

ARTICLE

High-frequency oscillatory ventilation — a clinical approach



Pediatric Critical Care Medicine, Duke University Children's Hospital, Durham, North Carolina, USA

Donna S Hamel, RRT, RCP, FAARC

Ira M Cheifetz, MD, FCCM, FAARC

Since its inception over a decade ago, HFOV has become an increasingly utilised and effective strategy for the treatment of acute lung injury and acute respiratory distress syndrome. During HFOV, the lungs are recruited and stabilised to avoid the cyclic stretch and shear exerted on the alveoli which occur during conventional ventilation by repeated alveolar collapse and re-expansion. Patients with deteriorating gas exchange despite increasing ventilatory settings can be successfully managed with HFOV as it provides significant lung protection. However, as with any mode of ventilation, management strategies must be designed to minimise (or eliminate) ventilator-induced lung injury based on a patient's pathophysiology.

Mechanical ventilatory strategies have evolved dramatically over the past decade. The deleterious effects of mechanical ventilation have been widely

studied and are universally recognised.¹⁻⁷ When high peak airway pressures, elevated mean airway pressures, excessive FiO_2 , and/or large tidal volumes

are necessary to maintain adequate gas exchange, patients are at risk of developing ventilator-associated lung injury.^{8,9} High-frequency ventilation was first introduced in the late 1970s as an alternative method of mechanical ventilation designed specifically to reduce the complications associated with conventional mechanical ventilation.

High-frequency ventilation is defined as a delivered tidal volume that is less than anatomical dead space and delivered at a high frequency rate (> 120 breaths per minute for adults, > 150 breaths per minute for infants and children). This relationship between dead space and ventilation was discussed as early as 1915 when Henderson and colleagues theorised that gas exchange sufficient to support life could be achieved even at tidal volumes considerably less than dead space.¹⁰⁻¹² However, it was not until the 1970s that interest in a clinical application of high-frequency ventilation emerged. Studies during the 1970s clearly demonstrated in animal models of acute lung injury that adequate alveolar ventilation could be achieved with tidal breaths smaller than anatomical dead space and accelerated breathing frequencies.^{12,13} When ventilating with these extremely small tidal volumes, peak airway pressures are dramatically reduced leading to the belief that high-frequency ventilatory approaches minimise the adverse effects of volutrauma, barotrauma, and stretch injury associated with conventional ventilation.¹⁴⁻¹⁷

The two most common forms of high-frequency ventilation are high-frequency jet ventilation (HFJV) and high-frequency oscillatory ventilation (HFOV). HFJV is most commonly performed via the Life Pulse ventilator (Bunnell Inc., Salt Lake City, Utah, USA), which delivers pulses of gas at a high velocity through an orifice at a frequency of 240 - 660 breaths per minute. The small high-velocity breaths and fast rates coupled with passive exhalation provide an effective means for carbon dioxide elimination at reduced peak inspiratory pressures. Positive end-expiratory pressure and 'sigh' breaths are provided with a conventional ventilator used in tandem with the jet ventilator. Mean airway pressure during jet ventilation is achieved indirectly by the manipulation of other ventilatory parameters. While the Life Pulse high-frequency jet ventilator is an effective means for ventilating infants and small children, it is not FDA approved to support larger paediatric and adult patients.

HFOV effectively provides support to infants, children and adults with acute lung injury. HFOV allows the clinician to directly set and manipulate the mean airway pressure (PAW). During HFOV, the PAW is set to achieve an optimal lung volume. High-frequency oscillation allows the clinician to open the lung and keep it open, thus improving outcomes by decreasing the shear forces associated with the repetitive opening of collapsed alveoli.¹⁸ Tidal volumes (i.e. oscillations)

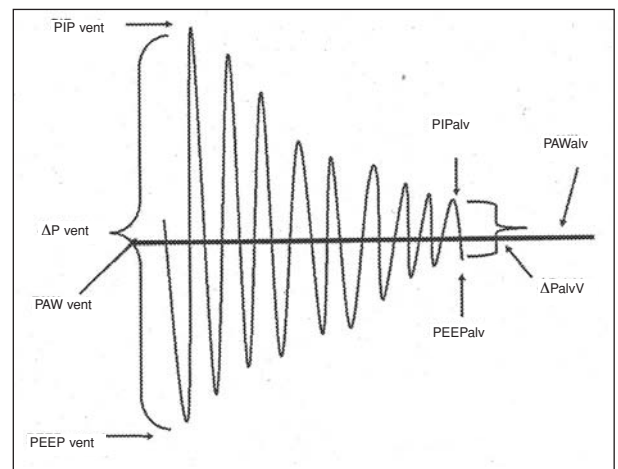


Fig. 1. Pressure attenuation during HFOV. The pressure generated by the high-frequency oscillator attenuates as gas moves along the oscillator circuit, endotracheal tube, and conducting airways.

are then superimposed on the PAW allowing for the utilisation of higher mean airway pressures at lower peak airway pressures. A key concept of high-frequency ventilation (both oscillation and jet) is that the swing from maximal to minimal airway pressure is attenuated as gas flow progresses from the ventilator to the alveoli (Fig. 1). This may also be described as an attenuation of the peak-to-trough swing across the mean airway pressure. HFOV is an attractive alternative to conventional mechanical ventilation for the respiratory management of a wide range of critically ill patients with acute lung injury.

