Vibratory Ventilation Decreases Filtration of Fluid in the Lungs of Newborn Lambs

J. Usha Raj, Robert B. Goldberg, and Richard D. Bland
From the Cardiovascular Research Institute and Department of Pediatrics, University of California, San Francisco, San Francisco, California

SUMMARY. To compare effects of vibratory and mechanical ventilation on fluid balance in the newborn lung, we measured pulmonary arterial and left atrial pressures, pleural and airway pressures, lung blood flow and lymph flow, and concentrations of protein in lymph and plasma of 19 healthy lambs, 2-4 weeks old, during a 2- to 4-hour period of spontaneous breathing, followed by 4-8 hours of mechanical ventilation at 30 breaths/min and 4-8 hours of vibratory ventilation, in which the lambs received 1650 whiffs of air/min. In 8 of 22 studies, we increased lung microvascular pressure by filling a balloon catheter in the left atrium with saline. There was no significant difference in mean airway pressure during the two types of ventilation. Despite higher lung vascular pressures, lymph flow was less and lymph protein concentration was greater during vibratory than during mechanical ventilation. These findings are consistent with reduced lung fluid filtration, possibly from reduced pulmonary blood flow and increased perimicrovascular pressure, during vibratory ventilation. In eight lambs killed after 8 hours of vibratory ventilation, extravascular lung water was normal and microscopy showed no edema. We conclude that vibratory ventilation has no adverse effect on lung fluid balance and may benefit lambs by decreasing net filtration of fluid into their lungs. (Circ Res 53: 456-463, 1983)

IN 1942, Warren and Drinker reported that breathing movements have an important influence on lung fluid balance. They measured flow of lymph from the lungs of anesthetized dogs and found that it decreased when the lungs became motionless during brief periods of intratracheal insufflation with oxygen.

Bohn et al. (1980) demonstrated successful respiratory gas exchange for many hours in dogs receiving high-frequency oscillatory ventilation, in which normal breathing movements stop. To see what effect this type of ventilation would have on lung fluid balance, we measured steady state lung lymph flow, as an index of net filtration of fluid from the microcirculation into the pulmonary interstitium, of 19 healthy newborn lambs that received 4-8 hours of both vibratory and conventional mechanical ventilation. In 8 of 22 experiments, we increased lung microvascular pressure by saline-filling a balloon catheter in the left atrium of the lambs. With or without left atrial hypertension, lymph flow was less during vibratory ventilation than it was during conventional mechanical ventilation, and in lambs killed after 8 hours of vibratory ventilation, extravascular lung water was normal and microscopy showed no edema. These results indicate that vibratory ventilation has no adverse effect on lung fluid balance in healthy lambs, with or without increased pulmonary microvascular pressure.

Methods

Preparation of Lambs for Experiments

By methods previously described (Staub et al., 1975; Bland and McMillan, 1977), we surgically prepared 19 newborn lambs for collection of lung lymph and measurement of cardiac output and pressures in the pulmonary artery, left atrium, aorta, inferior vena cava, and pleural space. The lambs had two thoracotomies, one within 3 days of birth, and another 4-7 days later. During surgery, we used halothane and nitrous oxide anesthesia and a piston-type respirator for mechanical ventilation. Before and after surgery, the lambs remained with their ewes for feeding and warmth.

In the first operation, we placed polyvinyl catheters in the pulmonary artery and left atrium, in addition to a 3 Fr. thermistor (Gould Statham model SP5003, Gould, Inc.) in the pulmonary artery and an 8 Fr. rubber balloon catheter (Foley catheter, C.R. Bard, Inc.) in the left atrium. Through a leg incision, we threaded catheters into the abdominal aorta and inferior vena cava. In the second operation, we resected systemic lymphatics entering the caudal mediastinal lymph node and inserted a heparin-coated polyvinyl catheter (inner diameter 0.38 mm, outer diameter 0.89 mm) into the efferent duct of that node, which receives about two-thirds of total lung lymph in lambs (Humphreys et al., 1967). We tunneled the catheter beneath the pleura and through the chest wall, and secured it to the skin with a suture. We also placed a 4 X 2 cm silicone (Silastic, Dow Corning Corp.) balloon catheter in the pleural space for subsequent measurement of
Description of Experiments

