GAS TRANSPORT MECHANISMS DURING HIGH-FREQUENCY VENTILATION

Online Supplement

Thomas JA Scott,[1] Chinthaka Jacob,[1] David G Tingay,[2,3] Justin S Leontini[1,]

[1]Department of Mechanical and Product Design Engineering, Swinburne University of Technology, Hawthorn, Victoria, Australia
[2] Neonatal Research, Murdoch Children's Research Institute, Parkville, Victoria, Australia
[3] Department of Paediatrics, University of Melbourne, Institution, Melbourne, Victoria, Australia

Correspondence: *Thomas Scott (tjscott@swin.edu.au).*

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Table 1. Glossary of gas exchange mechanisms and terminology during High-frequency Ventilation.

Term	Definition
Advection	The transport of a substance due to bulk fluid motion (such as occurs during conventional tidal ventilation).
Capacitor	In the context of HFV, the component of the RLC circuit used to represent the elastic loads acting on the airway-lung system.
Corner frequency	In the context of HFV, and based on RLC-type modelling, it is the frequency where the pressure cost of flow is lowest for a system with high airway resistance (overdamped). In general, it might be considered the frequency of a system at which the energy might be lowest.
Inductor	In the context of HFV, the component of the RLC circuit used to represent the inertive loads acting on the airway-lung system.
Molecular diffusion	Diffusion of matter, from a region of high concentration to a region of low concentration, due to random molecular motion.
Natural frequency	In the context of HFV, and based on RLC-type modelling, it is the frequency where the pressure cost of flow is lowest. In general, it is the frequency at which a system naturally vibrates.
Nonlinear mean streaming	A non-zero average velocity of gas flow at a given location that can occur in the middle to upper generations of the airway during high-frequency ventilation.
Pendelluft	Gas transport between adjacent lung compartments due to varying compliance.
Resistor-Inductor-Capacitor (RLC-type) model	In the context of HFV, the modelling technique currently used to understand the dynamics of the airway-lung system during high-frequency ventilation. In general, an electrical analogy used to model a dynamical system.
Resistor	In the context of HFV, the component of the RLC circuit used to represent the viscous losses in the airway-lung system.
Taylor dispersion	Enhanced transport of a gas in the axial direction (along a tube) that is induced by a radial concentration gradient (across the tube).
Turbulent diffusion	The mixing, transport and diffusion of gas due to turbulent motion that can occur in the upper generations of the airway during high-frequency ventilation.
Womersley parameter	A dimensionless parameter used in biofluid mechanics to quantify the relative importance of viscous effects in pulsatile/oscillatory flows.

Definitions of gas transport mechanisms and terms associated with current modelling that are used throughout this manuscript.

Table 2. Baseline ventilation protocols for the treatment of infants born at or near term with severe pulmonary dysfunction and the treatment of infants born preterm acute pulmonary dysfunction.