Theory of gas exchange during HFOV

While the gas exchange mechanisms during conventional mechanical ventilation are convection ventilation or 'bulk flow', gas exchange during HFOV is enhanced by other mechanisms. Even with the small tidal volumes of HFOV, direct alveolar ventilation may occur to short path length units that branch from the primary airways. However, this only accounts for a small component of the gas exchange that occurs during HFOV.

Molecular diffusion is speculated to be a major contributor to gas exchange during oscillatory ventilation. Molecular diffusion describes gas exchange across the alveolar-capillary membrane and contributes to the transport of both oxygen and carbon dioxide in the gas phase near the membrane. In 1984, Slutsky and colleagues¹¹ theorised that the gas exchange mechanism during HFOV was caused by the coupled effects of convection and molecular diffusion. It is speculated that this is due to an increase in turbulence of the molecules during high-frequency oscillation.¹⁹ In that same year, Chang and colleagues²⁰ determined that a convective mechanism may predominate with the increased tidal volume at lower ventilatory rates, while a diffusive mechanism may

predominate with the decreased tidal volume at higher frequencies.

Taylor dispersion is also proposed as a significant contributor to gas exchange. Taylor dispersion occurs when a high velocity of gas travels down the centre of a tube, leaving the molecules on the periphery unmoved. When the high-velocity flow stops, gas molecules then diffuse evenly along the tube (Fig. 2).²¹⁻²³ A variation of this theory describes an asymmetrical velocity profile. During inspiration, the high-frequency pulse creates a 'bullet'-shaped profile with the central molecules moving further down the airway than those molecules found on the periphery of the airway (i.e. 'two steps forward' approach) (Fig. 3).^{22,23}

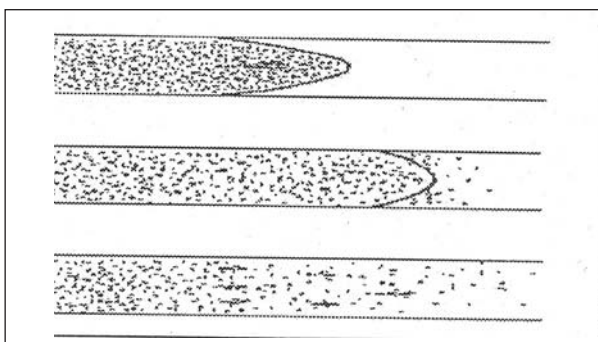


Fig. 2. Taylor dispersion occurs when a high velocity of gas travels down the centre of a tube, leaving the molecules on the periphery unmoved. When the high-velocity flow stops, gas molecules then diffuse evenly along the tube.

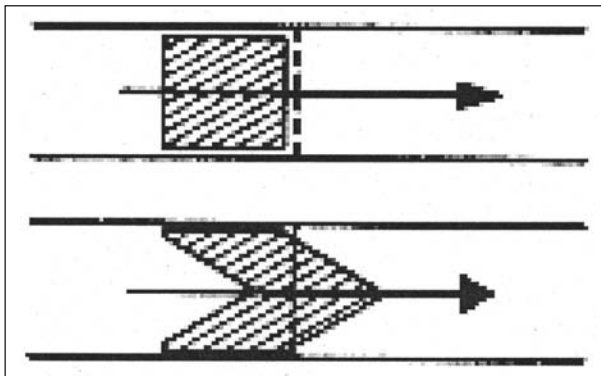


Fig. 3. Depiction of an asymmetrical velocity profile where, during inspiration, the high-frequency pulse creates a 'bullet'-shaped profile with the central molecules moving further down the airway than those molecules found on the periphery of the airway pattern.

Still another theory was proposed by Lehr *et al.*, who attributed effective gas exchange during HFOV to the Pendeluft effect.²⁴ At high frequencies, gas distribution becomes strongly influenced by time-constant inequalities. Gas from fast units (i.e. short time constants) will empty into the slow units (i.e. long time constants) (Fig. 4).