The average weight of the 19 lambs at the time of experiments was 7.3 ± 1.3 kg; their average age was 16 ± 4 days. During studies, the lambs rested in a prone position on a canvas sling that did not interfere with respiratory movements. A radiant warmer above the sling kept their body temperature constant. We intermittently flushed all vascular catheters with 0.5–1 ml of isotonic saline containing 10 U of heparin per ml. This volume of fluid had no significant effect on body weight, vascular pressures, or concentrations of protein in plasma. We continuously measured pressures in the pulmonary artery, left atrium, aorta, vena cava, and pleural space with calibrated transducers (Statham P23DC and 131TC, Statham Instruments) connected to a six-channel amplifier-recorder (Grass Instruments). Zero reference level for measurement of vascular pressures was a line drawn on the lambs’ skin at the level of the left atrium at the time of surgery. For measurement of pleural pressure, zero reference was atmospheric pressure. We measured cardiac output by thermal indicator dilution (Rudolph, 1974) at frequent intervals, and obtained samples of lymph in heparinized test tubes every 30 minutes. Hourly, we collected samples of arterial blood for measurement of packed cell volume (hematocrit), pH, blood gas tensions, and plasma protein concentration.

We did a total of 22 experiments: the left atrial balloon catheter was empty in 14 and filled with saline in 8. Each experiment consisted of a 2- to 4-hour control period, followed by two 4- to 8-hour experimental periods. In the control period, the lambs breathed spontaneously and had no sedation. During both experimental periods, they received pancuronium bromide (Pavulon, Organon Inc.) intravenously, 0.05 mg/kg body weight, as often as needed for paralysis, and morphine sulfate intramuscularly, 0.1 mg/kg, for analgesia and sedation. In one experimental period, the lambs had mechanical ventilation from a piston-type respirator (Harvard model 607, Harvard Apparatus) that delivered 30 breaths of air/min with an end-expiratory pressure of 1–2 torr and a tidal volume set to keep the partial pressure of carbon dioxide in arterial blood at 35–40 torr. In the other experimental period, the lambs received 1650 whiffs of air/min from an Emerson Airway Vibrator (JH Emerson Co.). We alternated the sequence of mechanical and vibratory ventilation, so that each was first in 11 experiments (seven at normal left atrial pressure, four at increased left atrial pressure).

Figure 1 is a schematic drawing of the airway vibrator apparatus that we used. It consists of a motor that drives a hard rubber diaphragm up and down 1650 times/min, delivering a tidal volume of no more than 25 ml. We used a loose-fitting 4.5- or 5-mm endotracheal tube (Rusch Inc.), the cuff of which was inflated during conventional ventilation and deflated during vibration so that gas could escape either through the trachea or through an 8 Fr. polyvinyl catheter (Argyl Feeding Tube, Sherwood Medical) attached to the endotracheal tube. Through that catheter, which was connected to a Statham 131TC strain gauge, we measured mean pressure in the distal airway continuously throughout mechanical ventilation and intermittently throughout vibratory ventilation. During vibration, we regulated airway pressure, oxygenation, and carbon dioxide elimination by changing the flow of fresh air entering the system. Air flow averaged 3.6 ± 1.3 liters/min in the 14 studies done on lambs with normal left atrial pressure and 5.2 ± 1.7 liters/min during the eight studies in which lambs had elevated left atrial pressure. Frequent suctioning of copious amounts of secretions in the oropharynx and upper airway was essential during vibratory ventilation.

Postmortem Studies

We resected the lungs of eight lambs at the conclusion of vibratory ventilation for 8 hours: left atrial balloon catheters were empty in four and filled with saline in four. We also removed the lungs of four lambs in which left atrial pressure was increased during 8 hours of conventional mechanical ventilation. To obtain the lungs of the lambs, we intravenously injected pentobarbital sodium (Diamond Laboratories), 20 mg/kg body weight, rapidly split the sternum, aspirated blood from the heart, and clamped both hilı at the prevailing airway pressure (9 ± 2 torr). We froze a piece of inflated lung in liquid nitrogen for subsequent microscopy and homogenized the remaining tissue for measurement of its blood and extravascular water content by a modification (Erdmann et al., 1975) of the method described by Pearce et al. (1965).

