Bubble CPAP: Is the Noise Important?
An *In Vitro* Study

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ABSTRACT

Continuous positive airway pressure (CPAP) is often used to provide noninvasive respiratory support in infants with Respiratory distress syndrome. The recruitment of atelectatic lung and appropriate lung volume maintenance are vital to the success of CPAP treatment. The noisy pressure waveform of bubble CPAP superimposed on pressure fluctuations as a result of spontaneous breathing may promote airway opening events as a result of stochastic resonance. The magnitude and the frequency of the superimposed noise are critical to this process. We hypothesized that the applied bias flow and mechanical properties of the lung would influence the magnitude and the frequency content of the noise transmitted to the lung. The effect of varying bias flow (6–10 L/min) and lung compliance (0.1–1.5 mL/cm H_2O) on the mean, range, and frequency content of the pressure fluctuations at the airway opening and within the lung was evaluated in an *in vitro* model lung. Increasing bias flow increased the mean and the magnitude of pressure oscillations at the airway opening and in the lung model. Decreasing compliance of the lung model increased the magnitude and the frequency content of pressure oscillations in the model lung. Lung mechanics and applied flow influence the magnitude of the noise superimposed on the transmitted pressure waveform and may influence lung volume recruitment in bubble CPAP. (*Pediatr Res* **57: 826–830, 2005**)

Abbreviations
CPAP, continuous positive airway pressure
P_{ao}, pressure at the airway opening
P_{fl}, pressure within the glass flask (model lung)
PIP, peak inspiratory pressure

There has been renewed interest in using continuous positive airway pressure (CPAP) to provide noninvasive respiratory support in infants with respiratory distress syndrome. The reports by Avery *et al.* (1) and more recently also that of van Marter *et al.* (2) highlighting the low incidence of chronic lung disease in preterm infants at the Columbia Presbyterian Medical Centre have focused attention on the specific respiratory care practices of that institution and particularly that of using bubble CPAP (3).

During bubble CPAP, the expiratory limb of the CPAP circuits vents through an underwater seal. The resulting bubbles create pressure oscillations that are transmitted back to the airway opening. Lee *et al.* (4) observed that the chests of infants who received bubble CPAP *via* an endotracheal tube vibrated in a similar manner and frequency to infants who received high-frequency oscillatory ventilation and questioned whether these vibrations may contribute to gas exchange. When comparing bubble CPAP with ventilator-derived CPAP in intubated infants, they showed that infants were able to maintain blood gas parameters despite reducing both minute volume and respiratory rate while on bubble CPAP and hypothesized that bubble CPAP may reduce work of breathing compared with ventilator-derived CPAP and augment gas exchange through promotion of facilitated diffusion. This hypothesis has not been scientifically tested, and no alternative rationale to support a physiologic advantage of this form of CPAP over other methods has been published in the literature. Although consideration has been given to the potential of improved efficiency of gas mixing during bubble CPAP, a second possibility is that the superposition of noise on the underlying constant pressure may promote lung volume recruitment and hence also reduce intrinsic work of breathing. If so, then the

frequency and the magnitude of the noise could be a vital factor in determining the success of bubble CPAP in recruiting atelectatic lung. In the current study, we aimed to evaluate how lung compliance and the applied flow altered the frequency content and the magnitude of the oscillatory component of the bubble CPAP pressure waveform in an *in vitro* lung model.

METHODS

To simulate the mechanical properties of the respiratory system of the intubated human newborn infant with hyaline membrane disease, we performed experiments in an *in vitro* model of the intubated newborn respiratory system similar to that used previously (5,6). The lung model incorporated an endotracheal tube (10 cm long, 4.0 mm ID) sealed into the neck of a 2-L glass flask. A commercially available version of the Columbia bubble CPAP setup (BubbleFlow; Fisher & Paykel, Auckland, New Zealand) set to deliver 5 cm H_2O was applied to size 2 nasal CPAP prongs (Hudson RCI, Temecula, CA) and connected to the *in vitro* lung model (Fig. 1).

