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TITLE: PULMONARY EXTRAVASCULAR WATER VOLUME DURING EDEMA

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The development of an in vivo measurement of lung water has been a long term goal of clinicians and physiologists. Multiple indicator dilution techniques have worked in normal man and animals. Under conditions of pulmonary edema, however, the accumulation of fluid redistributes or impairs blood flow. Since the volume of fluid is calculated from the product of blood flow and mean indicator transit time, the results are often variable and difficult to interpret in edematous animals. This paper describes a multiple indicator dilution method incorporating a lipid soluble tracer as a tissue marker, allowing quantitative measurement of lung water in edematous animals.

Fourteen dogs of mixed breed weighing between 18 and 25 kilograms were anesthetized with thiopental (10 mg/kg) and pentobarbital (20 mg/kg). The animals were intubated and mechanically ventilated with room air or oxygen enriched room air. A multiple indicator injectate was made up with chromium 51 tagged red blood cells indocyanine green tagged albumin, tritiated water and carbon^{14} tagged hexanol, in an isotonic mixture. One milliliter of the mixture was rapidly injected into the central venous circulation and arterial blood samples were collected in a rapidly rotating fraction collector at the rate of 2 samples per second. The study was divided into two groups of animals and three phases. In one group, following a control measurement, duplicate indicator dilution studies were repeated 1½ hours after the control period. In the second group, indicator dilution measurements were repeated 30 minutes and 1½ hours after the intravenous infusion of alloxan 75 mg/kg and saline 40 ml/kg. Alloxan causes pulmonary edema by producing a permeability defect in the endothelium. The alloxan was infused immediately after the control phase. Arterial blood samples were analyzed for Cr^{51}, C^{14} and tritium by the appropriate counting techniques. Indocyanine green was determined spectrophotometrically.

Following completion of all indicator dilution studies, the animals were sacrificed and the lungs were inflated and removed. Each lung was immersed briefly in liquid nitrogen solidifying the surface and rapidly sectioned into three horizontal planes. The lung sections were subsequently homogenized and freeze dried for determination of water, blood and lipid content.

Distribution volumes of the tracer materials were determined from the indicator dilution data by standard Sewart-Hamilton techniques for calculation of flow, and mean transit times. Pulmonary extravascular water volumes (PEWV) was calculated from the equation:

$$\underset{\text{mls/kg}}{PEWV} = \underset{\text{mls/sec}}{C.O.} \left(t_{THO} - t_{Cr^{51}} \right) / \text{body wt. (kg)}$$

Hexanol distributes in both water and lipid. Its oil/water partition coefficient is 10.9. Thus, the hexanol distribution volume is always larger than the tritiated water volume by about 20-30% under normal conditions. As edema fluid (water) accumulates the ratio $\frac{\text{THO volume}}{\text{Hex volume - THO volume}}$ changes dramatically. Because the blood flow term cancels in the above calculation the ratio is much more sensitive and consistent than the conventional PEWV calculation. The ratio is dimensionless representing proportion of water to lipid distribution volumes. The distribution volumes were then compared to the actual water contents of the lungs. The results for the non-edematous and edematous animals were tabulated.

		NON EDEMATOUS ANIMALS MEANS ± S.E.	EDEMATOUS ANIMALS MEANS ± S.E.
FLOW I	PEWV	3.54 mls/kg ±.79	5.07 ±.99
	THO / HEX-THO	2.93 ±.61	2.73 ±.42
FLOW II	PEWV	4.08 ±.54	8.01* ±2.22
	THO / HEX-THO	2.41 ±.51	12.7* ±5.9
FLOW III	PEWV	4.40 ±1.59	7.04 ±1.18
	THO / HEX-THO	2.00 ±.50	21.9* ±5.4
END OF STUDY	LUNG WATER mls/gm drylung	3.57 ±.15	5.85* ±.43

* $p < .01$ by Student's "t" test

The relationship between hexanol distribution volumes and tritiated water volumes correlates well with the formation of edema fluid in the lung. In every case where the lung water volume was increased by direct measurement, the water distribution volume increased relative to the hexanol volume ($p < .01$). The pulmonary extravascular water volume as determined by conventional techniques did not correlate with water content nearly as well in individual cases as had been shown previously.

It is concluded that the addition of a lipid soluble tracer to multiple indicator dilution studies offers the opportunity to follow edema formation and regression in individual cases. It is further concluded that the techniques may provide a means to estimate tissue perfusion or available surface area for exchange in permeability studies.

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