compliance promotes increased transmission of the oscillatory pressures to the lung periphery. In contrast, excessive humidification promotes condensation in the patient circuit, the tracheal tube and the airways, and compromises delivery of adequate tidal volumes.

9.4 Weaning from HFOV

As with any ventilatory modality, the goal of weaning during HFOV is to gradually withdraw support and encourage spontaneous breathing. Although many clinicians still wean from high-frequency back to conventional ventilation (possibly due to relative availability of different ventilators), weaning from HFOV directly to a non-invasive mode of respiratory support is possible, and often the preferred mode.

Weaning from HFOV to spontaneous ventilation is an intuitive process. Mean airway pressure is gradually reduced until levels consistent with the airway support provided with non-invasive respiratory support is attained. Oscillatory amplitude is gradually reduced until the patient assumes primary responsibility for CO_2 elimination through gentle spontaneous breathing. Although a theoretical argument can be put forward to decrease frequency as lung mechanics normalise and the corner frequency decreases, alterations to frequency are generally not necessary during the weaning phase in HFOV.

The time required for weaning will depend on the underlying pulmonary disease. In acute illnesses such as respiratory distress syndrome and persistent pulmonary hypertension of the newborn, weaning may be extremely rapid, lasting only hours. More chronic diseases such as bronchopulmonary dysplasia may require weaning of HFOV support over a period of days to weeks, and will vary from baby to baby according to concomitant morbidities.

10 Monitoring during HFOV

Careful continuous monitoring is essential to clinical management of any patient on mechanical respiratory support. Monitoring is especially important during HFOV as the reliance of gas exchange on the square of the tidal volume exaggerates changes in $PaCO_2$ with any change in the mechanics of the respiratory system and ventilatory circuit.

10.1 Monitoring of gas exchange and respiratory mechanics

Essential monitoring tools that should be in place prior to commencement of HFOV include peripheral oxyhaemoglobin saturation (SpO_2), transcutaneous carbon dioxide, and flow/tidal volume monitoring. Ideally, the tidal volume display should include a field for tidal volume/kg. As CO_2 removal during HFOV is dependent on the DCO_2 (frequency x V_T^2), DCO_2 monitoring is a useful adjunct monitoring variable to facilitate stability of $PaCO_2$ if ventilation frequency is changed to accommodate different stages of lung disease and/or mechanics.

Measurement of lung mechanics is more complex in HFOV than in conventional ventilation due to the damping of the oscillatory pressure waveform from the airway opening to the lung, and the dependence of this damping on both ventilatory settings and mechanics of the intubated respiratory system. When using intermittent conventional cycles as sigh breath, the tidal volume and the difference between PIP and PEEP measured during the conventional inspiration can be used to calculate dynamic compliance (C_{dyn}) provided an inspiratory pressure plateau is achieved[5].

Although it is tempting to apply a similar approach to assessment of compliance during HFOV in the absence of such intermittent conventional breaths, frequency dependent damping of the oscillatory pressure waveform makes this impossible to apply or interpret in a meaningful manner across the frequency spectrum.

Indeed, at frequencies of 15 Hz, tidal volume is relatively independent of lung compliance.

10.2 Monitoring of lung volume

With the importance of optimising lung volume being increasingly recognised as paramount to safe and lung-protective application of HFOV, tools to assess lung volume remain a focus of HFOV research. Periodic chest radiographs provide a crude indication of lung expansion: lung volume is optimal when expanded to the 8th or 9th posterior rib assessed in the mid-clavicular line (depending on gestation

[5] $C_{dyn} = V_{T,CV}/(PIP_{CV} - PEEP)$

and the presence/absence of pulmonary hypoplasia). Respiratory inductance plethysmography and electrical impedance tomography are proven in the research setting as useful tools to monitor relative and temporal changes in lung volume during initial volume recruitment procedures. Electrical impedance tomography is also useful for the detection of pneumothorax. Lung ultrasound is used increasingly in the setting of conventional ventilation to assess lung parenchymal pathology; application to HFOV is likely in the near future.

MONITORING DURING HFOV

Ventilatory parameters	Frequency ΔP and ΔP_{max} (Volume Guarantee mode) Mean airway pressure Set V_T and delivered V_T (Volume Guarantee mode) I:E ratio (or % inspiratory time) DCO_2 (frequency x V_T^2) FiO_2
Gas exchange	Blood gases Transcutaneous pO_2 and pCO_2 SpO_2
Lung volume & respiratory mechanics	Chest X-ray Respiratory inductance plethysmography Electrical impedance tomography Oscillatory pressure ratio ($\Delta P_{trachea}/\Delta P_{ventilator}$) C_{dyn} (intermittent mandatory sigh breath)
Circulatory system & systemic perfusion	Heart rate Systemic arterial blood pressure Central venous pressure Urine output

Table 2: Monitoring during HFOV.

10.3 Monitoring of circulatory system and systemic perfusion

The continuous application of moderately high distending pressures during HFOV places additional burdens on the interaction of the circulatory and respiratory systems. Additional beneficial monitoring in seriously ill infants on HFOV thus includes regular or continuous central venous pressure and system blood pressure.

Increased central venous pressure may provide warning of cardiorespiratory decompensation in the presence of very high mean airway pressures. Compromised cardiac function may also be evident from prolonged capillary filling time and reduced urine output. Intermittent functional echocardiography also provides information about cardiac contractility, cardiac output and right-ventricular pressure: this functional information may help clinicians identify early any adverse circulatory effects of changes in mean airway pressure strategy. Near infra-red spectroscopy (NIRS) recording of cerebral and peripheral tissue oxygen saturations may also inform on systemic impact of changes in HFOV strategy.

11 Indications for HFOV

Oscillatory ventilation has been applied in the clinical setting since the early 1980s. HFOV was used initially for rescue of infants failing conventional ventilation, and in many countries this remains the primary indication for use of HFOV. HFOV is an efficacious rescue treatment in lung diseases characterised by low distending lung volume and is a feasible alternative to ECMO under these conditions, providing that appropriate volume recruitment strategies are applied. The goal of rescue HFOV is to optimise the distending lung volume and in so doing. Achieving this goal will improve gas exchange through the highly efficient gas mixing that occurs during gas exchange whilst protecting the lung from the barotrauma that would result to achieve the same gas exchange at conventional breathing frequencies.
There is no clear evidence to guide clinicians when to commence rescue treatment with HFOV. Such guidelines need to consider the potential recruitable lung volume which is influenced by disease (eg hyaline membrane disease versus pulmonary hypoplasia) and also gestation (less mature infants have absent/underdeveloped

INDICATIONS FOR HFOV RESCUE TREATMENT

	Extreme Preterm	Very Preterm	Term
Tidal volume (mL/kg)	4.5 – 5.0	5.0 – 6.0	6.0 – 7.0
Peak inspiratory pressure (cmH_2O)	22 – 25	24 – 27	25 – 30
Breathing frequency (breaths/min.)	70 – 80	60 – 70	50 – 60

Table 3: Suggested conventional ventilation settings to consider commencement of HFOV as a rescue treatment.

alveoli and may become over distended at lower total lung capacities and tidal volumes relative to their weight). Rather than using absolute limits for peak pressure as the indication for switching to rescue HFOV, in clinical settings where HFOV is used primarily for rescue, clinicians should consider the nature of the disease being treated, the stage in the natural history of the lung disease, the susceptibility/resilience of that infant to iatrogenic injury and departure from gestation appropriate healthy breathing patterns when deciding when to initiate rescue HFOV.