Analytical Methods

We centrifuged samples of lymph and blood and measured the concentration of protein in the supernatant fluids by the biuret method (Gornall et al., 1949). Cellulose acetate electrophoresis (Microzone 110, Beckman Instruments) separated the protein fractions and allowed quantification of albumin and globulin. We measured the pH and partial pressures of oxygen and carbon dioxide in arterial blood on a Radiometer acid-base analyzer (Copenhagen).

Statistical Analysis

Results in the text and tables are expressed as the mean ± 1 SD. We used a paired t-test (Snedecor and Cochran, 1967) to compare measurements made during conventional mechanical ventilation with those obtained during vibratory ventilation, and we regarded as significant those differences that were supported by a P value of <0.05.
We compared only data for vibratory vs. conventional mechanical ventilation; a comparison of spontaneous breathing vs. the two forms of assisted ventilation would have been influenced by the medications that the lambs received, as well as the type of ventilation.

**Results**

**Normal Left Atrial Pressure Studies**

Figure 2 shows the time course of one experiment, demonstrating the significant changes that occurred in the 14 studies performed on lambs without left atrial pressure elevation. When intrathoracic pressures increased during vibratory ventilation, cardiac output and lymph flow decreased, and the concentration of protein in lymph increased. The switch from vibration to standard ventilation led to a decrease of intrathoracic pressures, an increase in cardiac output and lung lymph flow, and a decrease in lymph protein concentration.

Table 1 is a summary of data related to respiratory gas exchange and systemic circulation during the two forms of ventilation. Arterial pH and P\textsubscript{aco\textsubscript{2}} were not different during mechanical and vibratory ventilation, but arterial P\textsubscript{co\textsubscript{2}} was greater during tidal breathing than it was during vibration. Heart rate and pressures in the descending aorta and vena cava were not significantly different, but cardiac output was less during vibratory ventilation than it was during conventional ventilation.

Table 2 shows average intrathoracic pressures and data related to lung fluid balance for these 14 experiments. Pulmonary arterial, left atrial, and pleural

---

**Table 1**

Data Related to Respiratory Gas Exchange and the Systemic Circulation during Vibratory and Mechanical Ventilation in Fourteen Lambs with Normal Left Atrial Pressure

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Vibratory ventilation</th>
<th>Mechanical ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.41 ± 0.03</td>
<td>7.39 ± 0.04</td>
<td>7.42 ± 0.03</td>
</tr>
<tr>
<td>P\textsubscript{aco\textsubscript{2}} (torr)</td>
<td>81 ± 8</td>
<td>66 ± 9</td>
<td>72 ± 10*</td>
</tr>
<tr>
<td>P\textsubscript{co\textsubscript{2}} (torr)</td>
<td>44 ± 3</td>
<td>40 ± 2</td>
<td>38 ± 4</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>204 ± 22</td>
<td>194 ± 21</td>
<td>200 ± 15</td>
</tr>
<tr>
<td>Average aortic pressure (torr)</td>
<td>81 ± 9</td>
<td>86 ± 9</td>
<td>87 ± 11</td>
</tr>
<tr>
<td>Average vena caval pressure (torr)</td>
<td>5 ± 2</td>
<td>7 ± 2</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Cardiac output (liters/min)</td>
<td>1.93 ± 0.29</td>
<td>1.68 ± 0.40</td>
<td>1.87 ± 0.31*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 SD.

