High-frequency oscillatory ventilation: Mechanisms of gas exchange and lung mechanics

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Objective: **Overview of the mechanisms governing gas transport, mechanical factors influencing the transmission of pressure and flow to the lung, and the measurement of lung mechanics during high-frequency oscillatory ventilation (HFOV) in acute respiratory distress syndrome.**

Data Sources and Study Selection: **Studies indexed in PubMed illustrating key concepts relevant to the manuscript objectives. Pressure transmission during HFOV in the adult lung was simulated using a published theoretical model.**

Data Synthesis: **Gas transport during HFOV is complex and involves a range of different mechanisms, including bulk convection, turbulence, asymmetric velocity profiles, pendelluft, cardiogenic mixing, laminar flow with Taylor dispersion, collateral ventilation, and molecular diffusion. Except for molecular diffusion, each mechanism involves generation of convective fluid motion, and is influenced by the mechanical characteristics of the intubated respiratory system and the ventilatory settings. These factors have important consequences for the damping of the oscillatory pressure waveform and the drop in mean pressure from the airway opening to the lung. New techniques enabling partitioning of airway and tissue properties are being developed for measurement of lung mechanics during HFOV.**

Conclusions: **Awareness of the different mechanisms governing gas transport and the prevailing lung mechanics during HFOV represents essential background for the physician planning to use this mode of ventilation in the adult patient. Monitoring of lung volume, respiratory mechanics, and ventilation homogeneity may facilitate individual optimization of HFOV ventilatory settings in the future. (Crit Care Med 2005; 33[Suppl.]:S135–S141)**

KEY WORDS: resistance; inertance; compliance; oscillometry; gas transport; high-frequency ventilation; barotrauma; tracheal tube; respiratory function

The mechanisms governing gas flow, gas mixing, and pressure transmission during high-frequency oscillatory ventilation (HFOV) are fundamentally different to ventilation at more conventional respiratory breathing frequencies. They are integrally related to each other through the prevailing mechanical characteristics of the intubated respiratory system and frequency, symmetry, and magnitude of the applied pressure waveform. An appreciation of these mechanisms, and their implications for gas mixing efficiency, and the appropriate selection and matching of ventilator settings to the mechanical properties of the intubated respiratory system represent essential knowledge foundations for the clinician who uses HFOV to treat respiratory disease in the adult. This article aims to summarize the known mechanisms of gas mixing and to discuss the impact of lung mechanics on pressure transmission, flow generation, and the efficiency of ventilation and how each of these interact with each other during HFOV. A brief overview of the practical difficulties and progress achieved to date in measuring lung mechanics during HFOV is given and the relevance of measuring lung mechanics to optimization of clinical application of HFOV in acute respiratory distress syndrome (ARDS) is reviewed.

MECHANISMS OF GAS TRANSPORT AND GAS EXCHANGE

One of the fundamental principles underlying the increased efficiency of HFOV is the altered dynamics of gas flow distribution (1), challenging the traditional concepts of gas transport during conventional ventilation. A number of different mechanisms have now been identified as having a contributory role in promoting gas exchange during HFOV, including bulk convection, asymmetric velocity profiles, pendelluft, cardiogenic mixing, Taylor dispersion and turbulence, molecular diffusion, and collateral ventilation. These have been well illustrated previously (2) (see also Fig. 1) and are outlined subsequently. It is likely that they are not mutually exclusive and that a combination of the mechanisms augments gas transport during HFOV (3, 4).

Unlike conventional ventilation, bulk convection plays a relatively small role in gas transport during HFOV, although it is likely to contribute significantly to ventilatory exchange in the most proximal gas exchange units. In an anesthetized dog model, Spahn and colleagues (5) showed that decreasing delivered volume to a level below the HFO–circuit-related rebreathing volume (as opposed to the larger anatomic dead space) causes a sudden rise in the $Paco_2$. Their findings suggest that the efficiency of Co_2 elimination is critically dependent on the net oscillatory volume and that bulk convection has an essential role during HFOV. Turbulence in the large airways may also enhance gas mixing (2).

