Changes in lung volume, perfusion, ventilation and airway diameter in dogs with pulmonary oedema

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Summary

1. In dogs that were supported in the upright position and that were breathing spontaneously acute pulmonary oedema was induced either by extracellular fluid volume expansion (n = 5) or by increasing pulmonary microvascular permeability with alloxan (n = 5).
2. Before oedema was induced, the bronchi of the right lung were outlined with tantalum powder.
3. During a baseline period, standard chest radiographs were taken at inflation pressures from 0 to 2 kPa and the distributions of perfusion (with radioactive microspheres) and ventilation (with 133Xe) were measured. Arterial and mixed venous blood samples were taken to estimate the degree of venous admixture (physiological shunt) and pulmonary arterial and wedge pressures were measured.
4. After oedema had developed the radiographs and observations were repeated at a time when the pulmonary vascular pressures were insignificantly different from the baseline state.
5. With induction of oedema, particularly when due to volume expansion, the lower-lung zones decrease in volume. There were no significant changes in the upper zones.
6. Abnormal venous admixture occurred only in dogs with >20% loss of lower-zone volume; volume loss and physiological shunt were significantly correlated.
7. The distribution of perfusion changed little with induction of oedema. Volume-expanded dogs showed a slight diversion of perfusion away from the bases and towards the upper zones.
8. There was an approximately 30% reduction of ventilation to the lung bases and a corresponding increase to the upper zones.
9. With induction of oedema, bronchi were narrowed when there was a reduction of lung volume. There was a significant linear correlation between volume change and narrowing.

Key words: bronchial narrowing, pulmonary oedema, regional lung volume, regional perfusion, regional ventilation, ventilation–perfusion relationship.

Abbreviation: FRC, functional residual capacity.

Introduction

It has been previously shown (Snashall, Keyes, Morgan, McAnulty, Mitchell-Heggs, McIvor & Howlett, 1980) that when pulmonary oedema develops in the upright anaesthetized dog there is a loss of radiographic volume in the dependent zones of the lungs. This change was seen in mild as well as in severe oedema and was often the earliest radiographic change to be observed as oedema developed.

The changes in lung volume were estimated by measuring, from the radiographs, distances between intrapulmonary blood vessels and the pleural surface in the anteroposterior, lateral and vertical directions. One problem with this method was the identification of suitable vessels that were visible on all films before and after the development of oedema. The first purpose of the present study was to confirm our previous observations with tantalum bronchography (Nadel, Wolfe,
Graf, Youker, Zamel, Austin, Hinchcliffe, Greenspan & Wright, 1970) used to outline the lung and allow more accurate measurement of regional volumes. Secondly, we have examined the effect of different degrees of lung inflation on the oedema-induced loss of volume. Of particular interest was whether at low degrees of inflation evidence could be found of an increased closing volume, due to oedema (Hughes & Rosenzweig, 1970), causing an increase in lung volume.

There is evidence that lung-volume changes are important in determining the degree of hypoxia in pulmonary oedema. Forcible hyperinflation of the oedematous lung relieves hypoxia (Said, Longacher, Davis, Banerjee, Davis & Wooddell, 1964) and positive-pressure breathing, particularly with the addition of positive end-expiratory pressure, relieves hypoxia without decreasing the extent of the pulmonary oedema (Caldini, Leith & Brennan, 1975). To understand the relationship between lung volume and hypoxia, we have measured regional perfusion and ventilation before and after oedema development and have estimated the degree of venous admixture, quantified as the physiological parenchymal shunt (Robin, Laman, Goris & Theodore, 1977).

Methods

Procedure

Ten mongrel dogs of both sexes weighing 17–26 kg (mean 20.5 kg) were used. After induction of anaesthesia with intravenous thiopentone sodium (20 mg/kg), the dogs were intubated with a cuffed endotracheal tube and anaesthesia was maintained with halothane (0.5%) while gluco-chloralose (Merck, Darmstadt) (40 mg/kg) was slowly injected intravenously. Light anaesthesia was maintained with chloralose (10 mg/kg) every 2–3 h as required. A double-lumen balloon catheter was inserted, under fluoroscopic control, into a pulmonary artery via the right external jugular vein for measurement of pulmonary arterial and wedge pressures. These pressures were measured with strain gauges (Statham type P23A 114) and recorded continuously on a multichannel recorder. Vascular pressures were measured from a zero reference pressure at the level of the left atrium estimated radiographically.