* Significant difference between vibratory and mechanical ventilation, P < 0.05

---

**Table 2**

Intrathoracic Pressures and Data Related to Lung Fluid Balance during Vibratory and Mechanical Ventilation in Fourteen Lambs with Normal Left Atrial Pressures

<table>
<thead>
<tr>
<th></th>
<th>Pulmonary artery (torr)</th>
<th>Left atrium (torr)</th>
<th>Pleural space (torr)</th>
<th>Distal airway (torr)</th>
<th>Lung lymph flow (ml/hr)</th>
<th>Protein concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>18 ± 2</td>
<td>3 ± 1</td>
<td>-2 ± 1</td>
<td>0</td>
<td>2.20 ± 0.62</td>
<td>3.55 ± 0.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.61 ± 0.39</td>
</tr>
<tr>
<td>Vibratory ventila-</td>
<td>27 ± 4</td>
<td>8 ± 2</td>
<td>1 ± 2</td>
<td>9 ± 4</td>
<td>1.63 ± 0.58</td>
<td>3.54 ± 0.46</td>
</tr>
<tr>
<td>tion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.58 ± 0.43</td>
</tr>
<tr>
<td>Mechanical ventila-</td>
<td>23 ± 3*</td>
<td>6 ± 1*</td>
<td>0 ± 1*</td>
<td>7 ± 1</td>
<td>2.07 ± 0.59*</td>
<td>3.27 ± 0.39*</td>
</tr>
<tr>
<td>tion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.49 ± 0.36</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 SD.

* Significant difference between vibratory and mechanical ventilation, P < 0.05.
pressures were significantly greater during vibratory ventilation than they were during mechanical ventilation. Calculated pulmonary vascular resistance (not shown in Table 2) was 32% greater during vibration than it was during tidal breathing. The difference in average airway pressure was not significant (P > 0.10). Lung lymph flow was 21% less and lymph protein concentration was 8% greater during vibration than during conventional ventilation. Plasma protein concentration did not change significantly during these experiments.

Elevated Left Atrial Pressure Studies

Figure 3 illustrates the results of one of eight experiments done on lambs with left atrial hypertension. The differences are virtually identical to those that occurred without left atrial hypertension, but the magnitude of the decrease in lymph flow associated with vibration was greater during left atrial pressure elevation. Tables 3 and 4 show summary data for these eight studies, again demonstrating the

<table>
<thead>
<tr>
<th></th>
<th>Before left atrial pressure elevation</th>
<th>After left atrial pressure elevation</th>
<th>Vibratory ventilation, with increased left atrial pressure</th>
<th>Mechanical ventilation, with increased left atrial pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.40 ± 0.02</td>
<td>7.40 ± 0.02</td>
<td>7.38 ± 0.03</td>
<td>7.39 ± 0.02</td>
</tr>
<tr>
<td>$P_{ACO_2}$ (torr)</td>
<td>80 ± 7</td>
<td>87 ± 4</td>
<td>41 ± 3</td>
<td>41 ± 3</td>
</tr>
<tr>
<td>$P_{ACO_2}$ (torr)</td>
<td></td>
<td>43 ± 2</td>
<td>210 ± 18</td>
<td>210 ± 18</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td>210 ± 18</td>
<td>85 ± 6</td>
<td>85 ± 6</td>
</tr>
<tr>
<td>Average aortic pressure (torr)</td>
<td></td>
<td>6 ± 1</td>
<td>6 ± 1</td>
<td>2.16 ± 0.29</td>
</tr>
<tr>
<td>Average vena caval pressure (torr)</td>
<td></td>
<td></td>
<td>2.02 ± 0.28</td>
<td></td>
</tr>
<tr>
<td>Cardiac output (liters/min)</td>
<td></td>
<td></td>
<td>1.69 ± 0.17</td>
<td></td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 SD.

* Significant difference between vibratory and mechanical ventilation, P < 0.05

<table>
<thead>
<tr>
<th></th>
<th>Before left atrial pressure elevation</th>
<th>After left atrial pressure elevation</th>
<th>Vibratory ventilation, with increased left atrial pressure</th>
<th>Mechanical ventilation, with increased left atrial pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery (torr)</td>
<td>18 ± 2</td>
<td>23 ± 3</td>
<td>29 ± 4</td>
<td>26 ± 3*</td>
</tr>
<tr>
<td>Left atrium (torr)</td>
<td>2 ± 1</td>
<td>10 ± 2</td>
<td>14 ± 2</td>
<td>13 ± 2*</td>
</tr>
<tr>
<td>Pleural space (torr)</td>
<td>-2 ± 1</td>
<td>-2 ± 1</td>
<td>1 ± 1</td>
<td>0</td>
</tr>
<tr>
<td>Distal airway (torr)</td>
<td>0</td>
<td>0</td>
<td>8 ± 2</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Lung lymph flow (ml/hr)</td>
<td></td>
<td></td>
<td>2.48 ± 0.94</td>
<td>2.66 ± 1.09</td>
</tr>
<tr>
<td>Lymph protein concentration (g/dl)</td>
<td></td>
<td></td>
<td>3.61 ± 0.39</td>
<td>3.06 ± 0.47</td>
</tr>
<tr>
<td>Plasma protein concentration (g/dl)</td>
<td></td>
<td></td>
<td>5.51 ± 0.46</td>
<td>5.48 ± 0.34</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 SD.

