THE EFFECTS OF LIQUID VENTILATION ON CARDIOPULMONARY FUNCTION IN PRETERM LAMBS

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SUMMARY

The effects of fluorocarbon ventilation on cardiopulmonary function were studied in 8 preterm lambs, 132-136 days gestation. After mechanical ventilation with 100% oxygen (control period), the lambs were ventilated with fluorocarbon ($P_{iO_2} = 622$ torr). The liquid was then removed from their lungs and gas ventilation resumed (recovery period). During normothermic liquid breathing the alveolar-arterial O_2 gradient (A-a DO_2) decreased ($P < 0.01$) from control by 154 torr and remained decreased ($P < 0.05$) by 85 torr during recovery. Dynamic lung compliance (C_L) increased 50% ($P < 0.05$); PaO_2 increased 50% ($P < 0.05$); and $PaCO_2$ decreased 29% ($P < 0.01$) as compared to control values. The change in A-a DO_2 and PaO_2 before and after liquid ventilation was correlated ($r = 0.79$ and $P < 0.01$) with control C_L . There was a gradual decrease ($P < 0.01$) in mean arterial pressure from 62 ± 5.4 torr (control) to 53.1 ± 9.3 torr (recovery); however, there were no significant alterations in mean central venous pressure, heart rate, or mean electrical axis.

SPECULATION

These data demonstrate an improvement in gas exchange and dynamic lung compliance in preterm lambs after liquid fluorocarbon ventilation. Regression analysis suggests that the improvement in PaO_2 and A-a DO_2 was best in those lambs with the lowest initial lung compliance. Furthermore, the secondary effects of improved ventilation and pulmonary blood flow, in the long run could facilitate surfactant synthesis.

INTRODUCTION

Pulmonary gas exchange (4,6,11,14) and surface active properties (12) as well as functional (22,25,30) and structural changes in the lung (18) have been extensively studied in the adult mammalian species during and subsequent to fluorocarbon liquid ventilation. Corollary investigations into long-term toxicity have demonstrated no adverse morphologic, biochemical or histologic effects after ventilation with fluorocarbon liquid (7,13).

Recent studies have revealed the feasibility of ventilation with fluorocarbon in premature experimental animals (21,26,31). In contrast to the cardiopulmonary instability, which occurs during gas ventilation (19,27,29), premature lambs ventilated with fluorocarbon liquid exhibit good gas exchange and stable blood gas tensions (26). Numerous studies have indicated that respiratory distress and pulmonary instability in the newborn are associated with pulmonary surfactant insufficiency. Because in the liquid-filled lung the air-liquid interface is abolished, it has been suggested that this elimination of high surface forces could account for improved gas exchange and pulmonary stability (21). In addition to reduced surface-active forces and alveolar inflation pressures during liquid ventilation, there is evidence that surface forces may be reduced in immature lungs after ventilation with low surface tension (15 dynes/cm) fluorocarbon liquid (21,26). These findings contradict studies done with adult animals in which lung mechanics and gas exchange deteriorated after ventilation with fluorocarbon liquids (6,22,25,30).

The current literature offers limited data with respect to the effects of liquid ventilation on cardiopulmonary function of the immature lung; therefore, the first objective of this study was to quantitate comprehensive cardiopulmonary function data in the preterm lamb during and after such ventilation. There are also apparent differences in pulmonary function response to liquid ventilation between preterm and adult animals. With this in mind we sought to correlate the changes in lung function after liquid ventilation with respiratory maturity by measuring arterial blood gases, alveolar-arterial oxygen gradients, and lung mechanics. Based on the data presented herein as well as theoretical surface tension phenomena and ventilation-perfusion relationships, we have attempted to explain alterations in pulmonary function after liquid ventilation.