Asymmetric velocity profiles result in net convective transport of material. Although the more central particles are propelled down the length of the airway,

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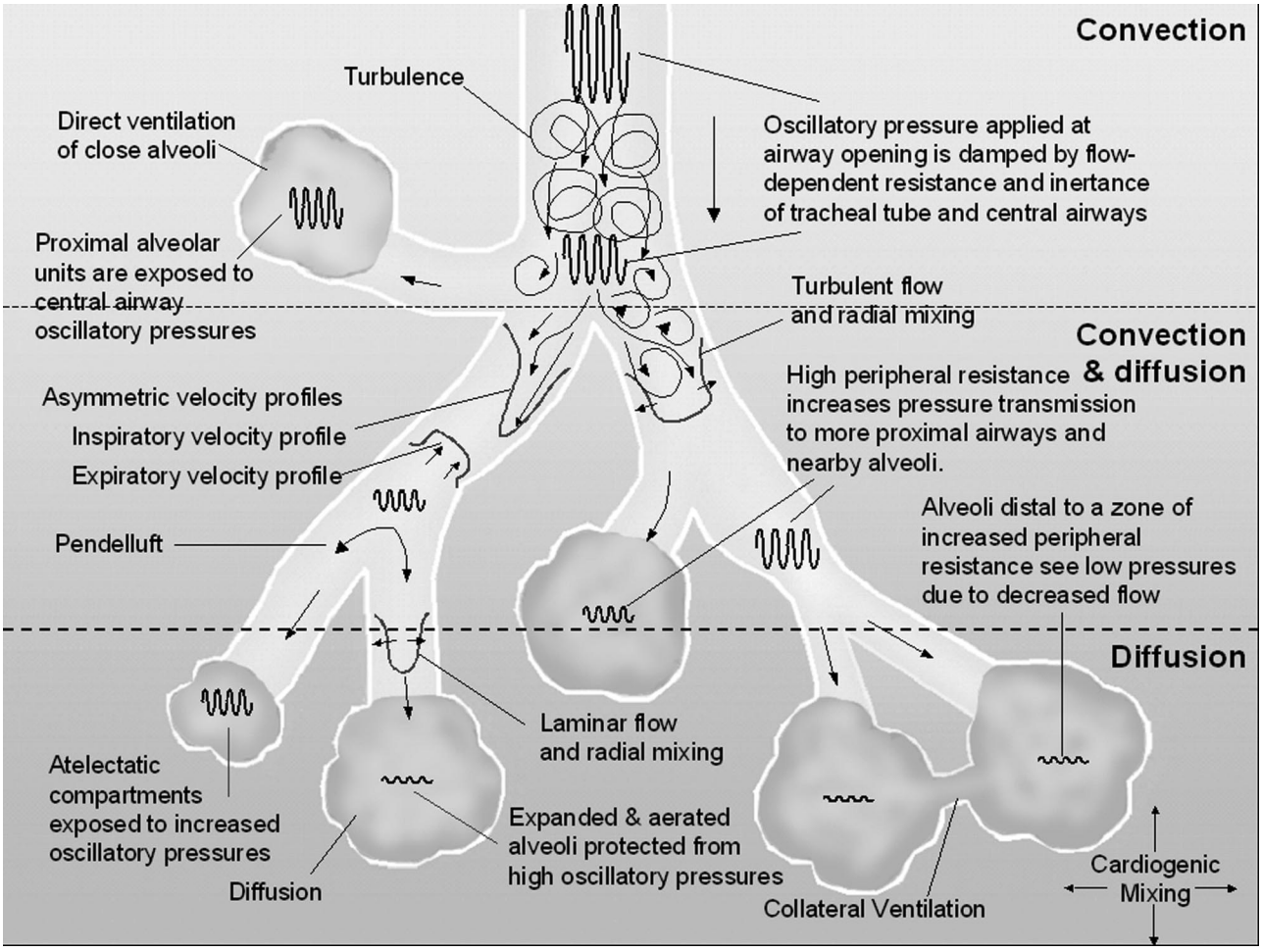