* Significant differences between vibratory and mechanical ventilation, P < 0.05.
TABLE 5
Postmortem Data for Lambs Killed after 8 Hours of Vibratory or Mechanical Ventilation

<table>
<thead>
<tr>
<th>Lambs</th>
<th>No.</th>
<th>Dry lung tissue</th>
<th>Extravascular lung water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibratory ventila-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal left atrial pressure</td>
<td>4</td>
<td>13 ± 0.1</td>
<td>4.6 ± 0.2</td>
</tr>
<tr>
<td>Elevated left atrial pressure</td>
<td>4</td>
<td>1.6 ± 0.5</td>
<td>4.5 ± 0.7</td>
</tr>
<tr>
<td>Mechanical ventila-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated left atrial pressure</td>
<td>4</td>
<td>14 ± 0.4</td>
<td>4.4 ± 0.6</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 SD.

Postmortem Studies
Table 5 lists the blood and extravascular water content of lungs obtained from lambs killed after 8 hours of either vibratory ventilation or conventional mechanical ventilation. There was no difference in extravascular lung water between lambs killed after 8 hours of increased left atrial pressure and either vibratory ventilation or standard ventilation. All three groups of lambs had significantly less blood in their lungs than they do when they breathe spontaneously without ventilatory assistance (2.2 ± 0.8 g/g dry lung) (Bressack and Bland, 1980). Figure 4 shows photomicrographs of sections of lung obtained from two lambs killed after 8 hours of increased left atrial pressure and either vibratory ventilation or conventional mechanical ventilation. In both, the lungs are well inflated and there is no evidence of pulmonary edema.

Discussion
Pulmonary edema is a frequent component of respiratory disorders that require assisted ventilation. It is therefore important to evaluate the effect on lung fluid balance of new techniques proposed to treat respiratory failure. Vibratory ventilation, at least as we applied it, had no adverse influence on lung fluid balance in healthy lambs with or without elevated left atrial pressure. Lung lymph flow, a reduction in lymph flow that occurred in the presence of higher pulmonary vascular pressures and less blood flow (28% greater pulmonary vascular resistance) during vibratory ventilation. Again, there was no significant difference in mean airway pressure during the two phases of ventilatory assistance.

FIGURE 4. Photomicrographs of frozen lung obtained from lambs killed after 8 hours of vibratory ventilation (left) and conventional mechanical ventilation (right). Both lambs had increased lung microvascular pressure from saline-filling of a balloon catheter in their left atrium, but neither lamb had pulmonary edema. 8.5x.
increased on average by 50% of the pressure applied of 10 cmH\textsubscript{2}O. They found that pleural pressure to the airway, and there was no significant change neously breathed against an applied airway pressure the lungs of unanesthetized sheep that sponta-

Woolverton et al. (1978) studied filtration of fluid in microvessels that participate in fluid exchange. They concluded filtration of fluid into the lungs. They concluded that vibratory ventilation shifted the distribution of protein in lymph. Alternatively, it is possible that vibratory ventilation shifted the distribution of lung vascular resistance toward the arterial side of the pulmonary microcirculation, caused by an increase in pulmonary blood flow. The combination of decreased lymph flow and an increased concentration of protein in lymph suggests that lung microvascular filtration pressure was less during vibratory ventilation than it was during tidal breathing. Because pulmonary arterial and left atrial pressures were greater during vibration than during mechanical ventilation, lung interstitial pressure also must have been greater during vibration to account for the reduced lymph flow and higher concentration of protein in lymph. Alternatively, it is possible that vibratory ventilation shifted the distribution of lung vascular resistance toward the arterial side of the pulmonary microcirculation. This is unlikely, however, because left atrial pressure also increased at least as much as did pleural pressure during vibratory ventilation.