METHODS

Animal Preparation

Eight preterm lambs at a mean gestational age of 134 days (147 ± 3 day term) and a mean birthweight of 3.4 kg (range 2.7-4.9 kg) were delivered by cesarean section while the ewe was restrained in a prone position. Epidural anesthesia, using 0.5-1.0 mg/kg of 0.75% bupivacaine HCl (Marcaine), was induced before the ewe was placed on the table. After the uterus had been exposed and opened sufficiently for the head of the lamb to emerge, a rubber glove containing warm saline solution was placed over the head of the animal to prevent inspiration of air. After a local infiltration with 1% solution (approximately 4 mg/kg), the right carotid artery and right external jugular vein were each cannulated with French No. 8 polyvinyl catheters. A cannula was inserted through a tracheotomy midway along the trachea, with its tip positioned proximal to the carina. After aspiration of lung fluid from the trachea, the rubber glove was removed from the animal's head and the lamb was delivered. The umbilical cord was then clamped, tied, and cut while 2.5 ml/kg of 50% sodium bicarbonate solution was administered intravenously. Simultaneously, placental blood was collected in a heparinized beaker and stored for later use. The lamb was wiped dry, weighed, and placed under a heat lamp, during which time the tracheal tube was connected to a volume-controlled piston pump (Harvard small animal respirator). At this time, pancuronium bromide (Pavulon, 0.1 mg/kg) was administered as an intravenous bolus and followed by a continuous infusion (0.1 mg/kg/hr).

Gas Ventilation (Control and Recovery) Procedure

Initially, tidal volume was set for 10-15 ml/kg at a pump frequency of 40-50 breaths/min, with equal periods of inspiration and expiration on 100% inspired oxygen concentration ($F_{iO_2} = 1.0$). In most cases, lambs were placed on positive end-expiratory pressure (PEEP) by connecting the outlet of the respirator to a gallon jug partially filled with water. The expired air line was immersed in the water and acted as a blow-off valve to provide 1-6 cm H_2O PEEP. Care was taken to maintain a peak intratracheal pressure of less than 55 cm H_2O in order to minimize pulmonary air leaks. The tidal volume, respiratory frequency and level of PEEP were then adjusted to optimize the arterial oxygen tension (PaO_2). An intravenous drip of 10% glucose solution containing 10 mEq of sodium bicarbonate per 100 ml was maintained at 3ml/kg/hr. If the pH fell below 7.25 after $PaCO_2$ was stabilized below 60 torr, additional bicarbonate solution was administered intravenously to correct the base deficit using the formula (3):

$$mEq \text{ base needed} = \text{-base excess (mEq/liter)} \times \text{body weight (kg)} \times 0.3.$$

The animal's rectal, esophageal, body surface and tracheal temperatures were monitored with a digital centrifigade thermometer and thermistors (Cole-Parmer, 8502-25).

Liquid Ventilation Procedure

Liquid ventilation with fluorocarbon was achieved using a previously described and modified liquid-breathing system (25,26). After control data were collected during mechanical ventilation (90 mins. duration), liquid ventilation was initiated.

Fluorocarbon liquid was warmed to 39°C to maintain the animal's body temperature during liquid breathing. The inspired oxygen tension (P_{iO_2}) and inspired carbon dioxide tension (P_{iCO_2}) of the liquid were sampled from the system before and during liquid ventilation of the animal. Oxygenated liquid was removed from the liquid-breathing system and placed in a suspended reservoir. A volume equivalent to the functional residual capacity (FRC) of the lungs was instilled from this reservoir via the tracheotomy tube into the animal's lungs. Postural and thoracic manipulations were performed to force out any large pockets of oxygen that might have become trapped in the lungs after instillation of the liquid. Such gas was free to escape into the reservoir rather than into the gas-free liquid-breathing system. Because the animal was previously ventilated with 100% oxygen, it is assumed that all gas remaining in the lungs was oxygen or carbon dioxide, which was either absorbed by the liquid or utilized by the animal's metabolism. The animal was then connected to the mechanically assisted liquid-breathing system. Very few bubbles of gas were observed through the clear polyvinyl chloride tracheostomy tube.

To measure the change in the animal's weight, a previously described strain gauge platform was employed (26). This was necessary to monitor both tidal volume (V_T) and functional residual capacity (FRC) and these measurements were accurate to within 1.0 ml of fluorocarbon liquid. Based on previous experiments (9,23), ventilation schemes were adjusted for effective carbon dioxide elimination and maintenance of physiologic arterial carbon dioxide tensions. Animals were ventilated for 45 mins. about a mean FRC of 26.5 ± 4.8 ml/kg, V_T of 14.2 ± 1.8 ml/kg and frequency of 9.6 ± 1.2 breaths/min. The fluorocarbon was then drained from the lungs and airways by tilting the animal. With postural and thoracic manipulations, a volume of liquid approximately equal to that instilled was collected by free flow. At this time (the recovery phase) the animal was reconnected to the gas ventilator ($F_{iO_2} = 1.0$) for another 30 mins. The tidal volume, respiratory rate settings, and inspiratory/expiratory time ratios were identical to those of the control period.