Study	Frequency (Hz)	Mean Airway Pressure	Pressure Amplitude
Studies from infants born at or near term [14]			
Clark *et al.* 1994 [41]	10	"Our goals were to maintain the lowest $F_iO_2$and normal lung inflation"	"a pressure amplitude sufficient to produce visible chest wall motion"
Rojas *et al.* 2005 [42]	10	"$2\mathrm{cmH_2O}$ above $\overline{\mathrm{Paw}}$ on CV at the time of enrolment"	"amplitude adjusted to obtain visual vibration of the chest wall and desired levels of $\mathrm{P_aCO_2}$"
Studies from infants born pre-term [15]			
Clark *et al.* 1992 [43]	10	"$\overline{\mathrm{Paw}}$ (measured proximal to the endotracheal tube) 1 to $2\mathrm{cmH_2O}$ greater than that being used on CV at the time of entry in the study"	"pressure amplitude that produced visible chest wall movement"
Courtney *et al.* 2002 [44]	10 – 15	"the initial mean airway pressure was at least 2 cm of water higher than that received during conventional ventilation"	NA
Craft *et al.* 2003 [45]	10 – 12	"Mean airway pressure was adjusted to maintain an optimal lung volume strategy as measured by a chest radiograph demonstrating expansion to eight to nine ribs and oxygenation saturation between 88% and 92% on an $\mathrm{F_iO_2}$ less than 0.40"	"Amplitude was adjusted to meet the goal $\mathrm{P_ACO_2}$"
Dani *et al.* 2006 [46]	10	$8\mathrm{cmH_2O}$	$30\mathrm{cmH_2O}$
Durand *et al.* 2001 [47]	10 – 15	"Mean airway pressure $(\mathrm{P_{AW}})$ at least $2\mathrm{cmH_2O}$ greater than patient was receiving on conventional ventilation."	"Amplitude $(\Delta\mathrm{P})$ adjusted based on physical examination and/or transcutaneous monitoring."
Gerstmann *et al.* 1996 [48]	10 – 15*	"The HFOV strategy was to begin CDP at $1-2\mathrm{cmH_2O}$ above $\mathrm{P_{AW}}$ used during the stabilisation period on CV"	"Ventilation was controlled by adjusting the power output to increase or decrease $\Delta\mathrm{P}$"
HiFi Group 1989 [49]	15	"The initial fraction of inspired oxygen and mean airway pressure were specified by the protocol to be the same as those required during stabilization on conventional mechanical ventilation. If the infants had not yet received	"the oscillatory amplitude was increased until chest-wall oscillations were rapidly apparent, and it was then adjusted as needed to correct hypocapnia or hypercapnia."

Study	Frequency (Hz)	Mean Airway Pressure	Pressure Amplitude
		conventional mechanical ventilation, the initial amount of inspired oxygen was set to be the same as that before intubation and the mean airway pressure was set to be $0.8\ to\ 1.0kPa\ (8-10\text{cm of water}).$"	
Johnson *et al.* 2002 [50]	10	$6-8\text{cmH}_2\text{O}$	"the amplitude was increased until the infant's chest was seen to be "bouncing""
Lista *et al.* 2008 [51]	10	$8-10\text{cmH}_2\text{O}$	40%
Moriette *et al.* 2001 [52]	15	"Initial mean airway pressure was set at $14\text{cmH}_2\text{O}$ when $\text{F}_\text{i}\text{O}_2 > 0.4$ and $2\text{cmH}_2\text{O}$ higher than with conventional ventilation when $\text{F}_\text{i}\text{O}_2 \leq 0.4$."	"Peak-to-peak pressure was set according to the PCO_2 level."
Ogawa *et al.* 1993 [53]	15	"lung volume was recruited in high frequency oscillatory ventilation by inflating the lungs fully by manual bagging just before starting and a high mean airway pressure was adopted"	NA
Plavka *et al.* 1999 [54]	15	"The proximal airway distending pressure $(\text{PA}_\text{W}\text{DP})$ was increased step by step to reach optimum lung inflation and alveolar recruitment and to optimize oxygenation as soon as possible"	"The pressure amplitude (DP) was adjusted to achieve adequate vibration of the thorax"
Rettwitz-Volk *et al.* 1998 [16]	15 – 20	"The initial settings were mean airway pressure and oscillatory amplitude to show good chest movement and $\text{F}_\text{i}\text{O}_2$ to maintain oxygen saturation as described above."	"The initial settings were mean airway pressure and oscillatory amplitude to show good chest movement and $\text{F}_\text{i}\text{O}_2$ to maintain oxygen saturation as described above."
Salvo *et al.* 2012 [55]	15	"mean continuous distending pressure (CDP), 6 to $8\text{cmH}_2\text{O}$"	"pressure amplitude producing visible chest vibrations"
Schreiber *et al.* 2003 [56]	10 – 15	"2 cm of water above that required during initial stabilization"	"an amplitude sufficient to jiggle the chest wall to the level of the umbilicus"
Sun *et al.* 2014 [57]	10	$6-8\text{cmH}_2\text{O}$	"The pressure amplitude was set in such a way that chest oscillations were visible with a frequency of 10Hz."