It is likely that a combination of these mechanisms (rather than a single mechanism) is responsible for the effectiveness of gas exchange during HFOV.²⁰ It is possible that all of these proposed mechanisms coupled

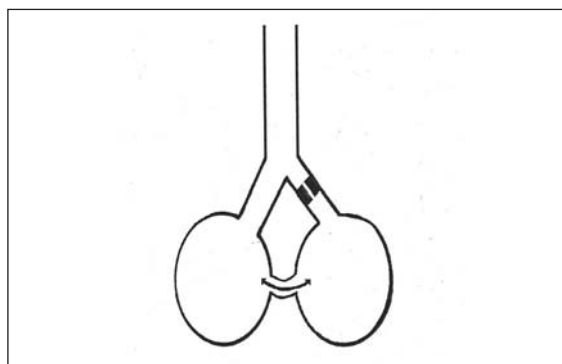


Fig. 4. The Pendeluft effect suggests that at high frequencies, gas distribution becomes strongly influenced by time constant inequalities. Gas from fast units (i.e. short time constants) will empty into the slow units (i.e. long time constants).

with cardiogenic mixing, in which the heartbeat adds to the gas mixing, contribute to the effective gas exchange abilities of HFOV.²³

HFOV specifications

Currently, the most commonly used devices to perform HFOV are the SensorMedics 3100A and 3100B ventilators (Viasys Healthcare, Yorba Linda, California, USA). These ventilators are electronically controlled piston-diaphragm high-frequency ventilators. The 3100A is designed to ventilate all patients regardless of weight; however, carbon dioxide elimination may be ineffective for some 'larger' patients. The 3100B oscillator is FDA approved only for patients weighing more than 35 kilograms.

The 3100A utilises bias flow rates of 0 to 40 l/min and is capable of delivering mean airway pressures between 3 and 45 cm H₂O. The 3100B has an increased bias flow ability (0 - 60 l/min) and can deliver higher mean airway pressures (3 - 55 cm H₂O). Inspiratory times range between 33% and 50% for the 3100A and between 30% and 50% for the 3100B. Both oscillators utilise similar frequency (3 - 15 hertz) and amplitude (8 - 90 cm H₂O) ranges; however, the lower bias flow ranges of the 3100A often make it difficult to achieve the higher mean airway pressures and larger amplitude requirements for 'larger' patients.

Physiology of gas exchange

During HFOV, oxygenation and ventilation are decoupled.²⁵ Oxygenation is primarily a function of FiO₂ and PAW. Mean airway pressure is used to inflate the lung and optimise the alveolar surface area for gas exchange (i.e. PAW equals lung volume).²³ PAW during HFOV is created by a continuous bias flow of gas past a resistance (inflation) of a balloon on the mean airway pressure valve. Therefore, the PAW is changed by adjusting the bias flow or the inflation of the balloon control valve (PAW adjust knob). Simply stated, PAW during HFOV is a clinician set value, not a byproduct of other variables. In fact, the PAW of the oscillator

without the piston moving is a continuous positive airway pressure (CPAP) system.

As with conventional ventilation, carbon dioxide elimination during HFOV is achieved by adjusting the minute ventilation. However, during conventional ventilation minute ventilation is defined as tidal volume times frequency ($V_t \times f$), whereas during HFOV, minute ventilation is equal to $V_t^{1.5-2.5} \times f$.^{26,27} Therefore, changes in tidal volume delivery have the most significant effect on carbon dioxide elimination.

Tidal volume delivery during HFOV is defined as the gas displaced by the movement of the oscillatory piston. The amount of piston movement is a function of delta P (i.e. amplitude), frequency, and per cent inspiratory time (% Ti).²⁵ The primary control of carbon dioxide elimination is the delta P.²⁸ Delta P displayed on the front panel is produced by adjustment of the power setting. The delta P produces a stroke volume (also referred to as amplitude). The amplitude itself is created by the distance that the piston moves resulting in volume displacement and a visible patient 'chest wiggle' (i.e. oscillation).

The secondary control of carbon dioxide elimination is the frequency setting. The power controls the force with which the piston moves, and the frequency controls the time allowed (distance) for the piston to move. Therefore, the lower the frequency the greater the volume displaced; and the higher the frequency, the smaller the volume displaced (Fig. 5). The % Ti also controls the time for movement of the piston and can therefore assist in carbon dioxide elimination as well. Increasing the % Ti is generally a technique used for ventilating larger patients.

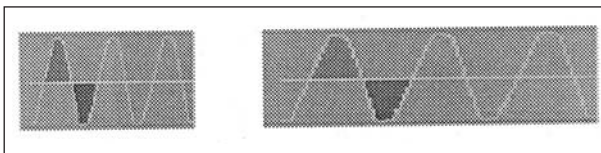


Fig. 5. Frequency and tidal volume during HFOV. The power controls the force with which the piston moves, and the frequency controls the time allowed (distance) for the piston to move. Therefore, the lower the frequency the greater the volume displaced; and the higher the frequency, the smaller the volume displaced.