Experimental Methods

Arterial blood gas tensions and pH were determined at 20-minute intervals on one ml samples after two ml had been withdrawn to clear out the carotid catheter. These two ml were then reinfused and followed by one ml of heparinized saline solution. If the hematocrit of the lamb fell below 40% as a result of blood sampling, fetal blood collected from the ewe's placenta was infused into the lamb. The blood samples were analyzed for PaO_2 , $PaCO_2$, using a radiometer amplifier and cuvettes with membrane-covered oxygen and carbon dioxide electrodes. A capillary glass electrode was used to measure the pH. All electrodes were enclosed in a water bath thermostated at 37°C. Blood gas and pH measurements were corrected to body temperature of the animal (17,20).

The alveolar-arterial oxygen gradient was determined from measured blood gas tensions and estimated mean alveolar oxygen tensions by using the alveolar gas equation and assuming that the alveolar $PaCO_2$ was equal to the $PaCO_2$ and that the respiratory exchange ratio was 1.0. In the recovery period the alveolar oxygen tension PAO_2 was corrected for the vapor pressure (57 torr at 37°C) of the fluorocarbon liquid.

Arterial blood was assayed for lactate and pyruvate concentration using a standard enzymatic technique (24). Blood samples (2 ml) were drawn into chilled test tubes. These tubes contained measured amounts of cold perchloric acid for precipitation of proteins and were immediately spun down in a refrigerated centrifuge at minus 40°C. The supernatant material was removed for analysis.

Pulmonary mechanics were measured in the control and recovery periods after arterial blood gases and pH of the lambs were stabilized. Mechanics of breathing were studied by simultaneously monitoring transpulmonary pressure, inspiratory and expiratory flow rates, and tidal volume on a Polygraph recorder (Grass Model 7). Intraesophageal pressure was measured with an esophageal balloon, 2.5 cm in length and 3.0 mm in diameter. The balloon was filled with 0.5 ml of air and positioned in the lower third of the esophagus. The esophageal catheter was protected at the mouth with a polyvinyl tube and was connected to one side of a differential strain gauge transducer (Statham PM131TC) with a low volume adapter inserted at the inlet. Tracheal pressure was transmitted by connecting the other side of the same transducer to the side tap on the tracheal tube. The recorded signal represented an estimate of transpulmonary pressure. Airflow was measured with a pneumotachograph (Fleisch #0) connected to a differential strain gauge pressure transducer (Statham PM283TC) of low volume displacement. Tidal volume was determined by electronic integration of air flow. The transducers and esophageal balloon were tested for transient response and did not introduce phase lag or damping in the frequency range encountered (0.1-4.0 Hz). The pneumotachograph was removed from the ventilating circuit except during measurements to minimize dead space.

Functional residual capacity was determined by a modified closed-circuit helium dilution technique (8). An electrically operated fast closing valve

(closure time within 3 msec) sequenced by a relay was used. When the valve was energized, the endotracheal tube connection was switched from the mechanical ventilator to a manually operated rebreathing bag. Dead space of the system, including the endotracheal tube and valve was 8.4 ml.

Values of respiratory rate were ascertained directly from the polygraph record and dynamic lung compliance was determined graphically by the method of Neergaard and Kirz (16). Lung resistance was computed by dividing the difference in transpulmonary pressure at midvolume points during inspiration and expiration by the difference in airflow at those instants. Each resistance and compliance determination was based on the average of at least three breaths. A constant tidal volume, level of PEEP, and frequency history preceded all measurements.

During gas breathing (control and recovery) oxygen consumption was determined by closed circuit spirometry method. The animal was mechanically ventilated from a 100% oxygen-filled circuit which consisted of: a spirometer to supply oxygen and to record its volume change, a Baralyme CO₂ absorber to remove expired CO₂, and a volume controlled piston pump (Harvard small animal respirator). The respirator incorporated an oscillating slide valve mechanism which restricted flow in the desired direction. Positive end-expiratory pressure could be incorporated into the system as needed, maintaining a closed loop. The system was found leak-free when tested for periods up to two hours. Oxygen consumption recordings were made using a wide scale strip-chart recorder (Varian, Model 1976).

Central venous pressure (CVP) and mean arterial pressure (MAP) were measured by connecting the jugular vein and carotid artery catheters to the Statham P23A transducer, respectively. Pressures were recorded on a Grass Model 7 polygraph recorder. Heart rate was obtained from blood pressure recordings. A standard 12-lead electrocardiogram was monitored on a Cambridge VS-111 EKG machine and recorded on a Grass Model 7 polygraph. Mean electrical axis (MEA) was determined using vector analysis.