Studies were performed across a range of lung model compliance (0.1–1.6 mL/cm H_2O) at each of three different flows (2, 6, and 10 L/min). Lung model compliance was varied by filling the glass flask with known volumes of water (5). Endevco pressure transducers were used to measure pressure at the airway opening (P_{ao}) and from within the model lung (P_{fl}). Pressure transducers were referenced to atmospheric pressure at the commencement of the study and before obtaining duplicate measurements at each combination of lung model compliance and inspiratory flow. Signals were filtered (200 Hz), amplified, digitized (Labdat; RHT Infodat, Montreal, Quebec, Canada), and stored on a personal computer for later analysis.

Analysis. Time-series recordings of P_{ao} and P_{fl} were transformed into the frequency domain using power spectral analysis to assess the extent of transmission of different frequency components to the lung. The mean and the range of the P_{ao} and P_{fl} pressure waveform were determined at each of the combinations of compliance and flow. The mean and the range of pressure measurements obtained at 8 and 10 L/min were compared with those at 6 L/min using one-way ANOVA. The frequency content and the power of the waveforms were assessed using power-spectral analysis (Anadat, RHT Infodat).

RESULTS

Representative time-series traces of the *in vitro* pressure measurements are shown for two different model lung compliances in Fig. 2. The P_{fl} was substantially higher than the P_{ao}
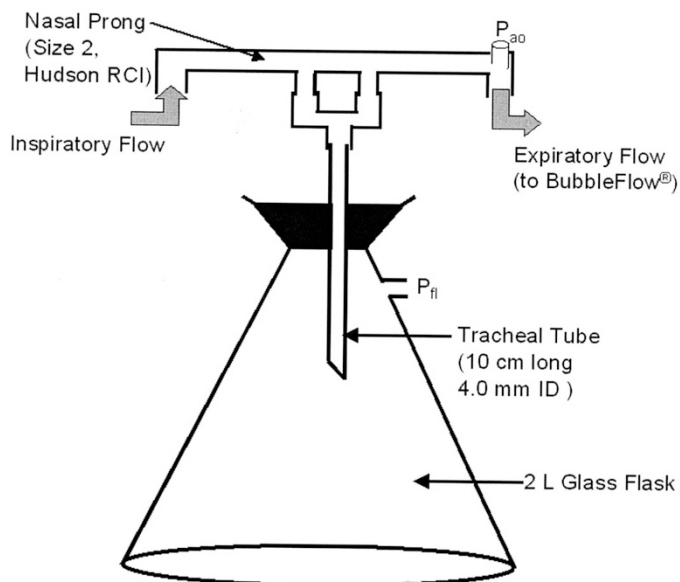
Figure 1. *In vitro* lung model. Compliance was varied by filling the glass flask with known volumes of water.
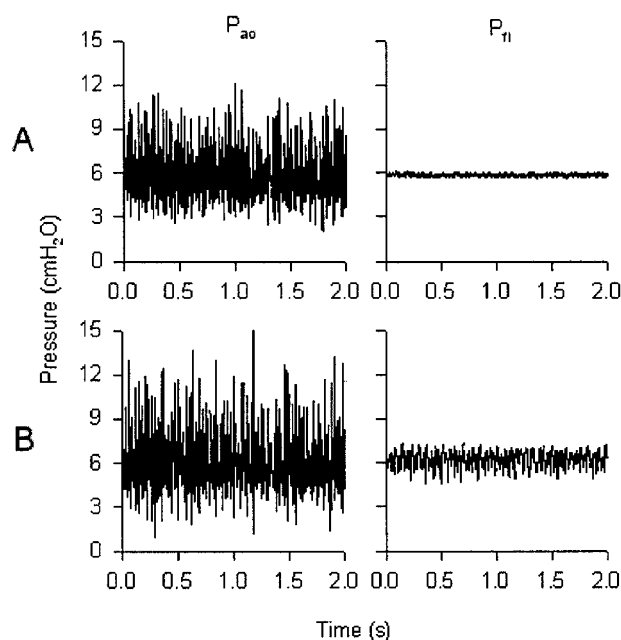
Figure 2. Representative time-series plots of pressure waveforms during bubble CPAP. Pressure measurements obtained at the airway opening (P_{ao}; *left*) and within the model lung (P_{fl}; *right*). Figure shows representative pressure measurements obtained at 1.5 mL/cm H_2O (*A*) and at 0.1 mL/cm H_2O (*B*).

