shown a doubling of the extravascular lung water but we know that this is a small percentage of the total lung weight; therefore, doubling of the extravascular lung water cannot explain doubling of the dry lung weight.

Dr. West: It should be noted that we are not sure that these lungs were indeed stiff and that pulmonary function studies should be made at this point. All that was shown was that the extravascular lung water was increased.

Dr. Emmanuel: That's correct.

Distributions of Ventilation-Perfusion Ratios in Acute Respiratory Failure*

Peter D. Wagner, M.D.; Raymond B. Laravuso, M.D.; Richard R. Uhl, M.D.; and John B. West, M.D.

Impairment of pulmonary gas exchange is a hallmark of acute respiratory failure, but its physiologic basis cannot be accurately defined with traditional analytic methods. Techniques such as the Riley three-compartment analysis do not permit differentiation between blood which is shunted through completely unventilated alveoli, and blood perfusing areas in which the ventilation-perfusion ratio \( \frac{V_a}{Q} \) is low but not zero. Although in theory the breathing of 100 percent \( O_2 \) should allow such a separation, it is likely that \( O_2 \) per se results in atelectasis of just those areas in which the \( \frac{V_a}{Q} \) ratio is low.\(^1\)\(^-\)\(^4\) Thus, the shunt estimated by this method may be considerably different from that present breathing room air, so that the breakdown of the total venous admixture into components due to shunt and ventilation-perfusion inequality may become subject to a large error. A possible additional factor contributing to the impaired gas exchange is increased resistance to diffusion of \( O_2 \) and \( CO_2 \) across the blood gas barrier. This further complicates the analysis, and most workers have been content to characterize the gas exchange abnormalities simply by the alveolar-arterial \( O_2 \) difference, venous admixture, and physiologic dead space, numbers which give little insight into the nature of the gas exchange lesion.

We\(^5\) have recently described a method in which the distribution of \( \frac{V_a}{Q} \) ratios can be measured as a virtually continuous function under steady-state conditions. In particular, it distinguishes between areas containing shunt and those in which the \( \frac{V_a}{Q} \) ratio is low on the one hand, and between areas containing dead space and those in which the \( \frac{V_a}{Q} \) ratio is high on the other. The method can be applied at any desired level of concentration of inspired oxygen (\( FIO_2 \)).

**METHODS**

A mixture of the six gases, sulphur hexafluoride, ethane, cyclopropane, halothane, diethyl ether, and acetone is dissolved in a suitable medium such as 5 percent dextrose in water, then infused into a peripheral vein for 20 minutes at the rate of 5 ml/min. Toward the end of the infusion, the concentrations of each gas are determined in the mixed expired gas and systemic arterial blood. It is necessary to know the concentrations in pulmonary arterial blood, but with the patient in a steady state of gas exchange, the concentrations of each gas in the pulmonary artery can be calculated from the Fick principle with sufficient accuracy that direct pulmonary artery sampling is not necessary (knowing cardiac output and minute ventilation, arterial and mixed expired concentrations, and blood-gas partition coefficients). However, pulmonary arterial lines are often present in patients with acute respiratory failure so that central venous blood is readily available.

Gas concentrations are measured by gas chromatography (Beckman GC-72-5). A flame ionization detector is used for all gases except sulphur hexafluoride, which is measured using an electron capture detector. Concentrations lie within the range .001-100 parts per million, well below levels that produce measurable changes in cardiopulmonary or central nervous function.

For each gas, the ratios of systemic to pulmonary arterial concentrations and mixed expired to pulmonary arterial concentrations are calculated, and from these the distributions of blood flow and ventilation with respect to ventilation-perfusion ratio are computed, respectively. These computations are performed by digital computer using techniques of numerical analysis. The results can be expressed graphically as two plots, namely, of blood flow on the ordinate and \( \frac{V_a}{Q} \) ratio on the abscissa, and of ventilation on the ordinate and \( \frac{V_a}{Q} \) ratio on the abscissa.

The method has been applied in dogs after induction of acute respiratory failure and in patients following chest trauma and respiratory failure. Distributions were measured first breathing either room air (in dogs, and some patients) or at the ambient \( FIO_2 \) deemed necessary for the care of the patient, and then after breathing 100 percent \( O_2 \) for 30-45 minutes, in order to assess the shortterm effects of oxygen on the \( \frac{V_a}{Q} \) distribution. We studied 30 dogs and 4 patients, and examples in 3 dogs and 1 patient will be given here.