Although it would have been possible to keep several of the preterm animals alive (26,27,28) this was not the purpose of the experiment; therefore, the animals were killed during the recovery phase. All data obtained during gas ventilation (control and recovery) were compared to those collected during approximately 45 min of assisted, liquid fluorocarbon ventilation. Statistical analysis with paired students 't' test were used to evaluate the data.

RESULTS

The trend in mean $\pm$ SE blood gas levels, P_iO₂ and A-a DO₂ are illustrated in Figure 1 for all eight lambs. As shown, during gas ventilation with 100% O₂ (control), mean PaO₂ was 140 $\pm$ 31 torr and significantly increased (P < 0.05) to 182 $\pm$ 24 torr after liquid ventilation. Mean PaCO₂ was markedly decreased from 35 $\pm$ 2.5 torr during the control period to 27 $\pm$ 4 torr during the recovery period (P < 0.01). In addition, the mean A-a DO₂ decreased significantly from 538 $\pm$ 32 torr during the control period to 384 $\pm$ 29 torr during liquid ventilation (P < 0.01). Mean A-a DO₂ was also decreased (P < 0.05) from the control values during recovery (453 $\pm$ 20 torr).

Arterial blood chemistry data for individual lambs are presented in Table 1 along with group mean $\pm$ SE values. As shown, arterial pH decreased from 7.36 $\pm$ 0.02 (control) to 7.29 $\pm$ 0.04 during liquid ventilation (P < 0.05) and returned to control values during the recovery phase. There was a concomitant increase (94%) in the base deficit during liquid ventilation from 4.1 $\pm$ 1.5 to 7.9 $\pm$ 2.2 mEq HCO₃⁻ (P < 0.05) in all lambs except one (2815). It is also noteworthy that arterial lactate concentration and the lactate-to-pyruvate ratio (L/P) demonstrated an increasing trend throughout the experiments.

A representative tracing of cardiopulmonary data during assisted gas breathing (control and recovery) is illustrated in Figure 2. As shown, mean arterial pressure decreased from control to recovery, whereas central venous pressure and heart rate are relatively unchanged. A striking feature in this tracing is that for similar tidal volumes the transpulmonary pressure is reduced by approximately 50% after liquid breathing. Control pulmonary function results and oxygen consumption measurements from 8 lambs are summarized in Table 2, with values for individual animals. As shown in Figure 3, dynamic lung compliance (C_L) increased 50% from 0.56 $\pm$ 0.08 ml/cm H₂O/kg during the control period to 0.76 $\pm$ 0.12 ml/cm H₂O/kg during recovery (P < 0.01). Concomitantly, peak intratracheal pressure decreased in all animals (p < 0.01) after ventilation with fluorocarbon liquid. Mean control values for FRC equaled 30.7 $\pm$ 5.0 ml which was in agreement with that reported for lambs of similar weight and gestation (27,28). Available data did not permit an accurate report of FRC measurements postliquid ventilation because fluorocarbon vapor interfered with the analysis of helium concentrations used in the gas dilution technique for determination of FRC. Finally, recovery inspiratory resistance, expiratory resistance, and oxygen consumption values were not statistically different from preliquid measurements. Figure 4 illustrates the relationship between PaO₂, the change in PaO₂ from control to recovery period Δ PaO₂, the change in A-a DO₂ from control to recovery period Δ A-a DO₂ and control C_L. As shown in the upper portion of this figure, there was a direct correlation (r = 0.82; P < 0.01) between control PaO₂ and C_L indicating a relationship between arterial blood oxygenation and mechanical properties of the immature lung. Arterial oxygen tension can be further described as a linear function of C_L by:

$$PaO_2 = 281.2 C_L - 45.8 \quad (1)$$

The increase in PaO₂ and decrease in A-a DO₂ after liquid ventilation were also found to correlate (r = 0.79; P < 0.01) with control C_L. As shown in Figure 3, the increase in PaO₂ and the decrease in A-a DO₂ after liquid ventilation could be respectively described as a linear function of C_L by:

$$\Delta PaO_2 = 339.2 C_L + 261.8 \quad (2)$$

and

$$\Delta A-a DO_2 = 332.8 C_L - 306.2 \quad (3)$$

Based on regression relationships (1), (2), and (3), those lambs with low C_L values demonstrated the lowest PaO₂ values in the control period. These same lambs showed the greatest improvement in PaO₂ and A-a DO₂ after liquid ventilation. In contrast, those lambs with high C_L values exhibited the highest PaO₂ values but showed the least improvement in PaO₂ and A-a DO₂ after ventilation with fluorocarbon.