Clinical indications

Patients with diffuse alveolar diseases, such as acute respiratory distress syndrome (ARDS), acute lung injury (ALI), bronchiolitis and air leak syndrome, may benefit from the use of HFOV. Most patients who require high ventilatory settings during conventional ventilation could potentially benefit from HFOV. Consider HFOV for patients with oxygen requirements greater than 0.60, peak inspiratory pressures greater than 32 cm H₂O, and mean airway pressures in excess of 15 cm H₂O. Patients without cyanotic congenital cardiac

lesions who have an oxygen index of greater than 13 on two consecutive arterial blood gases within a 6-hour period should also be considered candidates for HFOV.

Careful consideration should be employed when intracranial hypertension is present. The potential benefit of improved gas exchange at lower airway distending pressures should be carefully weighed against the risk of further increasing intracranial pressures.

Initiation of HFOV

When preparing patients for conversion to HFOV always consider the underlying pathology and thoroughly review the chest radiographs and arterial blood gases. It is also important to know the most recent mean airway pressure obtained during conventional ventilation. If the patient's pH is less than 7.25, consider buffering with sodium bicarbonate (NaHCO₃) before initiating HFOV. It should be noted that the use of sodium bicarbonate to buffer acidosis in this situation remains controversial. Growing evidence in the literature discourages this practice.²⁹

Most patients should have a functional arterial line. Pulse oximetry is absolutely essential. Transcutaneous oxygen and carbon dioxide monitoring is extremely useful. As patient size increases, the reliability of transcutaneous oxygen monitoring decreases. However, with newer technology available transcutaneous carbon dioxide monitoring is a very reliable trend monitor in most patients regardless of size. A central venous line may be helpful. A pulmonary artery catheter is not necessary and, in fact, is rarely utilised for this population of patients.

Sedation is required for most infants, and some may require paralysis. Essentially all paediatric and adult patients require sedation, and most will require paralysis at least initially. However, once the patient has entered the weaning phase, a trial without neuromuscular blockade should be done.

The patient should be suctioned before initiation of HFOV to assure the removal of excess secretions. Since de-recruitment may occur with suctioning, suctioning should be based on the patient's overall clinical status. Closed suction catheter systems can be used; however, it is essential to completely remove the suction catheter tip from the endotracheal tube (ETT) at the completion of suctioning. When catheters remain in the ETT, the delivered amplitude will be attenuated and a decrease in the 'chest wiggle factor' will be seen. Additionally, if a disconnect between the suction adaptor and the ETT occurs, there may be sufficient pressure to prevent the low pressure alarm from sounding. Oximetry and transcutaneous monitoring have the added benefit of notifying the clinician of adverse patient effects secondary to circuit disconnects.

Before transition from conventional to high-frequency ventilation, the clinician should ensure that the patient has adequate intravascular volume and cardiac output. Intravascular volume loading may be required on initiation of HFOV secondary to the associated increase in intrathoracic pressure.³⁰⁻³³ When available, the central venous pressure (CVP) should be monitored to assist in intravascular fluid management. Patients often require a low-dose inotrope infusion to augment cardiac output during the transition to HFOV.

On initiating HFOV, the FiO_2 should be set at 1.0. The bias flow should be set at 18 l/min or more for neonatal and paediatric patients. A 30 - 40 l/min bias flow is often required for larger paediatric and adult patients. An adequate bias flow is necessary to assure replenishment of the oxygen supply to the endotracheal tube and for optimal carbon dioxide removal from the circuit. If the bias flow is inadequate, circuit dead space increases and carbon dioxide removal can be impaired. The bias flow should be increased in increments of 5 l/min when carbon elimination is inadequate despite appropriate amplitude and frequency adjustments.

The mean airway pressure on the oscillator should be set at 4 - 8 cm H_2O above the level generated on the conventional mechanical ventilator for patients with diffuse alveolar disease.³⁴⁻³⁷ This increase is required secondary to the pressure attenuation which can occur along the oscillator circuit, endotracheal tube and airways. Additionally, the increased mean airway pressure is intended to augment lung recruitment in patients with acute alveolar injury (i.e. acute lung injury or acute respiratory distress syndrome). The frequency should be set according to the patient's weight and age (Table I). The % Ti should be set initially at 33% on the 3100A and 30% on the 3100B. The power setting control should be set at 6 and then adjusted to meet the desired amplitude. The power setting needed to provide an adequate amplitude (and chest oscillation) is dependent on the patient's size, weight and pulmonary compliance.