Figure 1. Gas transport mechanisms and pressure damping during high-frequency oscillatory ventilation (HFOV). The major gas-transport mechanisms operating during HFOV in convection, convection–diffusion, and diffusion zones include: turbulence, bulk convection (direct ventilation of close alveoli), asymmetric inspiratory and expiratory velocity profiles, pendelluft, cardiogenic mixing, laminar flow with Taylor dispersion, collateral ventilation between neighboring alveoli, and molecular diffusion (see text for details). The extent to which the oscillatory pressure waveform is damped is influenced by the mechanical characteristics of the respiratory system. Atelectatic alveoli will experience higher oscillatory pressures than normally aerated alveoli, whereas increased peripheral resistance increases the oscillatory pressures transmitted to proximal airways and neighboring alveolar units (adapted with permission (2), © 2005 Massachusetts Medical Society).

the peripheral particles diffuse radially, promoting axial gas exchange with expired alveolar gas (6). This phenomenon is particularly evident at the airway bifurcations where there is skewing of the inspiratory profile compared with a more symmetric expiratory velocity profile (7). The airway bifurcation phenomenon streams fresh gas toward the alveoli along the inner airway walls while "alveolar" gas is streamed away from the alveoli along the outer wall, and hence plays an important role in the longitudinal convective transport mechanisms during HFOV (8).

Taylor proposed that the longitudinal dispersion of tracer molecules in a diffusive process is augmented by radial transport mechanisms when laminar flow is applied in both the absence (6) or presence of turbulent eddies and secondary swirling motions (9). Fredberg (10) subsequently used a semiempiric analysis to predict that the combination of Taylor dispersion and molecular diffusion (augmented dispersion) accounts for almost all gas transport during HFOV.

Time-constant inequalities and phase lags between lung regions may set up bulk convective currents recirculating air between neighboring lung units (11–13). *In vitro* (14) and computational (15) lung models have shown that gas exchange during HFV may be markedly improved by the interaction of flow between asynchronous neighboring airways and has been graphically illustrated with stroboscopic filming techniques (2, 13). Asymmetries in inertance and compliance of peripheral airways and lung units are more important determinants of pendelluft than are asymmetries in resistance (16).

The superimposition of the rhythmic, strong contractions of the heart may further promote peripheral gas mixing by promoting the generation of flow within neighboring parenchymal regions rather than at the airway opening (17). The contribution of cardiogenic oscillation during HFOV has not been quantified, although it has been suggested that cardiogenic mixing may account for up to half of the oxygen uptake in the presence of totally apneic respiration (18). Collateral ventilation occurring through nonairway connections between neighboring alveoli has also been proposed as an additional mechanism of gas transport during both conventional and HFOV. The

relatively high resistance of the collateral channels to gas flow is likely to limit the extent to which this mechanism contributes to gas mixing during HFOV (19).

Spontaneous mixing of gas particles arising from Brownian motion contributes to the diffusion of gases in the respiratory tract. Gas velocities approximate zero in the alveolar region as a result of the very high total cross-sectional area. The dominant mechanism for gas mixing in this zone is molecular diffusion, with net transport of gas best described by Fick's law (10).

Studies in both theoretical models (10) and in healthy animals and humans (17, 20, 21) have demonstrated that tidal volume (V_T) has a greater effect on gas exchange than frequency (f) during HFOV. As such, ventilation efficiency during HFOV ($\dot{V}$) may be expressed as:

$$\dot{V} = f^a V_T^b \qquad [1]$$

where $b > a$. The values for a and b in this equation approximate 1 and 2, respectively, although the absolute values may be influenced by other factors such as the shape and complexity of the oscillatory pressure waveform. The more dominant contribution of V_T to ventilation during HFOV is the result of the oscillatory redistribution of gas from central to distal regions where molecular diffusion overcomes Taylor dispersion as the principal influence on gas transport (22). The transition frequency (frequency marking the transition from conventional to high-frequency gas transport mechanisms) varies in proportion to the ratio of metabolic rate to dead space and hence is lower in large animal species compared with small animal species and will be lower in adults compared with neonates (23). It has been shown that HFV gas transport mechanisms come into play, whereas V_T still exceeds airway dead space volume (V_D) (24) and that the transition frequency occurs when alveolar ventilation/frequency = 20% of V_D and V_T = 1.20 V_D (23).