Study	Frequency (Hz)	Mean Airway Pressure	Pressure Amplitude
Thome *et al.* 1999 [58]	10	"Paw was initially set 1 to $2\mathrm{cmH_2O}$ above the mean pressure during the previous stabilization with IPPV or, if HFV was started immediately after intubation, Paw was set at 10 to $12\mathrm{cmH_2O}$."	"ventilation was controlled by adjusting the amplitude"
Van Reempts *et al.* 2003 [59]	10	"Randomised infants were started on a MAP of $8\mathrm{cmH_2O}$ for infants < 29 weeks and $10\mathrm{cmH_2O}$ for neonates 29-31 6/7 GA with $\mathrm{F_iO_2}$ as needed."	"The pressure amplitude (delta P) was set at a value that produced visible chest wall movement."
Vento *et al.* 2005 [60]	10	$10\mathrm{cmH_2O}$	"set at 30% at the beginning, was increased, if necessary, until the infant's chest was seen to be "bouncing""

Baseline ventilator protocols obtained from references included in the Cochrane Database of Systematic Reviews: High frequency oscillatory ventilation versus conventional ventilation for infants with severe pulmonary dysfunction born at or near term (Review) [14]; and Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants (Review) [15]. * "Ventilator frequency was set to $10\mathrm{Hz}$, although in some very small infants this produced overventilation even at low power settings. In these small infants the oscillation frequency was increased to $15\mathrm{Hz}$, which reduced tidal volume output and decreased overventilation" GA: Gestational Age. NA: Not apparent. Note: References listed here are not exhaustive. Only references to studies included in the review have been tabulated here. Where applicable, only the major publication for the study has been included. Unless specified otherwise, tabulated values indicate protocol which high-frequency ventilation was initiated at.

Table 3. Baseline ventilation protocols for the treatment of adults with ARDS.

Study	Frequency (Hz)	Mean Airway Pressure	Pressure Amplitude
Deredak *et al.* 2002 [61]	5	"mPaw was set $5\mathrm{cmH_2O}$ greater than mPaw during CV immediately before conversion to HFOV."	"Pressure amplitude of oscillation (ΔP) was initially set to achieve chest wall vibration to the level of the midthigh."
Bollen *et al.* 2005 [62]	5	"HFOV was started with continuous distending pressure (CDP) at $5\mathrm{cmH_2O}$ higher than mean airway pressure (MAP) on CV and then adjusted to achieve and maintain optimal lung volume."	"Delta P was adjusted according to $\mathrm{P_aCO_2}$ and chest wall vibrations."
Demory *et al.* 2007 [63]	5	"Mean airway pressure was set at $5\mathrm{cmH_2O}$ greater than mean airway pressure measured during the ventilation optimization period."	"The pressure amplitude of oscillation was set to achieve a $\mathrm{P_aCO_2}$ close to the $\mathrm{P_aCO_2}$ measured during the ventilation optimization period."
Ferguson *et al.* 2013 [64]	NA	$30\mathrm{cmH_2O}$	"We minimised HFOV tidal volumes by using the highest possible frequency that would maintain arterial blood pH above 7.25."
Young *et al.* 2013 [29]	10	"$5\mathrm{cmH_2O}$ above the plateau airway pressure at enrolment"	NA
Mentzelopoulos *et al.* 2007 [65]	4 [5]	"mPaw of $3\mathrm{cmH_2O}$ above mean tracheal pressure measured distal to the endotracheal tube" [5]	"$30\mathrm{cmH_2O}$ above initial $\mathrm{P_aCO_2}$ during CV" [5]

Baseline ventilator protocols obtained from HFV trials for the treatment of adults with ARDS originally report in [5]. $\mathrm{P_aCO_2}$: Partial pressure of carbon dioxide. $\mathrm{F_iO_2}$: Fraction of inspired oxygen. IT: Inspiratory time. BF: Bias flow. mPaw: Mean airway pressure. CV: Conventional Ventilation. CMV: Conventional Mechanical Ventilation. NA: Not apparent. Unless specified otherwise, tabulated values indicate protocol which high-frequency ventilation was initiated at.