The bronchi of the right lung were outlined with tantalum powder (nominal particle diameter 1 μm; H. C. Starke, Berlin), which was dried previously in an oven at 90°C. The powder was insufflated through a catheter (Cournand; French gauge 7) directed into the segmental bronchi of the right lung under fluoroscopic vision. To prevent coughing and reflex bronchoconstriction the dogs were injected intravenously with atropine sulphate (0.6 mg).

Before the dog was placed in a vertical (head-up) position, the abdomen and hind limbs were bandaged firmly to prevent venous blood pooling.

The plan for the studies was to have a baseline period of observation, then to induce pulmonary oedema and to repeat all the observations in the oedematous state. These observations included chest radiographs, measurements of regional distribution of lung perfusion and ventilation, arterial and mixed venous blood gases and pulmonary vascular pressures.

Chest radiographs

Anteroposterior and right lateral radiographs were taken with a narrow (0.3 mm) focal-spot tube (Siemens, Sunbury-on-Thames, Middlesex, U.K.). The focus–film distance was 180 cm, so that the distance from focus to midpoint in the thorax was approximately 170 cm. Depending on the size of the dog, the settings of the X-ray tube were: for the anteroposterior radiographs, KV 78–90 and MA 80–100, exposure time 0.064–0.08 s; for the right lateral radiographs, KV 70–78 and MA 100, exposure time 0.064 s. The same settings were used before and after induction of oedema. Kodak XRP1 film and standard intensifying screens (Ilford) were used. An aluminium step wedge was included on each film for calibration of the film density. To prevent the dog from breathing at the moment of exposure, artificial hyperventilation with an Ambu bag was used for a few seconds before exposure. The radiographs were taken at times to coincide with end-diastole with a cardiac phase correlator (Nycotron, Oslo, Norway). The radiographs were taken with the chest inflated at pressures of 0, 0.5, 1.0, 1.5 and 2.0 kPa, before and after induction of oedema.

Regional lung perfusion

The regional distribution of perfusion to the lung was measured by embolizing the lungs with radioactively labelled microspheres [diameter 15 μm; 3-M (U.K.), Croydon, Surrey, U.K.]. At the end of the baseline period 1 μCi of 125I-labelled microspheres was injected intravenously, as a bolus, at the end of the expiration. After oedema development of 1 μCi of 85Sr-labelled microspheres was injected.
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Physiological shunt

In order to estimate the degree of physiological shunting (venous admixture) caused by oedema, mixed venous (pulmonary arterial) and arterial blood were sampled simultaneously, before and after induction of oedema. These were analysed for pH, $P_{O_2}$, $P_{CO_2}$ [blood gas analyser model 165 (Corning Eel) and oxygen saturation; IL 182 Co-oximeter. IL (U.K.) Ltd, Warrington, Cheshire, U.K.]. The shunt flow, $Q_{va}$, as a proportion of total flow was calculated with standard equations (Cotes, 1975).

Regional ventilation

In six dogs the regional distribution of ventilation was assessed during spontaneous tidal breathing by considering the relative changes in the ratio of regional tidal volume ($V_r$) to regional functional residual capacity (FRC) measured with $^{133}$Xe.

An integrated regional pulmonary function analyser (Ohio Nuclear, Solon, Ohio, U.S.A.) has been employed to facilitate preparation of a suitable $^{133}$Xe concentration and to process detector signals (Rawbone, 1976). $^{133}$Xe was mixed with air to a volume of 8 litres, in a wedge spirometer to give a maximum activity concentration of 0.8 mCi/l. The upright dog was connected to the spirometer in closed circuit and allowed to breathe to equilibration, which took an average of 150 s. Expired carbon dioxide was not absorbed from the circuit and therefore the breathing frequency and rate of equilibration increased. The increase in tidal volume was, in all cases, less than 10%. Respirations were monitored by the analyser.