**RESULTS**

Figure 1 shows representative distributions in three dogs following induction of acute respiratory failure. This was produced in one of three ways, namely, by injection IVI of 750,000 glass beads, 0.25 mm diameter (upper panel), by injection into the right ventricle of 0.1 ml/kg oleic acid (middle panel) and by inducing right lower lobe pneumococcal pneumonia (lower panel). The dog with embolism shows areas with very high \( \frac{V_a}{Q} \) ratios consistent with the partial obstruction of blood vessels without reduction in ventilation. In addition, there was a shunt of 8.8 percent, although the reasons for this remain obscure. On the other hand, the pictures in acute hemorrhagic pulmonary edema and lobar pneumonia are similar but grossly different from the picture of embolization. Here the major part of the distribution is normal, while the affected parts are for the most part totally unventilated (shunt) rather than poorly ventilated, indicating that complete rather than par-
Regardless of the cause of the lesion in these dogs, a consistent change occurred on breathing 100 percent O<sub>2</sub>, in that blood flow to unventilated alveoli appeared or increased. There was usually a concomitant reduction in the amount of blood in areas with low V<sub>A</sub>/Q ratios. An example of the effect of O<sub>2</sub> is given in Figure 2 in a dog with acute hemorrhagic pulmonary edema produced by oleic acid.

With the animals or patients both breathing air and 100 percent O<sub>2</sub>, the observed distributions quantitatively accounted for the simultaneously measured abnormalities of O<sub>2</sub> and CO<sub>2</sub> exchange. This was assessed by comparing arterial PO<sub>2</sub> and PCO<sub>2</sub> values predicted from

![Blood flow distributions](image)

**Figure 2.** Blood flow distributions breathing air and 100 percent O<sub>2</sub> in dog with acute hemorrhagic pulmonary edema produced by oleic acid. After breathing O<sub>2</sub> for 40 minutes, regions with V<sub>A</sub>/Q ratios less than about 0.1 were no longer present, while there was simultaneous increase in shunt, suggesting atelectasis in these regions of low V<sub>A</sub>/Q.

the V<sub>A</sub>/Q distributions with the arterial PO<sub>2</sub> and PCO<sub>2</sub> values measured at the time of determination of the distributions. In 68 individual comparisons, the regression equation between predicted and measured PO<sub>2</sub> and PCO<sub>2</sub> in mm Hg were:

PO<sub>2</sub> (predicted) = 1.012 * PO<sub>2</sub> (measured) + 0.65
over a range of from 31 to 640 mm Hg. Correlation coefficient was 0.986

PCO<sub>2</sub> (predicted) = 0.991 * PCO<sub>2</sub> (measured) + 0.30
over a range of from 25 to 81 mm Hg. The correlation coefficient was 0.984.

These close predictions suggest that virtually all the hypoxemia was caused by V<sub>A</sub>/Q inequality and that diffusion impairment was unimportant.

Figure 3 shows the distributions breathing 40 percent and 100 percent O<sub>2</sub> in a previously healthy woman 62 years of age who suffered closed chest trauma in an automobile accident, resulting in a left lower lobe infiltrate. The measurements were made 72 hours after adi-

![Ventilation-perfusion ratio distributions](image)

**Figure 3.** Ventilation-perfusion ratio distributions in patient with left lower lobe infiltrate following closed chest trauma. Distribution is bimodal, with about 20 percent of blood flow appearing in regions with low V<sub>A</sub>/Q ratios. Note that shunt, which is only 1.2 percent breathing 40 percent O<sub>2</sub>, rises to 5.3 percent breathing 100 percent O<sub>2</sub>.
mission, while she was on an Emerson ventilator (tidal volume 1,000 ml, frequency 8). Measurement of arterial blood gases revealed a Po2 of 90 (40 percent inspired O2) rising to 500 on 100 percent O2, a PCO2 level of 30 and pH of 7.54. It can be seen that approximately 80 percent of the cardiac output is perfusing lung within the normal range of VA/Q ratios, but that 20 percent appears in a region of very low VA/Q. In addition, there is a shunt of 1.2 percent. On breathing 100 percent O2, the shunt increased to 5.3 percent, while there was a small reduction in the blood flow to the low VA/Q areas.

**DISCUSSION**

We suggest at least two mechanisms acting synergistically to explain the role of O2 in creating or increasing the shunt. Both depend on the existence of low VA/Q areas and are based on the large rise in alveolar Po2 (as FIO2 is increased) from near mixed venous levels to near the inspired level (less PCO2). First, as PaO2 rises, the O2 uptake per unit of blood flow will greatly increase, and this may be so great as to exceed the delivery of fresh gas by alveolar ventilation so that the lung units collapses. This was previously suggested by Briscoe et al1 and may affect units in which the VA/Q ratio breathing air is about 0.1 or less (this value depending mainly on the mixed venous O2 saturation) The second possibility is the release of hypoxic vasoconstriction as alveolar Po2 rises. This increases the blood flow and therefore reduces the VA/Q ratio, and again this mechanism will be most marked in just those units where VA/Q ratio is low breathing air.