The promise of low tidal volumes and optimised distending lung volume offered by HFOV makes first intention, lung protective HFOV an attractive theoretical proposition for effective gas exchange at minimal cost of iatrogenic injury. Nonetheless, systematic meta-analysis of HFOV clinical trials suggest HFOV offers only a marginal reduction in the outcome of bronchopulmonary dysplasia and/or death for preterm infants with RDS (13, 18). Reasons for the equivocal outcomes of HFOV versus conventional ventilation frequency trials are varied, but undoubtedly include the timing of commencement (some infants will improve and wean ventilation rapidly regardless of ventilation modality) and the expertise of the clinical staff in understanding and applying both conventional and high-frequency ventilation modalities.

However, with the exception of early or a priori HFOV use, there remain relatively few controlled studies of the use of HFOV in many of the different clinical scenarios. Nonetheless, there remain theoretical advantages and anecdotal reports of success in using HFOV outside the immediate application of acute respiratory distress syndrome which are worthy of consideration and ongoing investigation. Homogeneous lung diseases are particularly amenable to HFOV. Successful application of lung protective HFOV for treatment of congenital diaphragmatic hernia may be in part responsible for recent trends to improved survival for this complex surgical condition. Similarly, HFOV is an effective treatment of persistent pulmonary hypertension of the newborn (PPHN), especially in the setting of secondary PPHN complicating a derecruited or consolidated lung.

The application of HFOV to inhomogeneous lung diseases is less clear. Successful HFOV rescue treatment of meconium aspiration (19) and exacerbations of bronchopulmonary dysplasia (20) are reported. The use of HFOV in the setting of pulmonary interstitial emphysema (PIE) is less clear. The only clinical trial of HFOV in the setting of PIE showed that HFOV offers benefits when applied to lungs with only mild PIE, but no advantage and possible harm in the setting of moderate to severe PIE (21). Systematic reviews highlight an association between HFOV and increased development of air leak, suggesting caution in the application of HFOV in the clinical setting of PIE (13, 18).

12 Strategies for HFOV in various lung diseases

12.1 Diffuse homogeneous lung diseases

Diffuse homogeneous lung disease includes respiratory distress syndrome, diffuse pneumonia and bilateral lung hypoplasia. Homogeneous lung diseases are ideal for treatment with HFOV. The primary goal is uniform recruitment and maintenance of lung volume to optimise oxygenation and ventilation with minimal barotrauma or volutrauma. Oscillation frequency is ideally set at or around the anticipated corner frequency of the lung. For more mature infants, a frequency of 10 Hz is appropriate. Extremely preterm and extremely low birthweight infants with homogeneous lung disease may be effectively and optimally ventilated at even higher frequencies of 12-15 Hz. Inspiratory to expiratory ratios of either 1:1 or 1:2 may be used.

PRACTICAL TIPS *T*

HFOV FREQUENCY

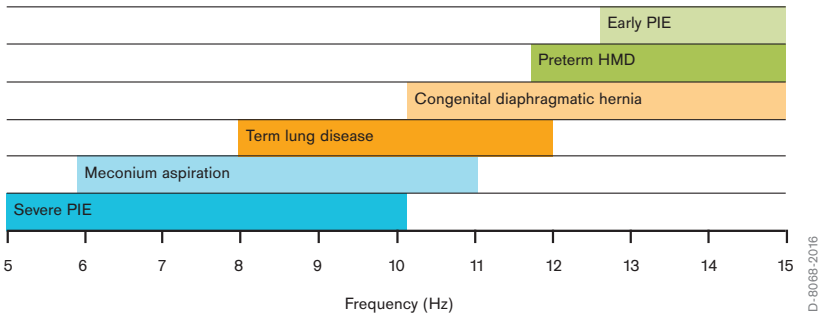

Figure 12-1: Suggested HFOV frequency ranges for common neonatal conditions.

Recruitment of the homogeneously collapsed lung ideally follows the algorithm shown in Figure 8-2 (Section 8.2.1) to find optimal distending volume, including administration of surfactant after initial recruitment, if suspicion of surfactant deficiency remains high. FiO_2 is weaned throughout the process. Recruitment continues as long as oxygenation improves and FiO_2 exceeds 0.25. Once optimal distending volume is achieved, subsequent weaning of mean airway pressure continues more

slowly as the patient improves, until mean airway pressures consistent with extubation to nasal continuous positive airway pressure are achieved.

Use of volume targeting (Volume Guarantee) during recruitment will ensure the patient is protected from both excessive cyclic tidal volumes and resultant rapid shifts in $PaCO_2$ during the recruitment process. Volume targeting also facilitates automated weaning from active oscillatory ventilation, towards predominantly spontaneous ventilation. In the absence of volume targeting, oscillatory amplitude should be decreased manually as the infant improves to encourage self-sustaining spontaneous efforts and ultimately extubation.

12.2 Inhomogeneous lung diseases

Inhomogeneous lung diseases are characterised by pathologies that differ markedly in presence and severity within different regions of the lung: they include focal pneumonia, pulmonary haemorrhage, meconium aspiration, unilateral lung hypoplasia and bronchopulmonary dysplasia. The primary goal of treatment is to oxygenate and ventilate effectively, allowing injured areas to heal whilst simultaneously avoiding new injury to more healthy lung regions: ultimately guiding the lung towards a more homogeneous state. Achievement of this goal is a significant therapeutic challenge due to regional differences in compliance and/or resistance: there is a risk of significantly over-distending or traumatising the more compliant lung units.

Theoretically, inhomogeneous lung conditions are likely to be better treated using a range of frequencies simultaneously, to target varying regional mechanical properties (22). This option is not yet commercially available. Clinicians therefore need to consider the likely mechanics and clinical course of the underlying pathologies and adapt their ventilation strategy accordingly.

Reduction of regional inhomogeneities – particularly when these are characterised by regional atelectasis -is enhanced by the use of higher rather than lower frequencies (23). The explanation for this homogenisation effect at higher frequencies is the higher flow velocities and increased acceleration of the flow waveform promote greater pressure losses in normally ventilated areas whilst simultaneously allowing pressure in atelectatic areas to increase to the threshold pressure at which recruitment occurs (24).