When titrating the power setting to achieve the optimal amplitude, the clinician should observe the patient for adequate 'chest wiggle' and therefore adequate chest oscillation. The amplitude is considered appropriate

Table I. Suggested high-frequency oscillatory frequency settings based on patient weight	
Weight (kg)	Suggested frequency (hertz)
1.5 - 2.0	12
2.0 - 5.0	10
5.0 - 12.0	9
12.0 - 20.0	8
21.0 - 30.0	7
> 30.0	6

when the patient has a visible oscillation from the chest to the upper thighs. Transcutaneous carbon dioxide monitoring is also useful for setting the amplitude. In larger patients, the transcutaneous values may not be identical to the arterial blood gas values; however, transcutaneous monitoring can be used successfully for the trending of gas exchange in most patients.

A decrease in chest oscillation is a clinical sign that pulmonary compliance has decreased. If a decrease in chest oscillation is noted, assess the airway to determine if there is an obstruction, then consider endotracheal tube suctioning. A unilateral reduction in chest oscillation indicates that the endotracheal tube may be in the right mainstem bronchus or a pneumothorax may be present. Check the endotracheal tube position and obtain a chest radiograph. Always reassess the chest oscillation following any change in patient position.

Patients with air leak syndrome require a low lung volume strategy even with HFOV. Therefore, a relatively lower mean airway pressure should be used. The PAW setting in unilateral air leak syndrome is dependent on the inflation of the unaffected lung. The clinician should accept less than optimal arterial blood gas values until the air leak resolves. Accept oxygen saturations of 85 - 90% with incremental increases in the FiO_2 as needed. Atelectasis is a possibility when ventilating with a low lung volume strategy. Hypercapnia with a pH of 7.25 or greater should be acceptable.^{38,39} When adequate oxygenation and ventilation are achieved, decrease the mean airway pressure and amplitude. A higher FiO_2 must often be accepted with air leak syndrome to provide for the lowest airway pressures and thus provide optimal lung protection. Once the chest tube air leak has resolved for least 24 hours, gently recruit the collapsed lung and begin weaning.

HFOV management strategies

Inadequate oxygenation requires adjustment of the mean airway pressure. PAW should be adjusted until optimal lung volume is achieved. Adjustments in PAW should generally be performed in increments of 1 - 2 cm H_2O for infants and children and 2 - 3 cm H_2O for adult patients. Lung volume is considered optimal when lung expansion is at the 9th thoracic vertebra (T9) on a chest radiograph. It is at this level that there should be a resultant increase in oxygen saturation which will allow for the reduction of FiO_2 . To optimise lung recruitment, consider a sustained inflation (volume recruitment) manoeuvre. Sustained inflation manoeuvres allow for a more rapid increase in lung volume compared with a gradual increase in the mean airway pressure.⁴⁰⁻⁴² Sustained inflation manoeuvres may be performed while on the HFOV by increasing the PAW by 5 - 8 cm H_2O for 30 - 40 seconds while the piston is stopped. At completion of a volume

recruitment manoeuvre, the mean airway pressure should be returned to the previous setting.

When performing a sustained inflation manoeuvre, risks do exist, such as haemodynamic instability and pneumothorax. Always monitor the patient's haemodynamic status when manipulating the mean airway pressure as perfusion must be matched to ventilation for adequate oxygenation to be achieved. It is also important to note that pulmonary vascular resistance is increased with either atelectasis or pulmonary overdistension.^{43,44} Therefore, the clinician should utilise chest radiographs and pulse oximetry to optimise lung recruitment while guarding against overexpansion. If the chest radiograph demonstrates optimal expansion, the FiO_2 has been maximised and oxygenation remains poor, increasing the % Ti to 50% will raise the distal PAW closer to the proximal values. Thus, increasing the % Ti will increase the effective PAW. It is important to note that increasing the % Ti will also increase the delivered tidal volume.

Managing carbon dioxide elimination is primarily performed by manipulating the power setting control. To reduce the PaCO_2 , increase the power setting control (i.e. amplitude) in 3 - 5 cm H_2O increments. Additionally, if the amplitude has been increased by 10 - 20 cm H_2O and there is a clinically inadequate decrease in the PaCO_2 , decrease the set frequency. The frequency should be manipulated in increments of 0.5 - 1 Hz. If the initial frequency is too high, unacceptable PaCO_2 levels may result. It is important to note that PaCO_2 may initially climb in large patients before it stabilises and then decreases. Therefore, allow a 5 - 10-minute stabilisation period after each parameter change. Permissive hypercapnia should be acceptable for most patients.⁴⁵

A decrease in chest oscillation ('chest wiggle') is a clinical sign that pulmonary compliance has decreased. The assessment of a change in chest oscillation is discussed in more detail under 'Initiation of HFOV'.