In studies of isolated, perfused rabbit lungs, Bø et al. (1977) and Nicolaysen and Hauge (1980) showed that increases in airway distending pressure reduce filtration of fluid into the lungs. They concluded that changes in alveolar pressure directly influence the hydraulic pressure in tissue surrounding lung microvessels that participate in fluid exchange. Woolverton et al. (1978) studied filtration of fluid in the lungs of unanesthetized sheep that spontaneously breathed against an applied airway pressure of 10 cmH\textsubscript{2}O. They found that pleural pressure increased on average by 50% of the pressure applied to the airway, and there was no significant change in lung lymph flow or lymph protein concentration. The authors concluded that, during continuous positive airway pressure breathing, increases in pulmonary microvascular pressure are offset by increases in liquid pressure transmitted to tissue surrounding the microcirculation, such that filtration remains constant and fluid does not accumulate in the lungs. Our results suggest that changes in lung perimicrovascular pressure during vibratory positive pressure breathing may more than offset increases in microvascular pressure that occur.

If intrathoracic pressure increases and remains nearly constant, as it does during vibratory ventilation, venous return to the heart and cardiac output are likely to decrease (Lenfant and Howell, 1960). Decreased pulmonary perfusion may reduce microvascular surface area for fluid filtration, thereby decreasing lung lymph flow.

The observed difference in lymph flow cannot be attributed to differences in mean airway pressure during the two methods of ventilation. In previous studies, we found that positive airway pressure per se had no effect on lung lymph flow in lambs (Raj et al., 1982), and Woolverton et al. (1978) showed that positive pressure breathing had no significant influence on steady state lung lymph flow in mature sheep. In this set of studies, mean airway pressure was similar during vibratory and conventional mechanical ventilation (P > 0.10). In five of 19 lambs, mean airway pressure was greater during tidal breathing than it was during vibration, mean pleural pressure was unchanged (0 ± 1 vs. 0 ± 2 torr), and in each case lymph flow was less and lymph protein concentration was greater during vibratory ventilation (Table 6). In those five lambs, cardiac output did not differ significantly during the two types of ventilation, suggesting that reduced pulmonary blood flow was not, by itself, responsible for the decrease in lymph flow observed during vibratory ventilation.

Increases in transpulmonary pressure accompanied by reductions in pulmonary blood flow may decrease fluid filtration both by decreasing micro-
vascular surface area and by lessening transmural filtration pressure across alveolar vessels (Bø et al., 1977; Permutt, 1979). These changes may be offset by the increase in fluid filtration that occurs in extravascular vessels when transpulmonary pressure increases (Permutt, 1979). We found no significant difference in the magnitude of the increase in mean transpulmonary pressure that occurred during vibratory vs. conventional mechanical ventilation. It is possible, however, that during the expiratory phase of tidal breathing, fluid filtration increases as transpulmonary pressure decreases. Such swings in fluid dynamics might account in part for the greater lung lymph flow and lower lymph protein concentration observed during mechanical ventilation.

We did not measure lung volume during these experiments and therefore cannot dismiss the possibility that patchy atelectasis may have developed from accumulation of secretions during vibratory ventilation. A non-uniform decrease in lung volume, with a corresponding redistribution of pulmonary blood flow, could have reduced effective surface area for fluid exchange, and this could have contributed to the decrease in arterial oxygen tension that occurred during vibratory ventilation as well.

In our lambs, it is unlikely that vibratory ventilation impaired lymphatic function because there was no increase in extravascular lung water content of lambs killed after 8 hours of vibration, even in the presence of elevated lung microvascular pressure. If lymphatic drainage had been retarded, we would have expected fluid to accumulate in the lungs (Nakahara et al., 1973; Cowan et al., 1976), which it did not. Furthermore, mechanical obstruction of lymph flow would not be expected to change the concentration of protein in lymph. Nevertheless, we cannot exclude the possibility that vibratory ventilation may have a small influence on drainage of lung lymph.