Although yet unproven, lower frequencies and short inspiratory to expiratory ratios may be more ideal in the setting of acute airtrapping and predominantly high resistance pathologies: the combination of a longer cycle time (low frequency) and relatively longer expiration than inspiration results in lower flow velocities and longer absolute expiratory times that will facilitate complete expiration of the lung (25). However, overcoming airtrapping is also critically dependent on maintaining a mean airway pressure sufficiently high to stent open the airways and hence avoid airway collapse during active expiration that may promote worsening of the gas trapping condition and may cause pneumothorax.

As with homogeneous lung diseases, the clinician must remain vigilant in adapting ventilatory strategy to the evolving disease process. Meconium aspiration, for example, commences as a condition with increased airway secretions, the removal of which may be enhanced by asymmetric inspiratory to expiratory ratios (eg I:E = 1:2). The presence of the secretions reduces airway diameter and impedes flow, whilst the meconium promotes acute inflammation of the airway walls: together these response promote high airway resistance and a downward shift of (optimal) corner frequency of the lung (see section 6.3). As the condition evolves, however, the pathology predominantly becomes more consistent with a chemical pneumonitis and patchy regional atelectasis. Consequently, later in the disease process a shift back to higher frequencies and consideration of lung recruitment may be beneficial.

12.3 Airleaks

Diseases characterised by air leak include pulmonary interstitial emphysema (PIE), bullous emphysema, pneumomediastinum, and pneumothoraces. Whereas HFOV should protect the lung from air leak, this protective effect is not well supported by the literature: systematic meta-analyses consistently show that HFOV is associated with a small increase in the presence of any air leak – which appears largely due to increased interstitial emphysema (13,18). Careful attention to avoidance of over distention (passive or cyclic) and targeting of treatment frequency to avoid inadvertent transmission of high oscillatory pressures may reduce the likelihood of developing air leak phenomena.

In the presence of gross air leak (eg pneumothorax), strategy should prioritise low tidal volume ventilation. Consequently, higher frequencies and avoidance of any superimposed conventional ventilation breaths are preferred. If significant PIE is present, then using lower frequencies with short I:E (eg I:E = 1:2) may enhance resolution of the disease (25).

Management of mean airway pressure is critical in the presence of air leak: aggressive lung volume recruitment is best avoided. Mean airway pressure should be reduced where possible then maintained at a pressure sufficient to stent small airways open (particularly in PIE when alveolar/airway attachments may be missing or damaged) to avoid progression of the air leak. Once the patient improves, continuation of HFOV for a further 24-48 hours may avoid recurrence. In the presence of unilateral PIE, positioning and/or selective single lung ventilation to promote collapse and rest of the affected lung, followed by gentle reinflation 1-2 days later may facilitate more rapid resolution.

12.4 Persistent pulmonary hypertension of the newborn (PPHN)

Strategy for use of HFOV in the presence of persistent pulmonary hypertension of the newborn needs to consider the underlying cause.

For infants with primary PPHN, with no significant underlying lung disease, the focus is on optimising the cardiocirculatory status: exclude or treat hypovolaemia and hypotension prior to commencement of HFOV; strive for normoventilation; and select a mean airway pressure that promotes lung perfusion by neither under- or over-distending the lung. Frequency selection is guided more by patient size than disease: higher frequencies are used for smaller and more immature babies. Babies with primary PPHN are often over-ventilated on conventional ventilation such that mean airway pressure on commencement of HFOV rarely needs to exceed that used during the preceding conventional ventilation. Often a decrease in mean airway pressure will increase cardiac output and significantly improve the patient's condition. Monitoring of central venous pressure is advantageous.

In contrast, when PPHN is secondary to another disease process, treatment needs to target the underlying pathology. Recruitment of underlying atelectasis, for example, may result in marked improvements in patient condition.

Concomitant treatment with HFOV and inhaled nitric oxide is more often successful than treatment with HFOV or iNO alone in the presence of severe PPHN, particularly for secondary PPHN associated with respiratory distress syndrome or meconium aspiration (26).

13 Complications, relative contraindications and limits of HFOV

13.1 Complications and side effects

13.1.1 Irritation

Commencement of HFOV is often associated with the patient becoming more unsettled. Irritation may be exacerbated by passive over distension of the lung and excessive oscillatory amplitude. Maintenance of quiet spontaneous breathing during HFOV will enhance oxygenation (30). Spontaneous breathing is encouraged by adjusting oscillatory amplitude to target permissive hypercapnoea. When patient discomfort or distress occurs, deeper sedation should be considered. Sedation should be reduced once hypercapnoea is settled, volume recruitment is complete and the patient is improving.

13.1.2 Secretions

Attention to provision of appropriate humidification is essential to ensure that secretions do not accumulate and plug the airways. Even small amounts of secretion or foam in the airways after surfactant administration can have a marked effect on the efficacy of HFOV: the increase in airway impedance (especially airway resistance) significantly decreases oscillatory tidal volumes and hence also the DCO_2. Importantly, oscillatory pressures also increase proximal to the build up of secretions and may promote local trauma.

13.1.3 Necrotising tracheobronchitis

Irritation progressing to necrosis of the tracheobronchial system may complicate HFOV, most often attributed to inadequate humidification and excessive mean airway pressure. There is no evidence that the incidence of necrotising tracheobronchitis is any different in HFOV to that occurring after conventional ventilation.

13.1.4 Haemodynamics

Increased vagal activity during HFOV may result in a slight reduction in heart rate. In contrast, high mean airway pressures may compromise both venous return to the heart and cardiac output as well as result in increased pulmonary vascular resistance. Clinically, the patient may try to compensate for reduced venous return with an increased heart rate. Each of these problems are minimised by careful attention to optimising blood volume and myocardial function and careful attention to mean airway pressure strategy to avoid lung over-distension and development of pulmonary hypertension. Development of peripheral oedema may be present due to the high intrathoracic pressures.

13.1.5 Intracranial haemorrhages

Concern about intracranial haemorrhage during HFOV stems from early studies when the use of HFOV was associated with adverse neurological outcomes (27). However, systematic reviews of more recent HFOV trials do not show the incidence of intracranial haemorrhage during HFOV to be different to that during conventional ventilation (13). Avoidance of intracranial haemorrhage is critically dependent on the use of appropriate lung volume recruitment and the use, correct interpretation and response to changes in monitoring variables: for example, as the lung is recruited with HFOV, early and responsive adjustment of ventilator settings such as ΔP_{hf} or tidal volume (volume-targeted modes) avoids inadvertent over-ventilation. Rapid fluxes in arterial carbon dioxide arising with breath to breath changes in tidal volume

associated with altered lung mechanics may translate to rapid changes in the intracerebral circulation: such fluctuations may be avoided with use of volume targeting, such as Volume Guarantee during HFOV, or careful adjustment of oscillatory amplitude in response to change in transcutaneous carbon dioxide when HFOV is operated without volume targeting.