Six sodium iodide scintillation detectors, with parallel cylindrical collimators, were positioned vertically against the dorsal aspect of the thorax, three on each side. These were positioned with reference to skin markers visible on the chest radiograph (Fig. 1) so that the upper detectors were aligned to the top of the thoracic cage. This caused, in several animals, the field of the lower detector to fall predominantly below the

![Fig. 1. Right lateral radiographs showing tantalum bronchograms of the right lung in one dog, before and after induction of oedema by extracellular fluid volume expansion (30% of body weight). Extravascular lung water/dry lung weight ratio = 8.2. The diaphragm has moved up. The bronchi in the lower zone are crowded together indicating a loss of volume which is confined to this zone.](image-url)
diaphragms, and this was particularly the case after the induction of oedema. There was some overlap of detector fields in the vertical plane but little overlap across the midline. The electrical output from the six ratemeters that was fed into a six-channel recorder, giving an analogue recording of the changing count rate during tidal breathing, which was proportional to regional \( V_T \) and that at end-expiration proportional to regional FRC, within the detector field. Values were calculated from the mean of five breaths.

The ventilation measurements from the right lung were ignored because of the tantalum powder in the airways on this side. It was frequently noticed that the pattern of the bronchograms changed with time and therefore it was uncertain that the distribution of ventilation would be unchanged.

In order to allow the comparison of regional distribution of ventilation before and after oedema and between animals, a regional tidal-ventilation index was derived, which is the ratio of regional \( V_T \) to regional FRC, both variables being represented as a proportion of total \( V_T \) and FRC respectively; the latter values are the sums of regional \( V_T \) and regional FRC from the three counters over the left lung. The index is therefore independent of regional volume or overall tidal volume. No account, however, has been taken of errors due to changing lung size and position during tidal breathing and with induction of oedema, or of the background chest wall counts.

**Induction of oedema**

Oedema was induced either by increasing microvascular permeability with alloxan (75 mg/kg, intravenously) (Eastman Kodak, Rochester, NY, U.S.A.) or by extracellular fluid volume expansion with Hartman’s solution infused at a rate of 2 ml min\(^{-1}\) kg\(^{-1}\) body weight \((n = 5)\). The volumes infused were 15–30% of body weight in different dogs \((15\% n = 2, 30\% n = 3)\) (Snashall, Weidner & Staub, 1977).

After volume expansion a period of 20–30 min was allowed for the pulmonary arterial and wedge pressures to return to the baseline value, before the post-oedema radiographs and observations were made.

**Analysis of lungs**

At the end of the experiment the dogs were killed with intravenous injection of pentobarbitone and the inflated lungs rapidly removed with the dog in the upright position. The lungs were immediately frozen in liquid nitrogen \((-196^\circ C)\). In a cold room at \(-20^\circ C\) each lung was divided into seven portions and each cut surface was examined macroscopically for the presence of perivasular and peribronchial cuffs of oedema and microscopically \((\times 30)\) for cuffing of small vessels and bronchioles. Each portion was separately analysed for its content of residual blood, extravascular water and dry lung weight. The method used was that of Pearce, Yamashita & Beazell (1965) as modified by Selinger, Bland, Demling & Staub (1975). Lung tissue was homogenized and the water content estimated by drying; residual blood content was estimated from the haemoglobin concentration of the centrifuged homogenate.

An aliquot of the homogenate of each portion of lung was placed in a gamma counter (model 8311, Nuclear Enterprises, Sighthill, Edinburgh, U.K.) and counted simultaneously for \(^{125}\)I and \(^{85}\)Sr. These counts were expressed per unit of blood-free dry weight of the lung portion.

