Changes in Ventilation and Perfusion during PEEP in Normal and Edematous Lungs*

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Ventilation with positive end-expiratory pressure (PEEP) increases arterial \( P_O_2 \) (\( PaO_2 \)) in hypoxemic patients1 and dogs2 with pulmonary edema. The increased \( PaO_2 \) indicates that a more favorable distribution of ventilation and perfusion results from PEEP therapy. This can be produced by supplying greater ventilation to perfused regions or by shifting perfusion away from underventilated regions to others of greater ventilation. To gain some insight into the mechanism for increased \( PaO_2 \) we used 133Xenon to measure regional ventilation (V), perfusion (Q) and volume (V) during 5, 10, 15 and 20 cm H\_2O PEEP in seven dogs with and six dogs without oleic acid-induced pulmonary edema.

The dogs were anesthetized with pentobarbital and placed in the supine position such that fixated detectors were aligned over four different lung regions (Fig 1). Two collinear detector pairs recorded radioactivity from the independent apical and lower lobes (regions 2 and 6) and another two pairs recorded from the dependent apical and lower lobes (regions 3 and 8). Each dog was mechanically ventilated with a Harvard 614 respirator set at a frequency of 20 breaths/min and a tidal volume of 20 ml/kg. Hyperventilation with resultant hypocapnia was necessary in order to control ventilation after producing pulmonary edema by right ventricular injection of 0.075 ml/kg oleic acid.

Regional perfusion was determined by injecting 2 mCi 133Xenon into the right ventricle. Just prior to injection the ventilator was stopped at mid-inspiration for 15 seconds to facilitate determination of peak radioactivity in the four lung regions. Regional ventilation was determined from the rate of 133Xenon wash-in from a closed circuit spirometer system, and regional volume was taken as the plateau height of radioactivity obtained after xenon in the lung had equilibrated with that in the closed circuit. Details of these procedures have been reported elsewhere.3 Distribution of \( Q \), \( V \) and \( V \) were normalized by making the total output from the four detector pairs equal to 100 percent. Each region then contained some fraction of the total response.

Regional function and \( PaO_2 \) were measured during intermittent positive-pressure ventilation (IPPV) before (baseline) and one hour after oleic acid injection. In dogs which did not receive oleic acid, a second series of measurements were taken one hour after obtaining the baseline values. IPPV was then replaced with either 5, 10, 15 or 20 cm H\_2O PEEP for one-half hour. IPPV was then reapplied for another half hour. The sequence of alternating between PEEP and IPPV was continued until all PEEP levels were studied. Perfusion and ventilation were determined at 20 and 25 minutes, respectively, during each half-hour period.

Oleic acid produced edema primarily in the dependent lower lobes (region 8) due to the high flow and relatively higher perfusion pressure in that region compared to the others. Both lung volume and ventilation decreased in region 8 at one hour after oleic acid injection but perfusion distribution was unaltered (Fig 2). These changes caused the \( V/Q \) ratio in region 8 to decrease as well. Increasing levels of PEEP caused a progressive increase in the volume of region 8. Ventilation also increased with PEEP through 15 cm H\_2O but at 20 cm H\_2O ventilation in region 8 decreased from the value obtained during 15 cm H\_2O. Perfusion distribution remained unchanged through 15 cm H\_2O PEEP but during the 20 cm H\_2O level it decreased slightly. Although \( V/Q \) ratio was obtained using zonal distribution for ventilation and perfusion rather than absolute values, there is a good relationship between changes in \( PaO_2 \) and \( V/Q \) ratio for region 8 (Fig 3). As \( PaO_2 \) increased with PEEP so did \( V/Q \) ratio in region 8.

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Figure 1. Detector configuration used for human evaluation. Only detectors 2, 3, 6 and 8 were utilized in this study of supine dogs.
This study has shown that pulmonary edema decreases volume and ventilation in region 8. These are the expected changes since histology of that region showed widening of the alveolocapillary barrier with hyaline membranes along patent alveolar walls. In addition, some alveoli were completely fluid-filled. Increased volume and ventilation with PEEP in region 8 may have resulted from pressure-induced spreading of intra-alveolar fluid and/or to the overcoming of decreased compliance. Decreased ventilation in region 8 during 20 cm H2O PEEP could have resulted from foam obstructed airways, but this is unlikely since the same PEEP level decreased ventilation of region 8 in dogs with normal lungs. A more reasonable possibility for decreased ventilation during 20 cm H2O PEEP is that turnover rate in the alveoli of region 8 decreased. Turnover rate is the relationship between alveolar size and tidal volume. As alveolar size increases a fixed tidal volume will result in a slower turnover rate for xenon in those alveoli. This in turn produces a slower rise to equilibrium activity during xenon wash-in and thus a lower ventilation.