13.1.6 Overinflation

Overinflation is the most frequent complication and cause for failure of oscillatory ventilation. It occurs most often in obstructive lung diseases such as meconium aspiration syndrome and pulmonary interstitial emphysema. Careful attention to appropriate frequency selection for the nature and stage of the underlying disease is essential to avoid this complication.

13.2 Relative contraindications

Acute pulmonary obstruction is the only relative contraindication to the use of HFOV. Acute obstruction may be present in the early stages of meconium aspiration, as well as during pulmonary haemorrhage, RSV bronchiolitis and bronchopulmonary dysplasia. Use of HFOV in the presence of obstruction risks barotrauma to the proximal airways, acutely inadequate gas exchange and exacerbation of gas trapping if a ball valve effect is present due to secretions.

13.3 Limitations of HFOV

Assuming a disease and patient appropriate strategy is selected, the success of HFOV is dependent on the capabilities of the high frequency ventilator to meet the proposed strategy. Even adults can be oscillated with an appropriately powered ventilator. Key to this goal is the achievement of adequate oscillatory volumes at disease specific optimal frequencies. Compliance of the patient circuit has a crucial impact on delivery of oscillatory tidal volumes: cyclic tidal volumes delivered to the patient are increased considerably with a low-compliant circuit including the use of a low volume humidifier chamber. Patient lung mechanics additionally influence the ability of the ventilator to deliver adequate tidal volumes for efficient gas exchange. The same ventilator that easily ventilates a large healthy patient may struggle to deliver adequate tidal volumes to a smaller patient. In this setting, effective ventilation may be achieved using increased I:E (eg I:E = 1:1) and lower frequency.
Recent and emerging modifications including volume targeting and inclusion of capability to use sigh breaths may also allow refinement of the strategy to achieve oxygenation and ventilatory goals whilst minimising iatrogenic complications.

PRACTICAL TIPS

FOR THE OPTIMAL SET-UP:

The set-up of patient circuit has a higher impact on ventilator performance during high frequency ventilation compared to during conventional ventilation. The patient circuit can be optimized as follows:

- Use breathing circuits with very stiff tubing walls and minimal volume in order to reduce the compressible gas volume and minimize compliance of the breathing circuit:
  - Use a circuit as short as possible.
  - Use a circuit with stiff tubing walls (smooth bore, no standard corrugated circuit).
- Prepare humidifier chamber as follows in order to reduce compressible volume to a minimum:
  - Use a small humidifier chamber to minimize chamber volume The chamber shall be filled with water to the maximum level as fluids are not compressible.
  - Avoid the use of incubator extensions as these increase tubing compliance and compressible volume. If the incubator temperature is high and extensions are needed, select the shortest extension with stiff tubing walls.
- Use heated circuits, if possible:
  - Use no or low-volume water trap in order to reduce the compressible volume.
- Avoid condensation in the breathing circuit to minimize resistance to air flow:
  - Avoid temperature drops in patient circuit by air conditioning or air draft.
  - Avoid restrictions of tube diameters by hose kinks or adapters.

14 Failure of HFOV

In most instances, HFOV improves the critical respiratory condition, at least temporarily. Failure is often a consequence of inappropriate strategy – that does not fully consider the patient's disease, the ventilator's capabilities, or the interactions between the two. Inappropriate HFOV strategy can lead to a rapid worsening of the patient's condition. Patients with homogeneous lung diseases are more likely (70-87%) to respond to HFOV than inhomogeneous diseases (50-79%), airleaks (63-80%), PPHN (39-69%), or CDH (22-27%) (21). Early identification of HFOV failure (persistently high FiO_2, oxygenation index, $PaCO_2$, or mean airway pressure and/or low A/a ratio) allows for prompt commencement of alternative therapies (eg high-frequency jet ventilation in inhomogeneous lung disease), and if necessary, transfer to a medical centre offering extracorporeal membrane oxygenation. In one study, an A/a ratio (Alveolar-arterial ratio) of < 0.08 six hours after commencement of HFOV best predicted HFOV failure and need for ECMO in neonates (31). Any patient with an increase in $PaCO_2$ and/or oxygenation index 2-6 hours after commencing HFOV that is not due to an immediate mechanical problem (eg blocked tube) is at risk of failed HFOV.

15 The future directions of HFOV

HFOV continues to evolve, despite being in clinical use for over 30 years. The introduction of volume targeting heralds further modifications such as targeted DCO_2 ventilation that will facilitate not only automated weaning, but also take the guess work out of appropriate changes to oscillatory amplitude with changes in frequency as disease state evolves. Future research will target more effective and lung protective ventilation for inhomogeneous lung diseases, where the use of multi-frequency ventilation may be particularly effective. Work also on the interaction between patient and ventilator, including the incorporation of demand flow, will allow patients to be treated with HFOV without the complications associated with deep sedation with/without paralysis, potentially increasing rapidity of recovering and ventilator weaning. Importantly, given the importance of effective monitoring (and its appropriate interpretation) to optimal HFOV strategy, we can expect further developments in bedside technologies such as respiratory plethysmography, electrical impedance tomography and oscillatory mechanics that facilitate identification of optimal distending lung volumes and early detection of adverse events such as pneumothorax.

16 Summary

HFOV is a mode of ventilation in clinical use for over thirty years. In many centres, HFOV is now an established alternative first-intention ventilation approach for respiratory disease not amenable to non-invasive therapies. It is also widely used as an alternative to conventional ventilation, when the latter fails. HFOV is often used to treat diseases such as respiratory distress syndrome, pneumonia, meconium aspiration syndrome, persistent pulmonary hypertension of the newborn and lung hypoplasia more successfully and more gently than ventilation at more conventional breathing frequencies. Compared to conventional ventilation, the greatest assets of correctly applied HFOV in this regard are improved oxygenation and ventilation with reduced risk of barotrauma and volutrauma.

A thorough understanding of the device being used, the complexities of interactions between ventilator and patient, and particularly the implications of lung mechanics for lung protective ventilation during HFOV is paramount to the successful clinical application of HFOV. Although we have made much progress in this regard, the learning curve remains steep: clinicians with an incomplete understanding of the concepts of HFOV and experience in its use may not observe the benefits that it offers – indeed, the potential for harm remains and hence vigilance in both application, monitoring, maintenance and ultimately weaning of the patient receiving HFOV remains of the utmost importance.