**Assessment of the radiographs**

**Lung-volume changes**. Changes in the regional volumes of the right lung were estimated from the anteroposterior and right lateral radiographs with use of the tantalum bronchograms to identify the same portion of lung at different inflation pressures, before and after the induction of oedema. For the upper zone the portion of lung was above the heart and for the lower zone, below the heart. From the bronchograms it could be seen that the upper-zone measurements were made on the upper lobe and lower zone on the basal lobe. In each zone the most peripheral bronchus that could be seen in all films, before and after induction of oedema, was identified and the distance from this bronchus to the pleural surface was measured in three directions at right angles (Fig. 1). The product of these three dimensions was taken as an indication of the volume of the region of lung measured, allowing estimation of changes in volume with inflation and oedema.

**Validation of measurements of volume change**. In four dogs the percentage change in total intrathoracic volume was estimated from the tantalum bronchograms, taken at FRC, and at inflation pressures of 0.5, 1.0, 1.5 and 2.0 kPa during the baseline period. The method described above was used to measure the vertical dimension from the highest apical bronchus to the diaphragmatic surface and the anteroposterior and lateral dimensions, at a level approximately
one-third of the distance from the diaphragm to the apex. These volume changes were compared with directly measured thoracic gas-plus-tissue volumes. Duplicate measurements of FRC were made by helium dilution with the dog rebreathing approximately 1.5 litres of a helium/oxygen mixture for 12 breaths. The increments of volume at each inflation pressure were measured with a spirometer. Lung tissue and blood volume were assumed to equal 1% of the body weight.

**Airway-diameter changes.** Changes in the luminal calibre of bronchi, outlined with tantalum powder before and after oedema, were assessed. These bronchi were between 0.2 and 1.5 cm in diameter in the baseline state, being lobar, segmental, subsegmental and sub-subsegmental divisions. The diameters of three to eight bronchi in each dog were measured at each inflation pressure, before and after oedema. The same section of airway was identified in each film. Where possible, straight cylindrical segments between bifurcations were chosen and were measured with dividers at right angles to the direction of the bronchus.

**Statistical analysis.** The variables, before and after oedema development, were compared in the same dog with Student’s paired t-test (two-tailed) and compared between groups with the unpaired t-test. Linear regressions were calculated with the least-squares method. A value of $P < 0.05$ was considered as significant.

**Results**

**Extravascular water and dry lung weight**

Similar amounts of oedema developed in volume-expanded and alloxan-injected groups. Mean extravascular water/dry lung weight ratios were $6.2 \pm 1.4$ and $6.7 \pm 1.3$ respectively. The mean value in upright control dogs measured in this laboratory is $4.3 \pm 0.3$ ($n = 5$). However, the insufflation of tantalum powder into the right lung artifically increased dry lung weight and therefore decreased the extravascular water/dry lung weight ratio. In dogs without bronchography the ratio of dry weights of the right and left lung was previously found to be $1/1$ ($n = 5$), and in this series with bronchography the ratio was $1.6/1.0$ ($n = 5$). It was calculated that on average 1.5 g of tantalum powder remained in the right lung at the end of the experiment. Mean extravascular water/dry lung weight ratios in the left lungs were $7.1 \pm 1.6$ and $6.3 \pm 1.3$ in the volume-expanded and alloxan-injected groups respectively.

**Regional volume changes**

With the development of oedema there was a fall in lower-zone lung volume shown by most dogs, that on average varied from 15 to 22% at inflation pressures from 0 to 2 kPa (Fig. 1). Taking the two groups together the change was statistically significant at all inflation pressures except 1 kPa. In the volume-expanded group all dogs showed a loss of lower-zone volume that varied from 22 to 30% at different inflation pressures and were significant at each pressure (Fig. 2). Smaller decreases were seen in alloxan-injected dogs (3–12%), which were not significant at any pressure. There were no significant changes in upper-zone lung volumes, although these increased in volume-loaded dogs by 7–12%.
TABLE 1. Mean (± SD) changes in lung dimensions with oedema and deflation