In larger patients with an unacceptable PaCO_2 , the % Ti provides an additional means for improving carbon dioxide elimination. While it is recommended that the % Ti be set at 30% when utilising the 3100B and 33% when utilising the 3100A, if the amplitude has been maximised and the frequency has been minimised, increase the inspiratory time towards 50%. Increasing the % Ti will increase the delivered tidal volume and, therefore, should improve ventilation. Additionally, for patients with cuffed endotracheal tubes, minimally deflating the cuff may improve ventilation by allowing for passive exhalation around the endotracheal tube throughout the entire breath cycle (Fig. 6).

Patient assessment

Obtain an initial chest radiograph approximately 1 hour after the initiation of HFOV. Then obtain a chest radiograph every 12 hours for the first 24 hours of

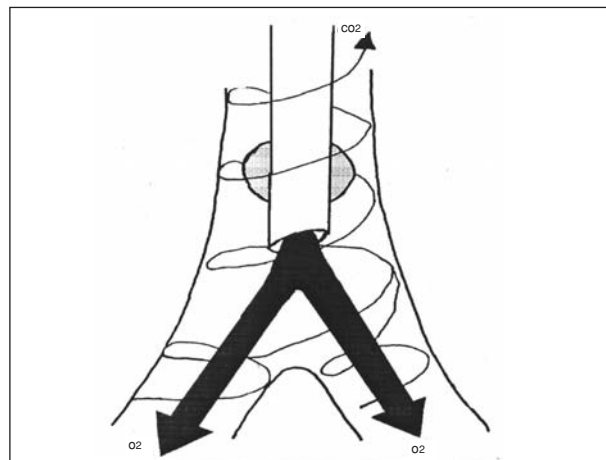


Fig. 6. Endotracheal tube air leak. During HFOV, passive exhalation of gas around the endotracheal tube throughout the entire ventilatory cycle occurs when the endotracheal tube cuff is deflated. Care must be taken when deflating the cuff to be sure that the oscillator can still maintain the set mean airway pressure. To achieve this balance, the cuff is often only minimally deflated.

HFOV. After the initial 24 hours, chest radiographs can generally be obtained once daily. While obtaining the chest radiograph, it is not necessary to stop the piston or reposition the head. Do not remove the patient from the oscillator and manually ventilate as this will not provide the information necessary to manage the oscillator as lung expansion will have changed.

Assessment of breath sounds during HFOV is difficult and identifying cardiac sounds is nearly impossible. To assess breath sounds it is not necessary to stop the piston. Listen for the intensity and quality of sounds throughout the chest. Breath sounds should be symmetrical. Always take any changes in breath sounds seriously. When a change is noted, stop the piston for further evaluation. When the piston is stopped the patient is on CPAP. Obtain a chest radiograph if there is any concern. When assessing cardiac sounds the piston must be stopped. Listen quickly to the heart sounds and restart the piston.

Weaning and conversion to conventional mechanical ventilation

The initial approach to weaning should be a reduction in the most toxic ventilatory parameter(s). Patients with diffuse alveolar disease should begin with a reduction in the FiO_2 . Once FiO_2 has been reduced to less than 0.60, begin weaning the mean airway pressure. The PAW should be decreased in increments of 1 - 2 cm H_2O for oxygen saturations greater than approximately 88% while maintaining adequate lung volume. De-recruitment occurs much more slowly than recruitment.¹⁷ In the event that lung volume is lost during the process of weaning, adequate lung volume can be quickly achieved with a sustained inflation manoeuvre followed by an incremental increase in the PAW.

The frequency should be increased in increments of 0.5 - 1 Hz until it is returned to the appropriate rate based on the patient's age and weight. Once the appropriate frequency is achieved, begin weaning the amplitude. The amplitude should be decreased in increments of 3 - 5 cm H₂O using the transcutaneous monitor as a guide. The % Ti should be returned to 30% for 3100B patients and 33% for patients ventilating with the 3100A before conversion to conventional ventilation.

Once the lung process has stabilised, the oscillatory support has been minimised and the arterial blood gases have improved, consider transition to conventional mechanical ventilation. While every patient is different, consider changing when the FiO₂ is less than 0.40, the PAW is 14 - 20 cm H₂O, and the amplitude is less than 30 cm H₂O. If the endotracheal tube cuff was deflated during HFOV, consider re-inflating it. Most patients make the transition to a pressure-limited mode (i.e. decelerating inspiratory flow) of ventilation with a peak inspiratory pressure less than 30 cm H₂O. The targeted tidal volume should be 6 ml/kg.^{2,46} The suggested FiO₂ is less than or equal to 0.50 with a PEEP of approximately 10 cm H₂O. The respiratory rate should be at the appropriate physiological rate for the patient's age.

- Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-lung strategy on mortality in acute respiratory distress syndrome. *N Engl J Med* 1998; **338**: 347-354.
- Brochard L, Roudot-Thoraval F, Roupie E, et al. Tidal volume reduction for prevention of ventilator induced lung injury in acute respiratory distress syndrome. The multicenter trial on Tidal Volume Reduction in ARDS. *Am J Respir Crit Care Med* 1998; **158**: 1831-1838.
- Kolobow T, Moretti MP, Fumagalli R, et al. Severe impairment in lung function induced by high peak airway pressure during mechanical ventilation. *Am Rev Respir Dis* 1987; **135**: 312-315.
- Papadakos PJ, Apostolakis MJ. High-inflation pressure and positive end expiratory pressure. Injurious to the lung? Yes. *Crit Care Clin* 1996; **12**: 627-634.
- Marshall RP. Current strategies for mechanical ventilation in acute lung injury. *Hosp Med* 2000; **61**: 678-679.
- Tsuno K, Prato P, Kolobow T. Acute lung injury from mechanical ventilation at moderately high airway pressures. *J Appl Physiol* 1990; **69**: 956-961.
- Thompson WK, Marchak BE, Froese AB, Bryan AC. High-frequency oscillation compared with standard ventilation in pulmonary injury model. *J Appl Physiol* 1982; **52**: 543-548.
- Marini JJ. Microvasculature in ventilator-induced lung injury: target or cause? *Minerva Anesthesiol* 2004; **70**: 167-173.
- Simonson DA, Adams AB, Wright LA, Dries DJ, Hotchkiss JR, Marini JJ. Effects of ventilatory pattern on experimental lung injury caused by high airway pressure. *Crit Care Med* 2004; **32**: 781-786.
- Gerstmann D. Major benefit of small tidal volumes during high-frequency ventilation. *Crit Care* 2003; **31**: 328-329.
- Slutsky AS, Drazen JM. Ventilation with small tidal volumes. *N Engl J Med* 2002; **347**: 630-631.
- Wetzel RC, Gioia FR. High frequency ventilation. *Pediatr Clin North Am* 1987; **34**: 15-38.
- Martinon-Torres F, Rodriguez-Nunez A, Matinon-Sanchez JM. Advances in mechanical ventilation. *N Engl J Med* 2001; **345**: 1133-1134.
- Von der Hardt K, Kandler MA, Fink L, et al. High frequency oscillatory ventilation suppresses inflammatory response in lung tissue and microdissected alveolar macrophages in surfactant depleted piglets. *Pediatr Res* 2004; **55**: 339-346.
- Imai Y, Slutsky AS. Comparison of lung protection strategies using conventional and high-frequency oscillatory ventilation. *J Appl Physiol* 2001; **91**: 1836-1844.
- Gerstmann DR, Wood K, Miller A, et al. The Provo multicenter early high-frequency oscillatory ventilation trial: improved pulmonary and clinical outcome in respiratory distress syndrome. *Pediatrics* 1996; **98**: 1044-1057.
- Arnold JH, Hanson JH, Toro-Figuero LO, Gutierrez J, Berens RJ, Anglin DL. Prospective, randomized comparison of high-frequency oscillatory ventilation and conventional mechanical ventilation in pediatric respiratory failure. *Crit Care* 1994; **22**: 1530-1539.
- Rimensberger PC, Pristine G, Mullen BM, Cox PN, Slutsky AS. Lung recruitment during small tidal volume ventilation allows minimal positive end-expiratory pressure without augmenting lung injury. *Crit Care Med* 1999; **27**: 1940-1945.
- Abbasi S, Bhutani VK, Spitzer AR, Fox WW. Pulmonary mechanics in preterm neonates with respiratory failure treated with high-frequency oscillatory ventilation compared with conventional mechanical ventilation. *Pediatrics* 1991; **87**: 487-493.
- Chang H. Mechanisms of gas transport during ventilation by high frequency oscillation. *J Appl Physiol* 1984; **56**: 553-563.
- Fredberg JJ. Augmented diffusion in the airways can support pulmonary gas exchange. *J Appl Physiol* 1980; **49**: 232-238.
- Haselton FR, Scherer PW. Bronchial bifurcations and respiratory mass transport. *Science* 1988; **208**: 69-71.
- Bouchet JC, Godard J, Claris O. High-frequency oscillatory ventilation. *Anesthesiology* 2004; **100**: 1007-1012.
- Lehr JL, Butler JP, Westerman PA, Zatz SL, Drazen JM. Photographic measurement of pleural surface motion during lung oscillation. *J Appl Physiol* 1985; **59**: 623-633.