17 Appendix

17.1 High Frequency Ventilation with the Dräger Babylog VN500

High-frequency in the Babylog VN500 provides active inspiration and active expiration with a sinusoidal pressure waveform (at I:E of 1:1) at a stable mean airway pressure. The HFOV settings are frequency (f_{hf}), amplitude ($Ampl_{hf}$), mean airway pressure (MAP) and inspiratory to expiratory ratio (I:E). The Babylog VN500 incorporates three major improvements relative to its Babylog 8000 plus predecessor to enhance the power and quality of HFOV:

1. the inclusion of a stronger mechanism to ensure that the oscillatory pressure becomes negative during expiration;
2. the servo control of inspiratory flow;
3. the ability of volume targeted HFOV;
4. the ability to directly control I:E by the user.

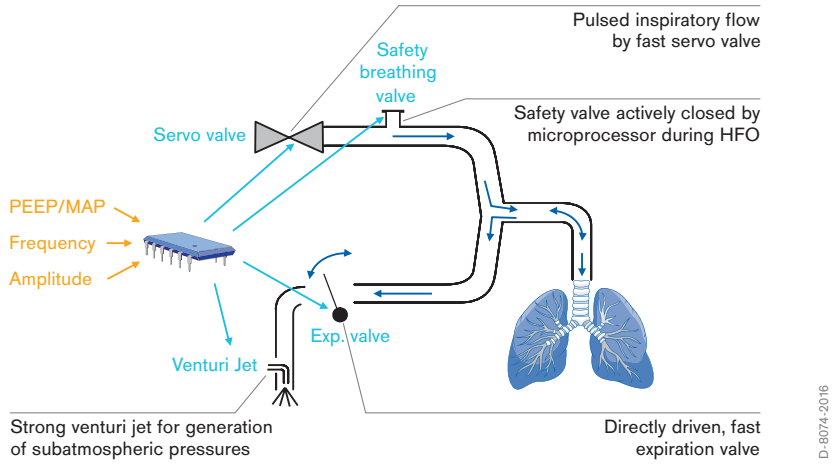

Figure 17-1: Principle of operation of the Babylog VN500.

The adjustable I:E ratio is depending on frequency: I:E of 1:1 are available over the complete frequency range from 5-20 Hz, whilst I:E of 1:2 are achievable from 5-15 Hz and 1:3 from 5-10 Hz.

SETTING RANGES

I:Ehf	Oscillation frequency range
1:1	5 to 20 Hz
1:2	5 to 15 Hz
1:3	5 to 10 Hz

Different actuators are used by the Babylog VN500 system to control the HFOV pressure waveform: the inspiratory valve, the expiratory valve and the ejector inside the expiratory valve. All three actuators are used to generate a pressure signal (waveform) at the y-piece (airway opening) with the operator determined settings of frequency, amplitude, mean airway pressure and I:E ratio. The integration of a powerful ejector (suction nozzle) into the expiratory valve allows the Babylog VN500 to reach higher amplitudes at low mean airway pressures. The ejector creates a sub-atmospheric pressure at the expiration valve, actively removing air out of the hose system. This mechanism allows generation of even sub-atmospheric peak pressures at the y-piece, ensuring rapid pressure reduction to actively empty the patient's lung, and consequently avoidance of intrinsic increased endexpiratory pressure (airtrapping). As explained in chapter 5, this sub-atmospheric pressures do not reach alveolar level.

The Babylog VN500 provides a base flow within the patient circuit during HFOV, facilitating spontaneous breathing. Spontaneous breathing is important to enhance ventilation distribution during HFOV, and becomes increasingly important for maintenance of gas exchange during weaning. Additional flow is provided during the inspiratory phase of each HFOV cycle, to achieve the set pressure amplitude.
The Babylog VN500 monitors the average inspiratory device flow delivered to the patient circuit which is important information in the application of nitric oxide. Inspiratory device flow is not stable under all conditions and is dependent on the selected HFOV setting, presence of leak around the tube, hose resistance and compliance. This measured value of device flow only indicates flow delivered by the ventilator to the patient circuit and not the flow delivered to the patient's lungs. External flow sources are not taken into account.
Amplitudes as high as 90 cmH_2O are achievable at frequencies of 5 Hz. As in other HFO ventilators, the maximum amplitude decreases with increasing frequency: absolute amplitudes achieved are dependent on circuit configuration and patient mechanics. Use of a stiff, dedicated HFOV patient circuit and low volume humidifier chamber is recommended in larger patients to fully access the capabilities of the Babylog VN500.

The airway pressure is measured from inspiratory and expiratory pressure sensors after consideration of inspiratory and expiratory hose resistances. The inspiratory and expiratory valves are controlled such that the measured mean airway pressure (MAP) equals a set MAP.
In the Babylog VN500, mean airway pressure is adjustable from 5 to 50 cmH_2O.

DRÄGER PATIENT CIRCUITS

Dräger provides a circuit portfolio, which is optimized for use with Dräger-ventilators. The following breathing circuits are recommended for HFOV, if highest performance is needed. Also other circuits can be used with the Babylog VN500 but the HFO performance might be diminished.

- **BlueSet heated HFV (N) (reusable)**
- **VentStar Helix heated (N) Plus (disposable)**

17.1.1 Adjusting HFOV with the Babylog VN500

Commencement of HFOV is achieved via the **Ventilation settings** dialog window, which can be opened in one of 3 ways:

1. Touching the **Ventilation settings** button (A) in the main menu bar (on the right).
2. Touching the up arrow (↑, B) button in the therapy bar.
3. Touching the displayed ventilation mode (C) in the header bar.

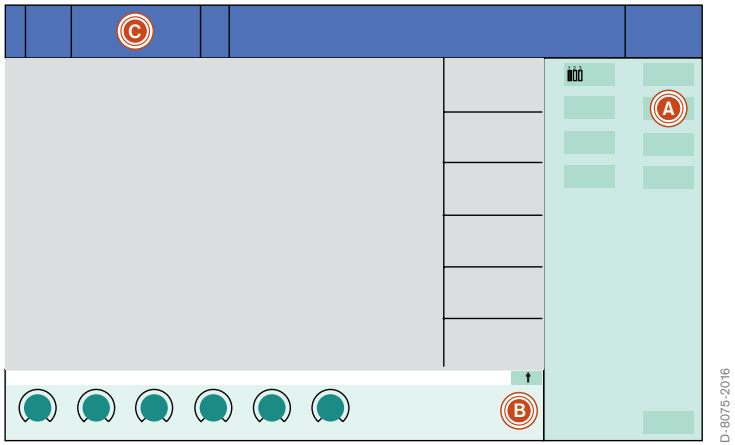

Figure 17-2: Options for opening the ventilation settings dialog window from the main screen.

By default, the **Ventilation settings** dialog window has a number of tabs (B) permanently assigned to specific ventilation modes. By default these are set at the factory to include PC-CMV, PC-AC, PC-SIMV and PC-PSV. These start up default modes can be changed to include PC-HFO as an option.