Despite efforts to maintain body temperature, hypothermia (35.9°C) was observed during the control period. With an average liquid temperature of 38.6°C measured at the trachea, mean rectal temperature increased from 35.9°C (control) to 36.5°C during liquid ventilation. Likewise, mean esophageal and surface temperature increased 36.8°C, and 35.8°C to 37.5°C, respectively. All temperatures returned to control levels during the recovery period.

There were no significant alterations in mean CVP = 3.7 $\pm$ 0.7 cm H₂O and heart rate of 166 $\pm$ 11 beats/min during the course of experiments. There was a gradual decrease (P < 0.01) in MAP from 62 $\pm$ 5.4 torr (control) to 53.1 $\pm$ 9.3 torr (recovery), but this trend has been previously reported in both preterm lambs (29) and humans during the first few postnatal hours. From the EKG recordings, mean group data for mean electrical axis were 258 $\pm$ 10 SE degrees during the control period and did not significantly change during the liquid ventilation and gas recovery periods.

All animals survived liquid ventilation except for lamb 2814 which developed a pneumothorax during the control period and died after 30 min of liquid ventilation.

DISCUSSION

This study confirms that the physiologic profile of the premature lamb is one of biologic instability in the first few hours after birth (5,19,29). These preterm lambs were unable to breathe and all required mechanical ventilation on 100% oxygen during the control period. As expected, all animals exhibited some degree of intra- and extra-pulmonary shunting (5,33) during the control period. This was probably due to atelectasis and persistent fetal circulation which is characteristic of the premature animal and is suggested by the mean arterial PaO₂ of 140 $\pm$ 31 torr and A-a DO₂ of 538 $\pm$ 31 torr with an inspired P_iO₂ of 713 torr. Functional residual capacity and pulmonary resistance data were consistent with the literature for lambs of similar weight and gestation; however, dynamic lung compliance, 0.57 ml/cm H₂O/kg was markedly lower. The unstable blood gas levels, metabolic acidosis and hyperlactatemia in these animals were in agreement with those found by Stahlman et al (29) in severely distressed lambs. Conventional techniques for respiratory management (mechanical ventilation, 100% inspired O₂, 2-6 cm H₂O end distending pressure) improved blood gas levels and acid-base status from spontaneous ventilation values, but no further improvement was observed during this early neonatal period of mechanical gas ventilation and is in agreement with previous observations (19,27,29).

The improvement in gas exchange during and after liquid ventilation suggests cardiopulmonary changes that are not typical to preterm lambs during the postnatal period. Mean A-a DO₂ decreased by 154 torr to 384 $\pm$ 29 SE torr during liquid ventilation (Fig. 1). The improvement of PaO₂ and A-a DO₂ continued throughout the recovery period and was accompanied by a decrease in PaCO₂. The measured increase in PaO₂ is even more dramatic when one considers that the alveolar P_AO₂ was reduced in the recovery period by the additional vapor pressure of residual fluorocarbon (57 torr at 37°C) in the lungs. In previous studies with adult animals and lambs (6,22,25,30) similar improvements in arterial oxygenation and A-a DO₂ were not observed during or following liquid ventilation. However, these animals were more mature and had better gas exchange and lower A-a DO₂ before liquid ventilation. Our present data demonstrate (Fig. 4) that animals with the most severe respiratory problems (i.e., lowest lung compliance and arterial oxygen tension) show the greatest improvement in PaO₂ and A-a DO₂ following liquid ventilation.

The improvement in gas exchange in spite of a reduction in P_iO₂ during liquid ventilation could involve several possible interrelated mechanisms. The air-liquid alveolar interface is abolished in the liquid-filled lung, thereby reducing high surface forces and possibly eliminating nonuniform ventilation which exist in the premature lung. Studies have demonstrated that pulmonary blood flow in the saline-filled lung is more evenly distributed than in the gas-filled lung (32). This may be particularly significant in distressed preterm lambs which exhibit extensive intrapulmonary shunting and elevated pulmonary vascular resistance (33). Reduction in atelectasis and a better ventilation/perfusion distribution would decrease intrapulmonary shunting and ultimately improve arterial oxygenation thus effecting a reduction in A-a DO₂ as illustrated in Figure 4.