- Schindler M, Seear M. The effects of lung mechanics on gas transport during high frequency oscillation. *Pediatr Pulmonol* 1991; **11**: 335-339.
- Scalfaro P, Pillow JJ, Sly PD, Cotting J. Reliable tidal volume estimates at the airway opening with an infant monitor during high frequency oscillatory ventilation. *Crit Care Med* 2001; **29**: 1925-1930.
- Jaeger MJ, Kurzweg UH, Banner MJ. Transport of gases in high frequency ventilation. *Crit Care Med* 1984; **12**: 708-710.
- Slutsky AS, Kamm RD, Rossing TH, et al. Effects of frequency, tidal volume and lung volume on CO₂ elimination in dogs by high frequency (2-30Hz), low tidal volume ventilation. *J Clin Invest* 1981; **68**: 1475-1484.
- Laffey JG, Engelberts D, Kavanagh BP. Buffering hypercapnic acidosis worsens acute lung injury. *Am J Respir Crit Care Med* 2000; **161**: 141-146.
- Traverse JH, Korvenranta H, Adams EM, Goldthwait DA, Carlo WA. Impairment of hemodynamics with increasing mean airway pressure during high frequency oscillatory and jet ventilation. *Pediatr Res* 1988; **23**: 628-631.
- Traverse JH, Korvenranta H, Adams EM, Goldthwait DA, Carlo WA. Cardiovascular effects of high frequency oscillatory and jet ventilation in normal and septic piglets. *Biol Neonate* 1989; **96**: 1400-1404.
- Osioviich HG, Suguihara C, Goldberg RN, Hehre D, Martinez O, Bancalari E. Hemodynamic effects of conventional and high frequency oscillatory ventilation in normal and septic piglets. *Biol Neonate* 1991; **59**: 244-252.
- Kinsella JP, Gerstmann DR, Clark RH, et al. High frequency oscillatory ventilation versus intermittent mandatory ventilation: Early hemodynamic effects in the premature baboon with hyaline membrane disease. *Pediatr Res* 1991; **29**: 160-166.
- Arnold JH. High-frequency ventilation in the pediatric intensive care unit. *Pediatr Crit Care Med* 2000; **1**: 93-99.
- Goddon S, Fujino Y, Hromi JM, Kacmarek RM. Optimal mean airway pressure during high-frequency oscillation: predicted by the pressure-volume curve. *Anesthesiology* 2001; **94**: 862-869.
- Van Genderingen HR, van Vught AJ, Duval EL, Markhorst DG, Jansen JR. Attenuation of pressure swings along the endotracheal tube is indicative of optimal distending pressure during high-frequency oscillatory ventilation in a model of acute lung injury. *Pediatr Pulmonol* 2002; **33**: 429-436.
- Arnold JH. High-frequency ventilation in the pediatric intensive care unit. *Pediatr Crit Care Med* 2000; **1**: 93-99.
- Clark RH, Slutsky AS, Gerstmann DR. Lung protective strategies of ventilation in the neonate: What are they? *Pediatrics* 2000; **1**: 112-114.
- Slutsky A. Mechanical Ventilation: American College of Chest Physician's Consensus Conference. *Chest* 1993; **104**: 1833-1859.
- Bond DM, Froese AB. Volume recruitment maneuvers are less deleterious than persistent low lung volumes in the atelectasis-prone rabbit lung during high-frequency oscillation. *Crit Care Med* 1993; **21**: 402-412.
- Byford LJ, Finkler JH, Froese AB. Lung volume recruitment during high frequency oscillation in atelectasis prone rabbits. *J Appl Physiol* 1988; **64**: 1607-1614.
- Ferguson ND, Chiche JD, Kacmarek RM, et al. Combining high-frequency oscillatory ventilation and recruitment maneuvers in adults with early acute respiratory distress syndrome: The Treatment with Oscillation and an Open Lung Strategy (TOOLS) Trial pilot study. *Crit Care Med* 2005; **33**: 479-486.
- Cheifetz IM, Meliones JN. Hemodynamic effects of high-frequency oscillatory ventilation: a little volume goes a long way. *Crit Care Med* 2000; **28**: 282-284.
- Zellers TM, Luckett PM. Cardiopulmonary interactions. In: Levin DL, ed. *Pediatric Intensive Care*. Vol. 1. 2nd ed. New York: Churchill Livingstone, Quality Medical Publishing, 1997: 1813.
- Hickling KG. Low volume ventilation with permissive hypercapnia in the adult respiratory distress syndrome. *Clin Intensive Care* 1992; **3**: 67-78.
- The Acute Respiratory Distress Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; **342**: 1301-1308.