(Fig. 3 *top*). Lung compliance did not influence the P_{ao} or the P_{fl}. An increase in flow was associated with increased mean pressure at both measuring sites.

For any given flow, there was a marked increase in the range of the pressure oscillations within the lung model as lung compliance decreased despite the absence of any change in the range of
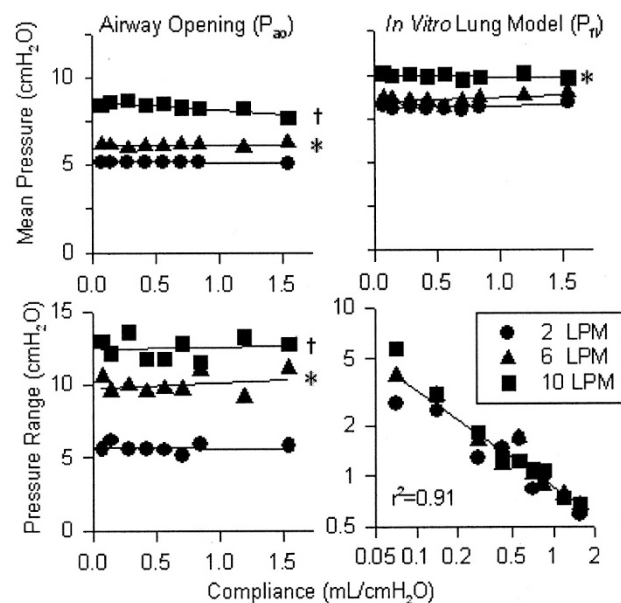
Figure 3. Influence of flow and compliance on mean and oscillatory range of pressure during bubble CPAP. (*Top*) Mean pressure. (*Bottom*) Range of oscillatory pressures in bubble CPAP pressure waveform. *$p < 0.05$ and †$p < 0.001$ *vs* 6 L/min. Duplicate measurements were obtained at each compliance and flow.

pressure oscillations measured at the airway opening (Fig. 3 *bottom*). The relationship between lung model pressure range and compliance conformed to a power law. An increase in flow was associated with an increase in the range of pressures measured at the airway opening, whereas there was negligible effect on P_{fl} except at low compliance.

Transformation of the oscillatory pressure waveforms from the time domain into the frequency domain using power spectral analysis showed that compliance alters not only the power but also the frequency content of the transmitted waveform with an apparent shift of the dominant frequencies to the right as compliance decreased (Fig. 4). The mean value of those frequency components with power >75% of the maximum power decreased from 15.5 to 8.7 Hz as compliance increased from 0.1 to 1.2 mL/cm H_2O (Fig. 5). There was a negative power–law relationship between the decrease in mean peak frequency and increasing compliance

DISCUSSION

The main findings of this study are that the magnitude and the frequency of pressure oscillations transmitted to the model lung during bubble CPAP are influenced by both the applied bias flow and the load impedance (mechanical characteristics) of the lung model.
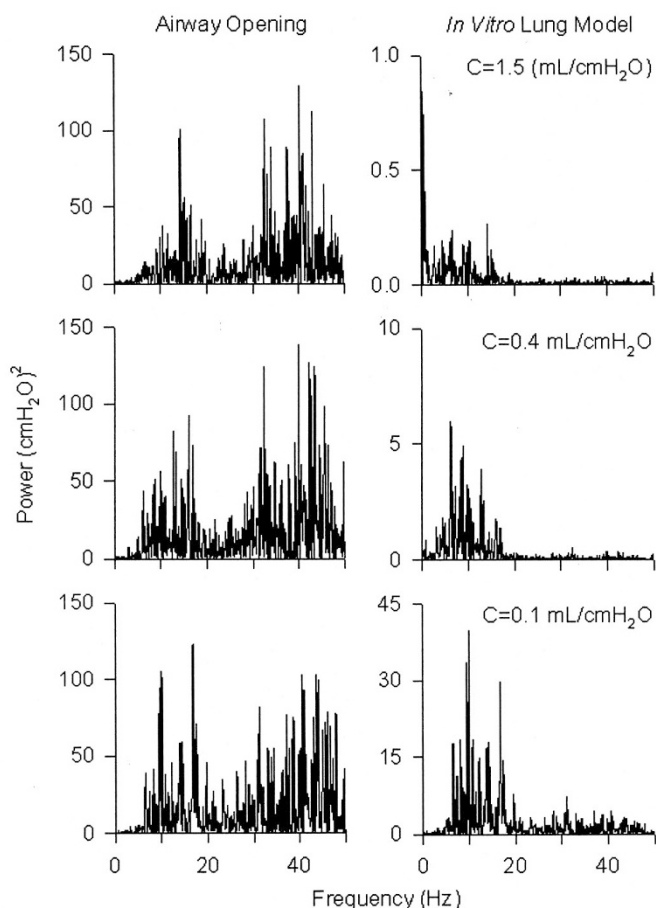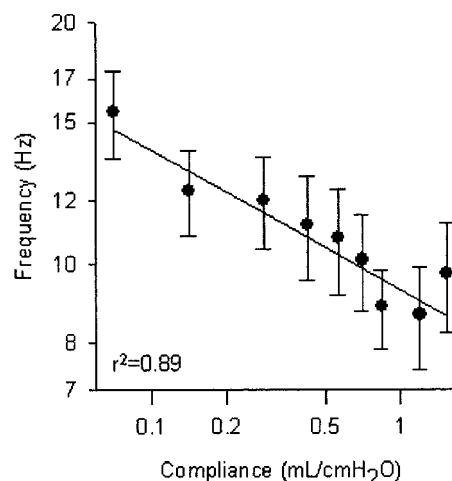