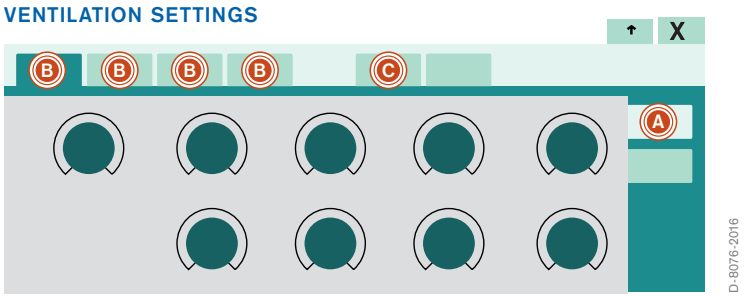

Figure 17-3: Ventilation settings dialog window.

Alternatively, the user can access PC-HFO by first selecting **Other modes** (D) tab, and then touching the button for PC-HFO from the available modes (E). This action turns the D tab to yellow. The user must confirm the change in ventilatory modality to PC-HFO with the rotary knob. Once confirmed, PC-HFO will be displayed in the (C) tab, and will be the active ventilation mode.

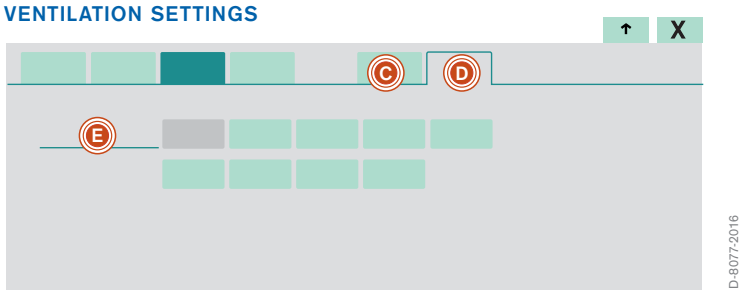

Figure 17-4: PC-HFV is activated from the Other Modes window.

Additional options for PC-HFO are accessed by pressing the tab for additional settings (G). These options include activation and setting of parameters for PC-HFO with Volume Guarantee (VG), and PC-HFO with Sigh. A sigh under high frequency oscillation is an intermediate conventional cycle.

PC-HFO-Volume Guarantee

During PC-HFO with Volume Guarantee, the Babylog VN500 automatically determines the oscillatory amplitude required to achieve the set oscillatory tidal volume **VT_{hf}**. The **$Ampl_{hf}$** therapy control is inactive when Volume Guarantee is switched on. If **VT_{hf}** can not be achieved a low tidal volume alarm is generated.

PC-HFO-Sigh

Sighs are a normal physiological protective mechanism for lung volume homeostasis. In the absence of airleak, incorporation of a sigh in HFOV may facilitate short-term re-recruitment of the lung after suction, or as an infrequent sigh to maintain lung volume and prevent development of atelectasis.

The frequency of the sigh is adjusted by altering **RRsigh**. The **Psigh** is the pressure applied during the resulting conventional pressure-controlled breath, which is maintained for a duration **(Tisigh)** set by the operator. The rise time and rise form of the sigh breath are determined by the **Slope** or **Insp Flow** according to the configuration of the ventilator interface. Sighs can also be manually triggered at any time with the **Man. Insp/hold** function: for manually triggered sighs, the duration of the sigh is determined by how long the operator continues to hold the **Man. Insp/hold** button.

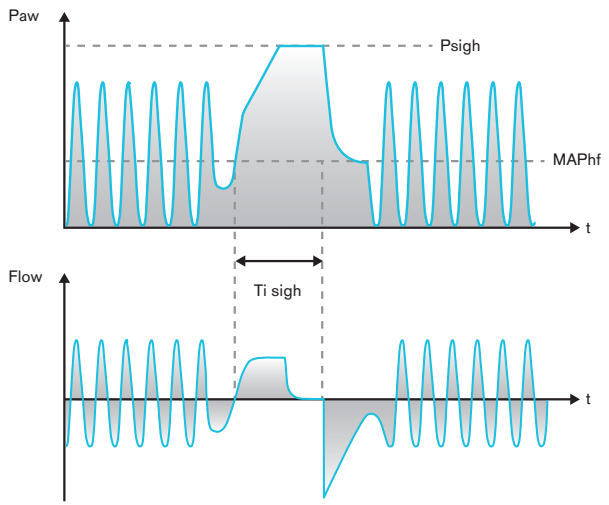

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Figure 17-5: Ventilator parameters for sigh breaths during HFO.

17.2 Clinical Case Report – Benefits of HFOV with Volume Guarantee

Mother (G_6P_0) presented with ruptured membranes 6 days prior to delivery. Labour induced due to appearance of malodourous liquor discharge suggestive of antibiotics. Maternal antenatal steroids and antibiotics administered 8.5 hours prior to delivery.

Preterm female infant born vaginally at 22 w and 5 days gestation with a birthweight of 430 g and head circumference of 19 cm. Apgar scores were 5 at 1 min, 6 at 5 minutes and 6 at 10 minutes. Electively intubated with a 2.5 mm tracheal tube and surfactant administered within first 10 minutes (200 mg/kg Curosurf™, Chiesi Farmaceutici).

Ventilation was commenced in the delivery room with peak inspiratory pressure (PIP) of 25 cmH_2O, positive end expiratory pressure (PEEP) of 6 cmH_2O and a fractional inspired oxygen (FiO_2) of 0.4. Ventilation was increased during resuscitation to 32/6 with an FiO_2 of 1.0, before infant started to improve and FiO_2 could be decreased.

The initial arterial blood gas at 30 min of life reflected the significant difficulties experienced gaining control of ventilation and gas mixing: pH 6.9, $PaCO_2$ 95 mmHg, PO_2 78 mmHg, BE -9.7 mmol/L, Lactate 8.3 mmol/L. The arterial blood gas improved over the next 75 min although a moderately severe mixed respiratory/metabolic acidosis persisted at 2 hours of age: pH 7.13, $PaCO_2$ 66.5 mmHg, PaO_2 47.6 mmHg, BE – 6.4 mmol/L with an FiO_2 of 0.9 and mean airway pressure 13 cmH_2O (oxygenation index (OI) = 24.6).

An X-ray at 2 hours of age was suggestive of early pulmonary interstitial emphysema. Volume Guarantee had been turned off, as even the minimum tidal volume of 2 mL was excessive for this 440 gm infant. At 4 hours of age the mean airway pressure was 10 cmH_2O, PIP 26 cmH_2O and PEEP 6 cmH_2O. The attending physician consulted with a colleague experienced with use of the Babylog VN500: a decision was made to commence HFOV with concomitant Volume Guarantee to minimise further lung damage to the infant from excessive ventilatory pressures.