During liquid ventilation arterial pH decreased significantly; however, a concomitant increase in base deficit despite constant bicarbonate infusion indicates a significant increase in the metabolic component of the acidosis and was in agreement with previous liquid breathing experiments (10,11). The present study demonstrates a significant increase (44.6%; P < 0.05) in arterial lactate concentration during liquid ventilation which has not been previously reported in preterm animals. Arterial L/P was significantly elevated indicating an increased state of anaerobiosis in which the lactate-to-pyruvate equilibrium was shifted toward lactate (1). The accelerated anaerobic metabolism and lactate production may reflect the decreased tissue oxygen delivery and redistribution of cardiac output in adult cats previously reported as a consequence of liquid ventilation (10). In addition, hyperlactatemia and acidosis may also be associated with the severity of respiratory distress reported for premature lambs (29).

Rufer and Spitzer (21) have shown that after liquid ventilation, the static lung compliance of immature mini-pigs approaches that of the mature animal. In similar experiments with premature lambs, peak intratracheal pressures measured after return to gas breathing were significantly lower than preliquid ventilation values (26). Our studies are in agreement with these studies in that intratracheal pressure decreased (30%; P < 0.05) postliquid ventilation. In addition to previous work, we found that dynamic lung compliance increased (50%; P < 0.01) with no significant alterations in pulmonary resistance. In contrast several investigators have reported a marked deterioration in pulmonary mechanics of adult species after fluorocarbon ventilation (22,25,30). An important difference between the preterm and adult studies is the maturity of the respiratory system of the experimental animal. Minimal surface tension can vary from as low as 2 dynes/cm in an adult to as high as 63 dynes/cm in an infant with respiratory distress (2). Because the surface tension of fluorocarbon is 15 dynes/cm, residual fluorocarbon lining the alveolar surface would tend to reduce surface forces in distressed lungs and increase them in adult lungs. Based on surface properties of the lung, then distressed lambs such as those in this study are more likely to demonstrate an improvement in lung compliance, PaO₂ and A-a DO₂ than adults or more mature newborns.

It is possible that improved surface properties of the lung are not entirely responsible for increased lung compliance after liquid ventilation. Studies in newborns with respiratory distress syndrome have shown an improvement in dynamic lung compliance after surgical closure of a patent ductus arteriosus due to a speculated decrease in intrapulmonary blood volume and turgidity of the vascular (15). In the present study there was no direct evidence of ductal closure, in fact in many cases blood gases suggest that there was persistent right to left shunting during the recovery period; therefore, a decrease in blood flow through the ductus arteriosus due to improved gas exchange and blood oxygenation could only account for a small portion of the increase in lung compliance. Our data are insufficient to establish a decisive role for any of these additional factors.

Other possible explanations for the observed changes in pulmonary function measurements can be excluded with reasonable certainty. A change in the loca-

tion of the esophageal balloon between measurements was unlikely because the balloon was secured with tape to prevent movement during the experiment. Instrument calibrations, tidal volume, respiratory rate, pneumotachograph adaptors, and tracheal cannula position all remained constant throughout individual experiments. Before pulmonary function measurements, the tidal volume, end distending pressure, and breathing frequency were maintained constant to prevent alterations of lung volume which might otherwise have produced changes in lung mechanics. Finally, the transducer, pneumotachograph, and esophageal balloon were tested dynamically for transient response and did not introduce phase lag or damping in the frequency encountered (0.1-4.0 Hz).

In conclusion, this study demonstrates that it is possible to maintain good gas exchange in distressed premature lambs during normothermic liquid ventilation and that there is a subsequent improvement in PaO_2 and dynamic lung compliance. Furthermore, the secondary effects of improved ventilation and pulmonary blood flow could, in the long run, facilitate surfactant synthesis. One might question whether this form of ventilation may have a long-term deleterious effect on the developing newborn lung, but we cannot directly address these issues. It is noteworthy that long-term experiments (7,14) in adult dogs indicated scant morphologic, biochemical, and/or histologic evidence of toxicity after ventilation with fluorocarbon liquid.

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Figure 1: Inspired oxygen tension ($P_i\text{O}_2$), alveolar-arterial oxygen gradient ($A-a\text{DO}_2$), arterial oxygen tension (PaO_2), and arterial carbon dioxide tension (PaCO_2) during control, liquid, and recovery ventilation. * $p < 0.05$; ** $p < 0.01$.