Figure 5. Effect of compliance on dominant frequencies transmitted to lung during bubble CPAP. Graph demonstrates mean (±95% confidence interval) frequency of spectral components at which power was >75% of maximum power within a representative measurement at each compliance and a flow of 6 L/min.

Study limitations. Although an *in vitro* lung model may seem to be a grossly simplified representation of the respiratory system, it has proved useful in the past for investigating aspects of pressure and volume transmission during high-frequency oscillatory ventilation (5–7). Predictions about pressure transmission in the preterm lung have been shown to be reproducible in animal studies (8–10).

No leak was incorporated in the *in vitro* lung model; therefore, it is likely that the amplitude of the oscillations transmitted to the model lung are greater than those observed in the clinical situation. However, it is clear that some oscillations are transmitted *in vivo*, with reports of visible chest vibrations when bubble CPAP is used in preterm lambs (11) and infants (4).

Implications of findings for lung volume recruitment. Promotion of lung volume recruitment under atelectatic conditions and maintenance of existing recruited lung are vital goals of CPAP treatment. Understanding how bubble CPAP may affect lung volume may allow us to better understand whether this technique potentially offers a specific advantage over other CPAP methods.

An apparent limitation of the present study is the constancy of lung compliance during each period in which bubble CPAP was applied. This modeling assumption would not hold under the pathologic circumstances of periodic recruitment-derecruitment of lung units or during the transition from an atelectatic to a permanently more recruited state. However, along the line of the findings in our measurements, we can predict the changes in bubble CPAP performance during the changes in lung mechanics. If, as a consequence of recruitment in inflation, compliance increases, then more flow would be directed to the lungs, which in turn would result in the decrease in both mean P_{ao} and the intensity of bubble formation (*i.e.* the oscillatory changes in P_{ao}). If derecruitment occurs, either in a recurrent way or as a consequence of pathologic processes, then a higher proportion of inspiratory flow is directed to the

Figure 4. Representative power spectral analysis of *in vitro* pressure waveforms during bubble CPAP. (*Left*) Airway opening. (*Right*) *In vitro* lung model. C, compliance.

expiratory line, resulting in higher values of mean P_{ao} and the oscillatory excursions, facilitating the reopening of atelectatic areas. The increase and decrease in lung compliance are in accordance with the need for a smaller or higher degree, respectively, of bubble CPAP ventilatory support.

Suki and colleagues (12,13) suggested that stochastic resonance effects may explain the augmentation of lung volume recruitment and improved oxygenation observed when biologic noise is added to breathing frequency and tidal volumes during conventional ventilation (14). Stochastic resonance is most simply described as the addition of noise to an input signal to enhance output in a nonlinear system. It is a widespread, naturally occurring phenomenon that can be seen reflected in the patterns of world weather, fluctuations on the stock market, population biology, and optimal functioning of neural networks, to name but a few. The essential ingredients for stochastic resonance are a nonlinear dynamic system, a weak biologic signal, and superimposed noise. Application of an optimal amount of noise to the underlying weak signal (input) achieves an optimal resonance (enhanced output) effect.