MECHANICAL FACTORS INFLUENCING PRESSURE, FLOW, AND VENTILATION DURING HIGH-FREQUENCY OSCILLATORY VENTILATION

With the exception of molecular diffusion, all of these mechanisms of gas transport in the airways during HFOV are dependent on convective fluid motion (25). Whereas gas transport is driven by convective fluid motion, the mechanics of the respiratory system are also an important consideration as convective fluid motion is driven by the pressure differences imposed by the chest wall or the ventilator (25). In this respect, the impedance of the combined ventilator, circuit, tracheal tube, and respiratory system is an important determinant of the efficiency of ventilation during HFOV. Impedance is a global term that encompasses the mechanical properties of elastance (1/compliance), resistance, and the inertance. Although inertance is essentially negligible at conventional breathing frequencies, it assumes a much greater role at higher frequencies and cannot be ignored during HFOV.

In relatively simple terms, impedance represents a mechanical barrier to flow and as impedance increases, higher-pressure swings are required to generate an equivalent flow (and hence also volume delivery to the gas exchanging component of the lung). As pressure differences that drive flow also distend tissues, one of the major goals of HFV ventilation strategies is the achievement of adequate gas transport with low tidal volumes while avoiding pressures that either overdistend (causing barotrauma) or cause airway closure and alveolar collapse (atelectrauma). An understanding of how the distribution of impedance along the combined ventilated respiratory system impacts on the transmission of the mean and the amplitude of oscillatory pressure swings and flow to various lung compartments is vital to the appropriate clinical application of this ventilatory technology.

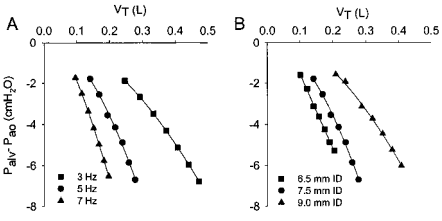

Figure 2. Effect of frequency and tracheal tube diameter on mean pressure drop. Simulations were performed using a previously published theoretical computer model (46) using mechanical input parameters that reflect current use of high-frequency oscillatory ventilation in the adult population (see Table 1). A square-wave oscillatory pressure waveform with 33% T_I was used to drive the model, including a range of airway opening amplitudes (30–90 cm H_2O) at *A*, three different frequencies (3, 5, and 7 Hz) and *B*, for three tracheal tubes of differing internal diameter (*ID*) (6.5 mm, 7.5 mm, and 9.0 mm). Ventilator and model lung characteristics used for the simulations are summarized in Table 1. For any given tidal volume (V_T), the magnitude of the difference in mean pressure between the alveolus and the airway opening (P_{alv}–P_{ao}) increases with increasing frequency and decreasing TT internal diameter.

Table 1. Model parameters for simulation of pressure transmission in adult lung during high-frequency oscillation ventilation

Parameter	Baseline value (range)
Frequency, Hz	5 (2–8)
T_I, %	33
Amplitude, cm H_2O	70 (30–90)
K_1, cm $H_2O \cdot s/L^a$	1.5 (1, 2.4)
K_2, cm $H_2O \cdot s^2/L^{2a}$	3.4 (1.5, 6.8)
I, cm $H_2O \cdot s^2/L^b$	0.1 (0.133, 0.07)
C_g, mL/kg	0.2
R_c, cm $H_2O \cdot s/L$	0.2
$R_p$tot, cm $H_2O \cdot s/L$	0.5 (0.25–5)
C_{tot}, mL/kg	40 (20–300)

C_g, gas compression in airways; R_c, linear resistance in central airway compartment; $R_p$tot, total resistance of peripheral compartment; C_{tot}, total compliance of peripheral compartment.

[a]Rohrer tracheal tube constants estimated by extrapolation from published values for smaller tubes. Baseline value representative of 7.5 mm ID tracheal tube with values for 6.5 mm and 9.0 mm ID tracheal tubes given in brackets; [b]values in brackets show those in simulations for 6.5 mm and 9.0 mm tracheal tubes, respectively.