The fact that perfusion distribution to region 8 did not change after producing edema is surprising in the light of previous studies in which isolated lungs were used. In those studies perfusion to the dependent lung decreased after producing edema, presumably because interstitial fluid forms a cuff around the extra-alveolar vessels and thus, lessens the expanding pull of the surrounding parenchyma. This then increases resistance to flow in dependent regions where edema is most pronounced and shifts flow to more independent and less edematous regions. Interstitial fluid pressure is dependent on hydrostatic force, which, in turn, is directly proportional to vertical height. It is possible that the vertical height of supine dog lungs is not sufficient to raise interstitial pressure to the degree necessary to narrow dependent blood vessels. Staub et al. and Hughes et al. have also reported that perfusion distribution remained unchanged in supine dog lungs after producing edema. In the Hughes' study, dogs positioned vertically did have a dependent reduction in flow after edema, which suggests vertical height is important.

Of further interest is the fact that perfusion distribution to region 8 was maintained at all levels of PEEP except 20 cm H2O, which caused a slight decrease. It must be remembered that perfusion is represented as perfusion per unit volume. Since lung volume increased progressively and perfusion did not change in region 8 through 15 cm H2O PEEP, perfusion must have kept pace with increasing lung volume in that region. This may have resulted from the inverse relationship between lung volume and extra-alveolar vascular resistance. As lung volume increased, resistance to flow through extra-alveolar vessels decreased, which maintained perfusion per unit volume. On the other hand, with increased alveolar pressure we would expect increased alveolar vascular resistance, with subsequent reduction of flow. It is possible that the lowered compliance in region 8 dampened the effects normally seen on blood flow as alveolar pressure was increased. At 20 cm H2O PEEP perfusion was shifted away from region 8. This may have resulted from a near maximal lung volume at that end-expiratory pressure which produced only minor decreases in extra-alveolar...
vascular resistance, while at the same time high alveolar pressure overcame the protective effect of decreased compliance, with a resultant increase in alveolar vascular resistance.

REFERENCES

DISCUSSION
Dr. West: That was a very nice study. I think that most of the changes you observed were in the direction one might expect except for the differences in blood flow. However, as you pointed out, you were measuring blood flow per unit volume and the volume at the bottom of the lung decreased dramatically following oleic acid. Therefore, in fact perfusion must have fallen quite appreciably so that I don’t think it is true to conclude as you said that there is no change in distribution of blood flow. Moreover, this may not be an ideal method of measuring blood flow under these conditions because xenon can only be eliminated in the alveolar gas in regions that are aerated and I presume that some of these alveoli are full of hemorrhagic edema.

In your last slide which dealt with gas exchange, you showed a correlation between the arterial Po2 and the ventilation/perfusion ratio at the bottom of the lung. Now, there is nothing wrong with showing the correlation as long as you are not trying to imply that this ventilation/perfusion ratio has anything to do with gas exchange because I don’t think it has. A ventilation/perfusion ratio of 0.5 is a trivial reduction and, in fact, the normal lung has regions with ventilation/perfusion ratio as low as that. It brings out an important point that always comes up in these topographic studies, that is, that the inequalities of ventilation/perfusion ratio that can be detected by external counting are very minor compared to the differences that must be there within the counting field but which cannot be distinguished because of the relatively poor spatial resolution.

Dr. Jones: I think you are absolutely right. Perfusion must have decreased with volume. However, with fixed detectors outside the chest it is important to present perfusion/unit volume, since one can never assume that a detector field is composed entirely of lung parenchyma. You are also correct about the ability of xenon to measure blood flow during severe pulmonary edema. Only effective perfusion can be obtained with the method we used. In other words, we could not measure the amount of shunt, since the method detects only that blood which passes gas-containing alveoli. Because of this inability to measure shunted blood we cannot expect the ventilation/perfusion ratio to decrease dramatically. Most of the decrease in Po2 is due to shunted blood and it appears, as you have indicated, that little of the change in Po2 can be accounted for by the small changes in ventilation/perfusion ratio we obtained.

Dr. Neff: In the last slide showing increasing Po2 at the various levels of PEEP and the improvement of ventilation/perfusion ratio, I didn’t see a control. Did you have controls in relation to time? In other words were we not seeing improvement as it took you one-half hour to run through each one of your models and then do a control?

Dr. Jones: Each level of PEEP was interrupted with a period of IPPV, and we found no significant change between inter-PEEP IPPV values and those obtained one hour after oleic acid injection. This indicates that the improvements in Po2 and ventilation/perfusion ratio were PEEP-induced and not time dependent.

We did run controls but those data were not included because of the time limit on the presentation. The control group, without oleic acid, did not have significantly altered ventilation/perfusion ratio or P02 during PEEP. In fact, PEEP caused a slight decrease in P02. What this was due to is not clear, but it may be related to increased dead space ventilation in response to increased airway pressure.

Dr. Loosli: What would have happened to your measurements if the animal would have been in the ventral position rather than lying on its back?

Dr. Jones: I am not sure what would have happened. The only experiment we have done along those lines was to inject oleic acid while the animal was in the prone position and then after 15 minutes turned over on its back. Still we observed the severe dependent, that is, dorsal congestion. So I assume if we left the animal on its stomach throughout the experiment the ventral portions of the lung would have become severely hemorrhagic due to increased hydrostatic pressure in that region.

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