Measurements of terminal airway resistance (15) and more recent acoustic measurements in collapsed canine lungs during slow-volume recruitment procedures (16) have shown that the recruitment of terminal airspaces are governed by power-law distributions, arising from avalanches associated with threshold phenomena propagating down a branching tree structure. The application of biologically variable respiratory rates and tidal volume have demonstrated superior oxygenation and improved compliance in a porcine oleic acid model of lung injury (14,17–20). Noise superimposed on the peak inspiratory pressure (PIP) during conventional ventilation can promote recruitment of collapsed lung zones when the PIP is at or around the lower inflexure (13). Whereas PIP exceeding the mean PIP will promote recruitment of additional lung units, minimal loss of lung volume occurs when PIP lower than the mean PIP is delivered as this is occurring on the flat slope of the pressure-volume inflation curve. The net effect is one of volume recruitment of some collapsed lung units and stabilization of open units. There is some evidence that this approach may also promote production of endogenous surfactant (21). Previous research has considered this concept only in relation to cyclic mechanical ventilation, and the relevance of noise to potential for lung volume recruitment in bubble CPAP has not been considered.

In bubble CPAP, the oscillatory component of the pressure waveform is superimposed on the desired mean CPAP and also the low-frequency pressure fluctuations imposed by the patient's own spontaneous respiratory efforts. Although the net volume output of the superimposed oscillations is essentially zero, these are applied to a nonlinear dynamic system—the lung—with a potentially very different net effect. The noisy nature of the pressure waveform generated from the bubbling in the expiratory line may actually promote airway opening events and consequently lung volume recruitment if superimposed on subthreshold respiratory effort. Pressure fluctuations above the mean pressure will promote greater lung volume recruitment than pressure fluctuations that fall below the mean pressure, provided that the upper limit of the pressure fluctu-

ations lies above the point of the lower inflexure of collapsed lung units on the pressure volume curve (21).

A key feature of the stochastic resonance phenomenon is that there is an optimum level of noise with respect to both power as amplitude and frequency (bandwidth). The pressure waveform produced by bubble CPAP is an extremely noisy signal with dominant frequencies around the 5- to 20- and 40- to 100-Hz zones. Our *in vitro* model lung study showed that the frequency content and amplitude of the transmitted pressure waveform changes with lung compliance. In simple terms, these changes are associated with the low-pass mechanical filtering effect exerted by the lungs: the higher frequencies were more dominant, and a wider range of pressure fluctuations (and hence higher peak pressures) were present at low compliance. Parallel compartment modeling of a similar scenario during high-frequency oscillatory ventilation suggests that in the presence of inhomogeneous disease, adequately recruited compartments are protected from the larger pressure fluctuations as a result of more marked damping of the pressure waveform (9). In contrast, collapsed regions of the lung would also see the higher frequencies and amplitudes promoting volume recruitment within these regions and potentially enhancing gas mixing resulting from facilitated diffusion. We question whether this scaling of both frequency and amplitude of the bubble-derived noise may represent a natural filter, in essence optimizing the amount of noise transmitted to the lung during bubble CPAP for the prevailing physiologic conditions. The amount of noise could be influenced further by the choice of applied bias flow, obviously *via* the effect of bias flow on bubble production. The impact of bubble CPAP on lung volume recruitment needs to be studied in an *in vivo* model of moderate atelectasis against a CPAP technique that has a similar low external resistive load with study end points that include lung volume, indices of ventilation inhomogeneity, and lung mechanics.

CONCLUSION

In a closed system, increasing flow increased both mean pressure and range of pressure oscillations transmitted to a model lung during bubble CPAP, whereas decreasing compliance increased the frequency content and the magnitude of the transmitted oscillatory pressures. Use of bubble CPAP in the poorly compliant lung may promote lung volume recruitment through the mechanism of stochastic resonance and augment the efficiency of gas mixing. This hypothesis needs to be tested in an *in vivo* model of neonatal respiratory disease.

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