Ventilator and Circuit Considerations

Inspiratory–Expiratory Ratio. The selection of inspiratory to expiratory time ratio (T_I:T_E) influences the delivery of pressure and volume to the lung. Traditionally, clinicians used asymmetric T_I:T_E ratios (inspiration shorter than expiration) to avoid the development of gas trapping during HFOV. Early studies (26–29) indicating mean pressures in the lung higher than those recorded at the airway opening used low mean airway pressures that may have precipitated the development of choke points (30). Using an optimal volume strategy, airways are splinted open (31), and providing the inspiratory and expiratory cycles are of equal duration and expiration is active rather than passive, there is negligible change in mean pressure between the airway opening and the lung (32–34). In contrast, the use of a T_I = 33% actually results in a drop in the mean intrapulmonary pressure as a result of higher flow-dependent tracheal tube (TT) resis-

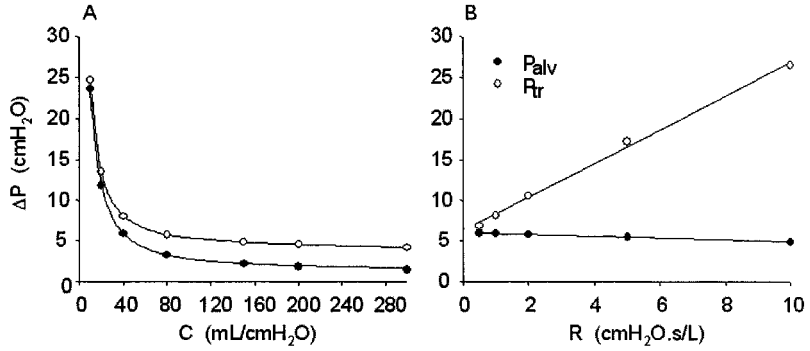

Figure 3. Effect of compliance and peripheral resistance on damping of the pressure waveform. Simulations were performed across a range of *A*, total lung compliance (10–300 cm H_2O) and *B*, total peripheral resistance (0.5–10 cm H_2O s/L) at a frequency of 5 Hz, 33% T_I for a 7.5-mm ID TT. There is a sharp rise in the magnitude of the oscillatory pressure waveform transmitted to both alveolar and tracheal compartments at low compliance. The amplitude of the tracheal oscillatory pressure waveform increases with increasing peripheral resistance.

tance during inspiration compared with expiration resulting from higher flows during the shortened inspiratory phase (32). The magnitude of the pressure drop increases with increasing frequency, and decreasing TT internal diameter (see Fig. 2) and relative duration of the inspiratory component (32), and in part explains the need to increase mean pressure above that used with ventilation at more conventional rates when initiating HFOV with T_I = 33% of total cycle time. It has previously been proposed that the use of asymmetric T_I:T_E may exaggerate the normal asymmetry of inspiratory and expiratory velocity profiles as a result of the proportionately higher inspiratory flows, further enhancing the efficiency of gas mixing; however, several studies (35–37) have failed to demonstrate a specific advantage of asymmetric flows on gas mixing efficiency. The consequences of T_I:T_E for gas mixing or the higher inspiratory flows associated with asymmetric T_I:T_E on induction of shear stress injury has not yet been adequately investigated.

Waveform. Ventilators differ in the shape of the pressure waveform delivered to the airway opening. Sinusoidal waveforms are normally delivered with equal inspiratory and expiratory cycle durations and thus have a single dominant frequency. More complex waveforms such as the near-square waves delivered by the SensorMedics 3100B (SensorMedics, Yorba Linda, CA) are by definition composed of a fundamental frequency and multiple higher harmonic frequencies. When asymmetric T_I:T_E ratios are used, the fundamental frequency (and its corresponding harmonics) will be different during inspiratory and expiratory oscillatory cycles. A comparison of gas-mixing efficiency between sinusoidal and complex waveforms has not yet been performed; however, it will be difficult to do so in a way that equivalent flow waveforms are produced if T_I:T_E ratios other than 1:1 are used. Ventilators determine the T_I:T_E based on the relative durations of the respective components of the pressure waveform. For the square wave, this estimate is a reasonably close approximation of inspiratory and expiratory flow cycles, which more accurately define the start of the inspiratory and expiratory periods. In contrast, a sinusoidal airway opening pressure waveform constructed with a 33% T_I actually generates an inspiratory flow that accounts for approximately 42% of the total cycle time (unpublished observations). As a consequence, the magnitude of the pressure drop across the TT is less for a ventilator delivering sinusoidal pressure waveforms than for a square waveform ventilator (32). Square waveforms are associated with sudden changes in flow and airway pressures, whereas more gradual and smooth changes are observed using sine wave ventilation. There has been a suggestion that square wave ventilation at conventional breathing frequencies is associated with increased incidence of air leak syndrome (38); however, the impact of waveform shape and the rapidity of change in flow and pressure for shear stress and lung injury during HFOV has not been assessed.