<table>
<thead>
<tr>
<th>Zone</th>
<th>Upper</th>
<th>Lower</th>
<th>Upper</th>
<th>Lower</th>
<th>Upper</th>
<th>Lower</th>
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<tbody>
<tr>
<td>Oedema</td>
<td></td>
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<tr>
<td>Alloxan</td>
<td>-3 (5)</td>
<td>-1 (10)</td>
<td>-4 (7)</td>
<td>-17 (20)</td>
<td>-3 (2)</td>
<td>-14 (6)</td>
</tr>
<tr>
<td>Volume expansion</td>
<td>15 (23)</td>
<td>9 (13)</td>
<td>1 (6)</td>
<td>-13 (8)</td>
<td>-4 (3)</td>
<td>-13 (9)</td>
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<tr>
<td>Deflation</td>
<td></td>
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<td>(n = 5)</td>
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<td>(n = 10)</td>
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FIG. 3. Correlation between intrathoracic volume change measured radiographically and volumetrically in four dogs. The lungs were inflated from FRC to airway pressures of 0·5, 1·0, 1·5 and 2·0 kPa and the change in air volume was measured with a spirometer. Lung volume at FRC was measured by helium dilution. The lung tissue and blood volume were calculated by assuming that they comprise 1% of body weight. The line of identity is shown.

dimension with little changes in the other two dimensions. Dimensional changes due to the induction of oedema differed from those due to lung deflation. When the lung deflated from 1·5 kPa inflation pressure to FRC during the baseline period, upper-zone volume decreased by an average of 19% and lower zone by 36%. This was accomplished in the upper zone mainly by a 13% fall in the lateral dimension, whereas in the lower zone all dimensions decreased to a similar extent (anteroposterior -14%, lateral -16% and height -13%).

Validation of measurement of volume change

The relationship between lung volume changes measured radiographically and spirometrically is shown in Fig. 3 ($r = 0·93$, $P < 0·01$). On
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Fig. 4. Distribution of perfusion to the left lung lobes before (-----) and after (----) oedema. Mean values (±1 sem) for the groups are shown: (a) volume-expanded and (b) alloxan-injected. The area shown for each lobe is proportional to the total perfusion to that lobe: UL, upper lobe; ML, middle lobe; LL, lower lobe.

Table 2. Pulmonary vascular pressures at the times of study

<table>
<thead>
<tr>
<th>Group</th>
<th>Pressure (kPa)</th>
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<tr>
<td></td>
<td>Baseline</td>
<td>Final</td>
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<td></td>
<td>Pulmonary</td>
<td>Pulmonary</td>
<td>Pulmonary</td>
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<td></td>
<td>artery</td>
<td>wedge</td>
<td>artery</td>
<td>wedge</td>
<td></td>
</tr>
<tr>
<td>Alloxan</td>
<td>12.0 ± 2.3</td>
<td>0.6 ± 2.6</td>
<td>13.4 ± 3.1</td>
<td>-0.6 ± 2.3</td>
<td></td>
</tr>
<tr>
<td>Volume expansion</td>
<td>11.8 ± 7.5</td>
<td>2.2 ± 4.6</td>
<td>10.2 ± 5.0</td>
<td>-1.0 ± 1.1</td>
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</tr>
</tbody>
</table>

average, volume change measured radiographically is a slight overestimate of volumetrically measured volume change; large (20–30%) deviations from the line of identity were seen in three out of 14 measurements.

Changes in regional perfusion with oedema

In general, the changes in the pattern of regional distribution of labelled microspheres after the development of oedema were slight (Fig. 4). In four volume-expanded dogs perfusion of the lower lobe decreased (mean -12.1 ± 5.6%) and the middle and upper lobe increased (mean 85.9 ± 85.6 and 11.4 ± 69.7 respectively). In the other volume-expanded dog there was no change in perfusion. This slight upward redistribution of perfusion was seen even though the pulmonary vascular pressures were allowed to return to approximately baseline values before the microspheres were injected (Table 2). The alloxan group of dogs showed little change in the distribution of perfusion.