Gabel et al. (1981) demonstrated that lymphatic channels from the diaphragm may feed the caudal mediastinal lymph node and thereby contaminate collection of lung lymph. We cannot exclude the possibility that vibratory ventilation lessened diaphragmatic contributions to outflow of lymph from that node, but our study design makes that an unlikely possibility. First, during our dissection of the caudal mediastinal lymph node, we always injected the diaphragm with Evans blue dye and resected any lymphatics that coursed toward the node. Second, all of the lambs that we studied were sedated and paralyzed during both forms of ventilation, and we did not electrically stimulate their phrenic nerves. Gunther and Demling (1981) showed that, without phrenic nerve stimulation, diaphragmatic contributions to the caudal mediastinal lymph node are negligible.

Unlike previous studies of high-frequency oscillatory ventilation (Bohn et al., 1980; Bunnell et al., 1978; Butler et al., 1980; Slutsky et al., 1980), we found that arterial oxygenation was less effective during vibration than it was during conventional mechanical ventilation. It is possible that species- and age-related differences may be responsible for this discrepancy. We used newborn lambs, rather than mature animals, which have considerable collateral ventilation in their lungs (Woolcock and Macklem, 1971). Newborn animals without lung injury have no apparent pathways for gas to flow between respiratory units (Boydren, 1977). The presence or absence of collateral ventilation may be important in determining the potential for oxygenation with vibratory ventilation. Bohn et al. (1980) reported that pigs, which have virtually no collateral ventilation (Sylvester et al., 1975), had lower arterial Po2 measurements during high-frequency oscillatory ventilation than during tidal breathing.

It is possible that the mechanics of the system that we used to apply vibratory ventilation may have contributed to the reduced arterial oxygenation that we observed. Because we deflated the cuff of the endotracheal tube during vibration, some of the secretions that collected in the oropharynx of the lambs may have entered the airways and caused obstruction. As we gained more experience in applying this technique, our skill at removing secretions and maintaining patent airways improved, so that oxygenation of the lambs was considerably better during the more recent studies in which we raised left atrial pressure. It is possible that intermittent lung inflations might have improved arterial oxygenation (Wright et al., 1981), but we avoided this because we wanted to observe lung fluid balance in lambs without normal breathing movements.

Irrespective of the cause for the reduced oxygenation, we cannot attribute the lower lymph flow rates observed during vibratory ventilation to the reduced partial pressure of oxygen in arterial blood of the lambs. Previously, we showed that reductions in arterial oxygen tension increase lung lymph flow and decrease the concentration of protein in lymph of newborn lambs (Bland et al., 1980, 1982; Bressack and Bland, 1980).

Our lymph flow data are similar to those reported by Warren and Drinker (1942), who studied anesthetized dogs during brief periods of oxygen inflation without breathing movements. Mitzner et al. (1981) also observed a decrease in the flow of lymph from the in situ perfused lungs of lambs. These results, coupled with ours, suggest that the bellows action of the lungs during normal breathing is at least partly responsible for regulating filtration of fluid from the microcirculation into the interstitium of the lungs. Judgment concerning the potential benefit of vibratory ventilation on fluid balance in the newborn lung awaits successful application of this technique to animals with incomplete lung development or severe pulmonary edema.

We thank the J.H. Emerson Company for providing an airway vibrator, G.E. Sedlin and T.A. Hazinski for help in preliminary exper-
References

Humphreys PW, Normand ICS, Reynolds EOR, Strang LB (1967) Pulmonary lymph flow and the uptake of liquid from the lungs of the lamb at the starting of breathing. J Physiol (Lond) 193: 1–29
Warren MF, Drinker CK (1941) The flow of lymph from the lungs of the dog. Am J Physiol 136: 207–221

INDEX TERMS: Vibratory ventilation • Mechanical ventilation • Lung fluid balance • Pulmonary edema • Newborn lambs • High-frequency positive-pressure ventilation
Vibratory ventilation decreases filtration of fluid in the lungs of newborn lambs.
J U Raj, R B Goldberg and R D Bland

doi: 10.1161/01.RES.53.4.456

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/53/4/456

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://cirres.ahajournals.org/subscriptions/