Frequency

Higher frequencies result in delivery of lower tidal volumes and also decrease the magnitude of the alveolar pressure swings (20, 39). What constitutes optimal frequency in HFOV is an issue often discussed by clinicians. In newborns, frequencies between 8 and 15 Hz are most often used, whereas lower frequencies are more often used for adults (40, 41). Given the relative importance of V_T in determining Co_2 exchange ($Vco_2 \propto f \cdot V_T^2$) (10, 20, 21, 42), the goal of frequency selection needs to minimize the pressure swings to both proximal and distal lung compartments while not compromising the V_T to the extent that insufficient ventilation takes place. From a mechanical point of view, in most adult clinical scenarios, this is likely to occur slightly below the resonant frequency near the corner frequency (F_c) of the lung (see subsequently) (25).

Tracheal Tube. The TT contributes over 50% of the total impedance of the respiratory system and accounts for approximately 90% of the inertance (43). During HFOV, the resistance of the tracheal tube is flow-dependent and can be described using Rohrer constants (32, 44). As resistance is inversely proportional to r^4 (where r = radius), small reductions in the internal diameter of the TT (i.e., from secretions or change in TT size) decreases (damps), the amplitude of the pressure waveform, and reduces resultant flow and V_T. A decrease in TT internal diameter also increases the magnitude of the drop in mean pressure between the airway opening and the lung parenchyma for any given ventilator amplitude (45, 46). Whereas these effects are quite marked in narrow neonatal tubes (46), appreciable changes in these parameters can still be observed in the range of TT used in the adult population as a result of the significantly higher flows.

Patient Factors

Whereas the traditional teaching approach for HFOV has emphasized extensive damping of the pressure waveform between the airway opening and the alveolar compartment (11, 47, 48), it needs to be appreciated that this knowledge was largely based on measurements made in models with highly compliant lungs. In contrast, theoretical (45, 46), *in vitro* (49), and *in vivo* (50, 51) models of lung disease have demonstrated that damping

at different points within the airways and alveoli is heavily dependent on the distribution, homogeneity, and mechanical characteristics of disease within the respiratory system.

HFOV was initially developed for use in the extremely noncompliant and immature lung of the premature neonate with hyaline membrane disease, which is typified by relatively diffuse homogeneous atelectasis associated with surfactant deficiency. The magnitude of pressure amplitudes transmitted to the lung in the newborn lung increases exponentially with decreasing compliance (46, 49, 50). In contrast to the neonate, the most usual application of HFOV in the adult is for ARDS. Like hyaline membrane disease, ARDS is characterized mechanically by a very poorly compliant lung, usually in the absence of altered resistance. In contrast to hyaline membrane disease, however, the pattern of lung involvement in ARDS may be relatively inhomogeneous (52, 53), and the cause of the illness may be the result of pulmonary or extrapulmonary causes (54, 55). Modification of a theoretical lung model using appropriate ventilator settings (41), tracheal tube constants, and respiratory mechanical parameters (56) for an intubated adult with ARDS demonstrates the relatively higher pressure transmission to the airways and alveolar compartment in the presence of poor compliance (see Fig. 3*A*).

Ventilation inhomogeneity poses a problem at conventional ventilation frequencies because the distribution of gas is largely controlled by the distribution of regional lung compliance, and thus heterogeneous regional expansion and ventilation necessarily follow. As ventilation frequencies approach the resonance frequency, however, gas transport is less dependent on regional lung compliance (57) and increasingly governed by the resistive (26), inertive (48), and branching angle properties of the central airways (58, 59). Theoretical studies have indicated that compliant alveoli are effectively spared from excessive oscillatory pressures with the larger alveolar pressure swings being directed to the more poorly compliant compartments (46).