These studies demonstrate the feasibility of the method in the acutely ill dog and patient with a variety of clinical syndromes. Not only are the results appropriate to the nature of the lung injury, but they also account quantitatively for the accompanying disturbances of O2 and CO2 exchange. The only requirements of the method are a 20-minute infusion (delivering only 100 ml of fluid), single samples of mixed expired gas and systemic arterial blood and measurement of minute ventilation and cardiac output. The procedure is easily performed at the bedside without the need for patient cooperation. The method may be useful in the differential diagnosis of the causes of acute respiratory failure, in following the patient’s course and in assessing the effects of therapy on gas exchange. Finally, it has been demonstrated that breathing of 100 percent O2 for as short a period as 30-45 minutes may result in a significant increase in the amount of shunted blood, so that in addition to deleterious effects on the patient, the extrapolation of the shunt calculated from O2 measurements to room air conditions may be considerably in error.

**REFERENCES**


only 20-30 percent of our patients. Did you find this in all patients investigated?

Dr. Wagner: Yes, we have found this phenomenon in all of the studies that we have done which include normal volunteers, dogs (on respirators) and sick patients who did not have adult respiratory distress syndrome. We found that the more normal the lung to begin with the less the change post-100 percent Fio2.

Noninvasive Measurement of Intrathoracic Fluids*

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The seriousness of impending pulmonary insufficiency following stress—hemorrhage, burns, operation, trauma, left ventricular failure, sepsis, and shock—has long been recognized by clinicians. However, its detection and quantitation frequently elude currently used diagnostic techniques until irreversible pulmonary insufficiency or cardiac failure occurs. Recent applications of the electrical impedance method for acquiring physiologic data show promise of providing a safe, noninvasive, and continuous measurement for early detection, localization, and quantitation of intrathoracic fluid accumulations.2,3

In a series of studies of four groups of healthy anesthetized dogs, the basal thoracic impedance (Z0) was evaluated as a means of detecting, localizing, and quantitating thoracic fluid accumulations. The Kubicek circumferential band electrode system4 and two variable "spot" electrode arrangements were used with a constant sinusoidal current applied to one pair of electrodes and the voltage reflecting thoracic impedance measured across the remaining pair of electrodes (Fig 1). In groups 1 and 2, pleural and pericardial effusion were simulated by the infusion and withdrawal of normal saline (37°C) from each hemithorax or pericardial space, respectively. Pulmonary edema was induced in group 3 either by alloxan or sucrose, or simulated by pulmonary lavage with saline. A fourth group was subjected to multiple penetrating thoracic wounds inflicted by a 13-gauge needle.

These studies indicate that transthoracic electrical impedance provides a sensitive index of thoracic fluid accumulation. Although the band and both spot electrode systems were sensitive to thoracic fluid changes, only the latter systems were useful in fluid localization. This is readily apparent from Figure 2 in which the percentage of thoracic impedance change associated with the infusion of saline into the right hemithorax of a dog is shown. A linear correlation (r>0.9; P<0.01) between Z0 and various thoracic fluid accumulations is characteristic of data for individual animals in all groups (Fig 3); the differences in conductivity of body fluids are reflected as differences in slopes (blood is less conductive than plasma or saline). Pleural and pericardial effusion typically produce an average total impedance change of 2.0 and 1.5 ohms per 100 ml of saline infused, respectively.

Alloxan- or sucrose-induced pulmonary edema produce a typical impedance change of 2 to 5 ohms for the band electrode array, with 4 ohms for the tetrapolar spot electrode array. This edema is accompanied by marked ventilatory obstruction and early deaths, attributable to the copious amounts of fluid and foam in the tracheobronchial tree. This method of producing edema does not permit simple quantification of fluid accumulations; however, by using unilateral pulmonary lavage, it is possible to maintain the animal while measuring im-

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Figure 1. Four terminal systems for the measurement of thoracic impedance. A. Flexible metal electrodes encircling neck and thorax. 50 kHz constant sinusoidal current (1 mA rms) was applied to electrodes 1, 4. Voltage changes reflecting thoracic impedance changes were picked up from electrodes 2, 3. B. Stainless steel "spot" electrodes (1 cm diameter) sutured to chest wall at level of sixth intercostal space. Twenty kHz constant sinusoidal current (1 mA rms) was applied to electrodes 2, 4, and impedance changes between other pairs of electrodes were recorded. C. Standard disposable ECG type electrodes were applied to thorax as shown. Twenty kHz constant sinusoidal current (1 mA rms) was applied to electrodes 1, 6, and impedance changes between electrodes 2, 3, or 4, 5 were recorded.