As the treating consultant was concerned about early evolution of PIE, HFOV was commenced with a frequency of 5 Hz and an I:E ratio of 1:2 and an amplitude of 20 cmH_2O, adjusted to obtain appropriate chest vibrations. Measured tidal volume was 1.3 mL (3 mL/kg = lower end of recommended VT at 5 Hz – see section 12). HFOV was commenced with mean airway pressure of 10 cmH_2O (approximately the same as the mean airway pressure on conventional ventilation) to avoid further progression of PIE.

Due to the infant's extreme prematurity and fragile skin, transcutaneous blood gas monitoring was not used. A blood gas obtained 5 min after commencing HFOV showed pH 7.31, $PaCO_2$ 40 mmHg, PaO_2 72.7, BE – 5.6 mmol/L. FiO_2 had decreased to 0.3 with a MAP of 10 cmH_2O. (OI = 3)

In the absence of transcutaneous monitoring and to avoid excessive blood sampling, Volume Guarantee was added to HFOV. Initial VT_{hf} was set at the measured VT_{hf} of 1.3 mL with $Ampl_{hfmax}$ set at 22 cmH_2O. FiO_2 decreased to 0.21. Amplitude was weaned automatically to 15 cmH_2O. A repeat blood gas 15 min later showed these settings were maintaining stable blood gases: pH 7.3, $PaCO_2$ 41.5 mmHg, PaO_2 57, BE-5.3. A further repeated blood gas two hours later showed $PaCO_2$ was remaining stable. Satisfied that the DCO_2 target was appropriate, the intervals between blood gas sampling were extended with confidence.

A repeat chest x-ray on day 2 suggested PIE is improved. The frequency was gradually increased to 9 Hz, and further to 13 Hz by day 4. With each increase in frequency, the set VT was decreased to maintain a stable DCO_2, reaching 0.9 mL (2 mL/kg) at a frequency of 13 Hz. Low dose inhaled nitric oxide (<5 ppm) was commenced by the attending consultant on day 4 when the OI has increased again from 4.7 to 8.4, and continued for 5 days.

Despite an episode of coagulase negative septicaemia, the ventilatory course remains relatively stable over the next 10 days, with the HFOV with Volume Guarantee maintained until day 13, when the loan Babylog VN500 ventilator was returned. The infant was placed back on conventional ventilation however deteriorated clinically with increasing FiO_2. After 36 hours, HFOV was recommenced with a different oscillator without capability of tidal volume monitoring or volume targeted HFOV. With increase of FiO_2 to 1.0, and non-response to volume recruitment, inhaled nitric oxide was recommenced (10 ppm) and a modified course of dexamethasone commenced (total cumulative dose 1.2 mg/kg over 3 weeks). Response to the intensification of treatment was moderately rapid. Oscillatory amplitude, FiO_2, MAP and iNO were weaned over a 12 day period and the infant was extubated from HFOV to nasal CPAP at 5 weeks postnatal age when she was 27[4] w postmenstrual age. Nasal CPAP was ceased at 35[5] w postmenstrual age, with cessation of all oxygen support at 42 w postmenstrual age and discharge at 5 months (44 w postmenstrual age).

Of interest is Figure 17-6 which shows the changes in the infants' $PaCO_2$ over the first 3 weeks of her illness. The stability of the $PaCO_2$ during HFOV with Volume Guarantee is clearly evident. The two deviations from the status quo representing brief episodes when she was briefly returned to conventional ventilation. Increased fluctuation in her $PaCO_2$ occuring after 2 weeks corresponds with the period when she was on HFOV without volume targeting or monitoring. Rapid fluxes in arterial partial pressure of carbon dioxide may translate to unwanted rapid changes in intracerebral circulation, that can be prevented with the usage of Volume Guarantee. This graph provides a clear illustration of the benefits of volume targeting for stability of $PaCO_2$ during HFOV, which was particularly beneficial in this extremely low gestational age infant.

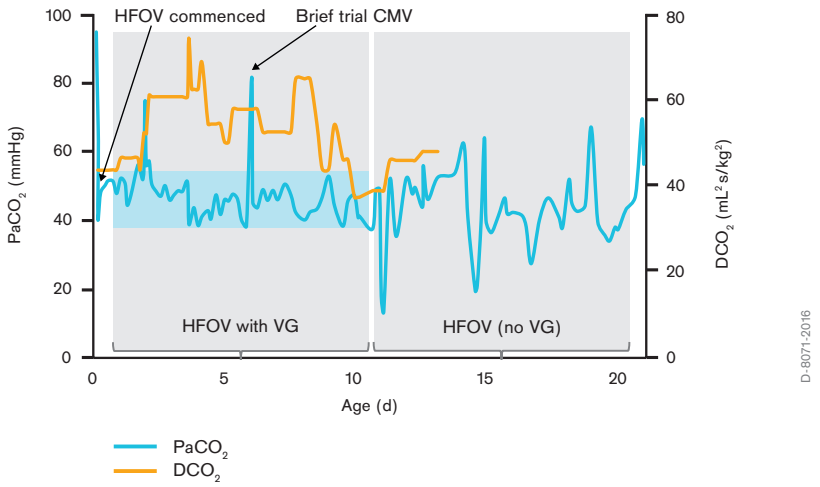

Figure 17-6: Stability of $PaCO_2$ and required DCO_2. Blue line: $PaCO_2$, orange line: DCO_2. Note increased variability (with some extreme values) after change in ventilator and discontinuation of HFOV with Volume Guarantee (VG). DCO_2 is corrected to the square of the body weight (kg^2). Average DCO_2 during the period of Volume Guarantee was 51.6 mL^2s/kg^2. No DCO_2 was recorded after VG was turned off.

The subsequent course of this extremely premature infant who received 96 % of her ventilation on HFOV is truly remarkable. Her initial cranial ultrasound scans were all normal, with only minor changes of calcifying vasculopathy within her basal ganglia at 415 w postmenstrual age. She has mild retinopathy (max Grade I, no plus) which resolved spontaneously. At 3 years of age, she had had only 8 hospital readmissions and a total of 16 days in hospital after initial hospital discharge. The majority of her readmissions were for bronchiolitis and lower respiratory tract infections and her admissions were primarily for oxygen support overnight during acute illness. Her current therapy is inhaled steroid and intermittent salbutamol. She has no respiratory symptoms between episodes. Growth centiles are weight (26th centile); height (12th centile) and head circumference 3rd centile. Her 3 year developmental assessment with the Griffiths Mental Developmental Scale – Extended Revised shows a General Quotient of 101. Her main issues were distractibility and some delay in vocalisation although she was speaking in short sentences.