HFOV is also applied in clinical scenarios other than the purely poorly compliant lung. Understanding the impact of respiratory mechanics on pressure and flow may help elucidate why such approaches have so far met with variable success. An increase in peripheral airway resistance (as might be expected to occur if using HFOV in a patient with small airways disease) will result in a marked increase in the pressure swings in the airways proximal to the obstruction, despite the preservation of relatively small pressure and volume fluctuations delivered to the alveolar compartment (see Fig. 3*B*) (46). In such cases, tuning ventilator frequency to the corner frequency of the affected lungs will reduce the likelihood of excessive pressure excursions in the proximal airways and limit associated shear stress (25).

PRESSURE COST OF VENTILATION

Although each of the factors outlined here influence the magnitude of pressure transmission from the airway opening to the lung, they also have consequences for the delivery of flow and the magnitude of resultant tidal volumes. A particularly instructive way to approach the complexities of these different interactions is to follow the approach of Venegas and Fredberg (25) by considering the pressure cost of achieving flow, which can be considered as the pressure cost per unit convective flow times the convective flow cost per unit alveolar ventilation. Their seminal 1994 paper highlighted some important principles for the clinical practice of HFOV and warrants special attention. The oscillatory pressure cost of flow decreases rapidly with increasing frequency, reaching a minimum at the resonance frequency:

$$f_0 = \frac{1}{2\pi\sqrt{IC}} \qquad [2]$$

where f_0 is the resonance frequency, C is the compliance, and I is the inertance. In overdamped lungs, minimal additional damping of the oscillatory pressure is achieved above the corner frequency:

$$f_c = \frac{1}{2\pi RC} \qquad [3]$$

where f_c is the corner frequency and R is the resistance, suggesting that there is benefit in increasing ventilation frequency up to but not beyond this point. As f_c increases, a beneficial decrease in oscillatory pressure continues to be achieved at higher frequencies than would be the case in the normal lung. Equally, increasing system resistance will shift the f_c to lower frequencies. This concept may explain why neonatal conditions such as meconium aspiration syndrome are most successfully ventilated using lower frequencies than those used for hyaline membrane disease.

The adult lung is a relatively overdamped system compared with the neonatal lung. Using published values for resistance, inertance, and compliance (60), a healthy adult lung would have $f_0 \approx 2.7$ Hz and $f_c \approx 0.32$ Hz. Assuming lung compliance of a patient with ARDS is decreased to 1/10th the normal value (i.e., approximately 20 mL/cm H_2O) (52), f_0, and f_c for the adult ARDS lung would approximate 8.6 Hz and 3.2 Hz, respectively. Whereas the absolute values of these parameters will ultimately depend on the relative changes in inertance and resistance, this rough estimation suggests values for f_c in keeping with current clinical practice of HFOV in ARDS.

A second and perhaps more important factor is the impact of inappropriate positive end-expiratory pressure (PEEP) selection. In the healthy lung, pressure cost of ventilation increases markedly at high PEEP values, and to a lesser extent also when alveolar recruitment occurs as a result of low PEEP (25). Venegas and Fredberg show that in the poorly compliant lung, the selection of PEEP is much more critical than the frequency, at least for frequencies above the resonant frequency of the lung, although frequency choice remains more important than in the normal lung. In contrast, pressure cost of ventilation increases dramatically above the corner frequency in the situation in which increased airway resistance is a dominant feature of disease (25).

MONITORING LUNG MECHANICS AND VENTILATION INHOMOGENEITY TO GUIDE VENTILATORY PRACTICE

The important interplay between respiratory mechanics and the selection of appropriate ventilation frequency and selection of mean airway pressure highlights the urgent need for bedside assessment of lung volume, distribution of ventilation, respiratory mechanics, and optimal ventilation frequency. Major advances in the noninvasive assessment of lung volume and regional inhomogeneity have been achieved over the last decade; however, these are the subject of two further articles in this supplement (chapters 7 and 8) and are not discussed further here. Progress is also being made in obtaining meaningful measurements of

lung mechanics during HFOV and warrants some discussion.

Ideally, measurement of lung function during HFOV would: 1) provide a comprehensive bedside assessment of lung function across a range of oscillatory frequencies during a limited time interval; 2) be achievable at (and without compromising) the prevailing lung volume; 3) generate detailed information about the function and integrity of the respiratory system with particular reference to lung volume and mechanics of the lung parenchyma; 4) provide measurement parameters that are comparable with those of patients ventilated at other (lower) frequencies; and 5) be applicable to the measurement of lung mechanics in both the acute and longer-term follow up of individual patients.

Until recently, estimation of respiratory mechanics during HFOV has most often been obtained using conventional passive mechanics, although this approach provides limited information about the lung parenchyma (often the primary site of pathology in the poorly compliant lung). In addition, the deflation maneuvers associated with such measurements may promote alveolar derecruitment and have not been found useful in determining optimum lung volume during HFOV (61). Likewise, the measurement of dynamic mechanics is also plagued by problems. Accurate measurement of the high instantaneous flows is difficult to achieve, as are meaningful measurements of dynamic compliance. Compliance is determined by assessing changes in volume-per-unit change in pressure, but tidal volume becomes increasingly independent of changes in compliance with increasing frequency (49). As a result, detecting change in underlying lung compliance during HFOV would require monitoring of intrapulmonary pressures. Because the amplitude of the oscillatory pressure waveform at the airway opening does not reflect changes in the intrapulmonary pressure amplitudes during HFOV, a more invasive approach is required. Using a catheter tip manometer, Van Genderingen and colleagues (51) have demonstrated an inverse relationship between respiratory compliance and the oscillatory pressure ratio (ratio of pressure swings at the distal and proximal ends of an endotracheal tube) and were able to use these measurements to define the optimal continuous distending pressure.

Sipinková et al. (62) obtained measurements of oscillatory mechanics during short bursts of HFOV across a range of tidal volumes (5.0, 6.6, and 10 mL) and frequencies (10, 15, 20, and 25 Hz) in rabbits and demonstrated changes in oscillatory mechanics from the pressure-flow relationship at the airway opening before and after vagotomy in adult rabbits at each of a range of oscillation frequencies and tidal volumes. Drawbacks of this approach are the need for different measurements at each frequency (potentially inducing time-variant results) and the relatively high amplitude of oscillatory signals required (which may introduce nonlinearities).

More recently, the low-frequency forced oscillation technique (FOT), which uses a broadband low-amplitude forcing signal has been used to monitor changes in lung mechanics associated with changes in lung volume (46, 50) during HFOV. The low-frequency FOT can meet each of the criteria listed here, and animal ventilators have been built incorporating similar measurements interspersed with normal ventilation at user-defined frequencies. A particular advantage of this approach is that it facilitates partitioning of respiratory mechanics into airway and parenchymal components (63). The inclusion of esophageal pressure catheters also enables chest wall impedance to be measured, a factor that may be quite important for ARDS and have implications for the successful application of HFOV (54). Gattinoni and coworkers highlighted the improved responses of patients with chest-wall stiffness to increased application of PEEP compared with those in whom the primary illness effected diminished compliance of the lungs (52). Practical limitations for clinical introduction of the low-frequency FOT will include the need for measurements during a relaxed respiratory pause and the success in achieving leak-free measurements in the presence of tracheal tube leak by application of pressure over the carina.

SUMMARY

Whereas some similarities can be drawn between ventilation at conventional breathing rates and HFOV, the added complexity introduced by the higher frequencies and the accompanying high flows significantly alters the mechanical balance. Changes in the relative importance of compliance, resistance, and inertance at different frequencies for any given lung condition in determining the magnitude of flow and pressure transmitted to the distal lung have important implications for clinical practice. Clinicians need to understand the concept of drop in mean pressure across the tracheal tube, and appreciate how this may be altered by frequency, internal diameter of the tracheal tube, and ventilator amplitude. Likewise, an appreciation of lung mechanics in the clinical setting may guide selection of those patients likely to benefit from HFOV and appropriate ventilator settings (especially frequency) to achieve low tidal volume ventilation while avoiding barotrauma to proximal alveolar units. Further development of tools to monitor lung volume, regional ventilation inhomogeneity, and lung mechanics would establish an objective basis for optimizing the clinical application of HFOV in the setting of ARDS.

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