17.3 Example: DCO_2 during lung volume recruitment with/without Volume Guarantee

A collapsed plasticised adult porcine lung (Nasco, Fort Atkinson, WI) was intubated (8.0 mm with a cuffed tracheal tube) and connected to the Babylog VN500 in HFO mode. Initial ventilator settings were frequency of 5 Hz, mean airway pressure (5 cmH_2O) and amplitude I:E 1:1. The lung was recruited then derecruited by stepwise increments then decrements in mean airway pressure with pressure changes made at 2 minute intervals. The recruitment was performed initially using Volume Guarantee at constant set tidal volume (20 mL) and a maximum pressure amplitude of 30 cmH_2O then repeated using constant amplitude (23 cmH_2O = starting VT_{hf} of 20 mL) without Volume Guarantee. Figure 17-7 shows the recorded tidal volumes, ventilator displayed pressure amplitude and DCO_2 recorded for each step change in mean airway pressure. Recruitment at a constant oscillatory pressure amplitude (ΔPhf) results in considerable fluctuations in tidal volume and consequently also DCO_2. Clinically, $PaCO_2$ and cerebral blood flow may also fluctuate considerably unless the clinician remains at the bedside to constantly adjust oscillatory amplitude in response to changes in lung mechanics. In contrast, when HFO is used in a Volume Guarantee mode, both tidal volume and DCO_2 remain constant, and the oscillatory amplitude is automatically adjusted according to changes in lung mechanics. In this setting, the patient will have more stable $PaCO_2$ and the clinician may focus on other issues. Setting $Ampl_{hfmax}$ appropriately is critical, however, to the safe use of Volume Guarantee. The $Ampl_{hfmax}$ effectively triggers the low tidal volume alarm, and hence the clinician should set the $Ampl_{hfmax}$ to reflect the amount of change in oscillatory amplitude they are prepared to accept automatic ventilator adjustment before notification of a change in the patient's condition. A buffer of 5 cmH_2O for $Ampl_{hfmax}$ above the average ΔPhf provides a reasonable buffer. It is similarly important that the $Ampl_{hfmax}$ is decreased as the patient's condition improves so that any deterioration in condition is picked up early.

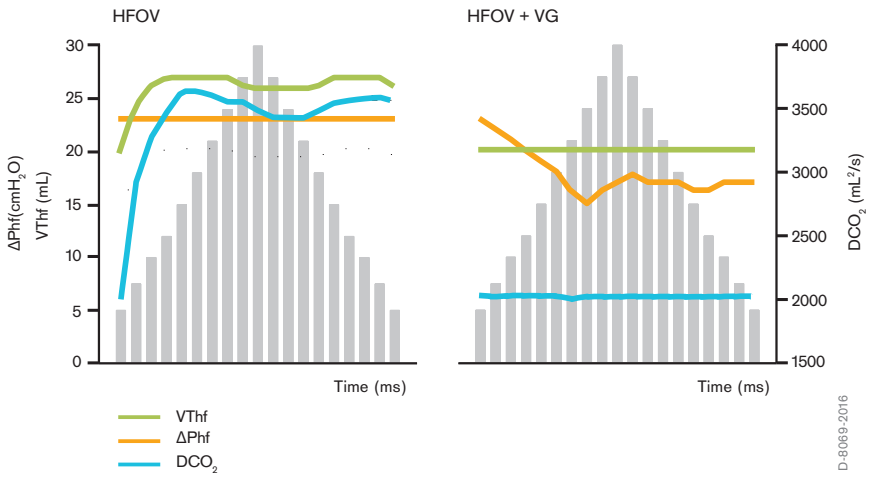

Figure 17-7: Changes in DCO_2, pressure amplitude and tidal volume during lung recruitment. Graphs show recruitment using HFOV without (left) and then with (right) Volume Guarantee. The orange line is the pressure amplitude. The green line is the tidal volume. The blue line is the DCO_2.

17.4 Abbreviations

AC	Assist control
BPD	Bronchopulmonary dysplasia
C	Compliance
CgDH	Congenital diaphragmatic hernia
C_{dyn}	Dynamic compliance
CLD	Chronic lung disease
CPAP	Continuous positive airway pressure
CV	Conventional ventilation
DCO_2	Gas transport coefficient
delta P	Peak inspiratory pressure minus PEEP
E	Elastance
ECMO	Extracorporeal membrane oxygenation
f	Frequency
f_0	Resonance frequency
f_c	Corner frequency
FiO_2	Fraction of inspiratory O_2 concentration
FRC	Functional residual capacity
HFV	High-frequency ventilation
HFJV	High-frequency jet ventilation
HFO	High-frequency oscillation
HFOV	High-frequency oscillatory ventilation
HMD	Hyaline membrane disease
Hz	Hertz: unit of frequency (cycles/second)
I	inertance
ICH	Intracranial haemorrhage

I:E	Inspiratory to expiratory ratio
IMV	Intermittent mandatory ventilation
IPPV	Intermittent positive pressure ventilation
Kg	Kilogram
MAP	Mean airway pressure
MV	Minute volume
PaO_2	Partial pressure of oxygen in arterial blood
$PaCO_2$	Partial pressure of carbon dioxide in arterial blood
PO_2	Partial pressure of oxygen
PCO_2	Partial pressure of carbon dioxide
Paw	Airway pressure
PEEP	Positive end expiratory pressure
PIE	Pulmonary interstitial emphysema
PIP	Peak inspiratory pressure
$Ampl_{hfmax}$	Maximum oscillatory amplitude
PPHN	Persistent pulmonary hypertension of the newborn
PVL	Periventricular leukomalacia
R	Resistance
RDS	Respiratory distress syndrome
RSV	Respiratory syncytical virus
SIMV	Synchronised intermittent mandatory ventilation
SIPPV	Synchronised intermittent positive pressure ventilation
SpO_2	Saturation of peripheral oxyhaemoglobin
τ	Time constant
Ti	Inspiratory time
Te	Expiratory time
TLC	Total lung capacity
TT	Tracheal tube
$\dot{V}$	Oscillatory flow
V_t	Tidal volume
VT_{hf}	Tidal volume during high frequency

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REGION MIDDLE EAST, AFRICA
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Branch Office
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Dubai, United Arab Emirates
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Fax +971 4 4294 699
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REGION ASIA / PACIFIC
Draeger Medical
South East Asia Pte Ltd.
25 International Business Park
#04-27/29 German Centre
Singapore 609916, Singapore
Tel +65 6572 4388
Fax +65 6572 4399
asia.pacific@draeger.com

REGION CENTRAL AND SOUTH AMERICA
Dräger Panama Comercial S. de R.L.
Complejo Business Park,
V tower, 10th floor
Panama City
Tel +507 377 9100
Fax +507 377 9130
contactcsa@draeger.com

CANADA
Draeger Medical Canada Inc.
2425 Skymark Avenue, Unit 1
Mississauga, Ontario, L4W 4Y6
Tel +1 905 212 6600
Toll-free +1 866 343 2273
Fax +1 905 212 6601
Canada.support@draeger.com

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