Physiological shunt

Venous admixture (Qsv > 0.10) causing hypoxia occurred in three dogs (two volume-expanded, one alloxan-injected) after oedema development. Their mean shunt was 0.26. The mean lung water ratio of these dogs (left lungs, 7.2 ± 2.0) was slightly greater than that of the
remaining oedematous dogs (6.5 ± 1.2). The mean lower-zone volume change in hypoxic dogs was -30.2%, whereas animals without significant shunting had on average no volume change (mean +0.35%). Owing to the small numbers, these differences are not statistically significant. These results have therefore been combined with those from five dogs in the previous series (Snashall et al., 1980) in which physiological-shunt measurements were made. These were four dogs in which volume expansion was performed as in the present study and one dog that developed oedema after pulmonary angiography. Three of the volume-expanded dogs developed shunts in excess of 0.10 as did the dog with oedema after angiography. Thus we have a total of seven dogs with $Q_{va} > 0.10$ (mean 0.32 ± 0.19), all of which had marked loss of lower-zone lung volume (mean -41 ± 15%) and eight dogs without significant shunting or volume loss (mean -0.1 ± 12%). The difference in the volume loss between these groups is significant ($P < 0.001$). The mean lung water ratios of these groups were not significantly different ($Q_{va} > 0.1$ group; extravascular water/dry lung weight ratio 6.4 ± 1.8; $Q_{va} < 0.10$ group extravascular water/dry lung weight ratio 6.3 ± 1.2) and there was no significant correlation between the extravascular water/dry lung weight ratio and physiological shunt ($r = 0.37, P > 0.05$), whereas volume change and physiological shunt showed a significant negative correlation ($r = -0.83, P < 0.001$, Fig. 5).

**Change in regional ventilation with oedema**

In the baseline period the regional ventilation index was similar in the volume-expanded and alloxan-injected dogs (Fig. 6). Ventilation per unit lung volume is two to three times greater at the

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**Fig. 5.** Relationship between lower-zone volume change and physiological shunt. In addition to dogs from the present series (○), values from a previous series, studied under similar circumstances, are included (▲) (Snashall et al., 1980). It is assumed that the appropriate regression line is hyperbolic, but there are insufficient points for curve fitting. Linear regression gives a significant relationship ($y = 0.008x -0.018; r = -0.83, P < 0.01$). Venous admixture is uniquely associated with lower-zone volume loss >20%.

**Fig. 6.** Distribution of tidal ventilation between lung regions under three vertically placed gamma counters over the left lung, before (-----) and after (---) oedema in (a) volume-expanded and (b) alloxan-injected groups.
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Lower-zone volume change (%) 
-35 -30 -25 -20 -15 -10 -5 0

-40

FJG.

7. Relationship between change of lower-zone lung volume and lower-zone airway diameter, showing the regression line (-----) and 95% confidence limits (-----) of the line (y = 0.61x -7.01; r = 0.75, P < 0.025). Each point represents the result in one dog and relates lower-zone volume change to the mean change in airway diameter in that zone.

base than at the apex of the lung. With induction of oedema, the tidal volume did not change significantly (mean reduction of 5%). Both groups showed an increase in ventilation index at the top of the lung (29% increase in volume-expanded dogs; 48% increase with alloxan). There were only slight changes in the region under the middle counter. In the lower region there was a 27% fall in ventilation index in the alloxan-injected dogs (P < 0.02) but only slight changes (mean increase of 6%) in the volume-expanded dogs.

Changes in airway diameter with oedema

Before and after the development of oedema, airway diameter was a function of inflation pressure. With the development of oedema in several dogs there was obvious narrowing of the Airways outlined by tantalum powder, by up to 40%. This narrowing was largely confined to the lower zones in dogs showing a loss of lower-zone lung volume and there was a significant correlation between loss of volume and narrowing (Fig. 7; r = 0.75, P < 0.025), but not between the extravascular water/dry lung weight ratio and narrowing (r = -0.44, P > 0.05). There were no differences in behaviour of large and small airways over the range of calibre studied.

Discussion

This study, using tantalum bronchography to outline the lung, has confirmed our previous finding that in pulmonary oedema there is usually a loss of volume in the dependent regions of the lung. This effect was most marked in volume-expanded dogs.

We have quantified lung-volume changes by measuring anteroposterior, lateral and vertical dimensions within the upper and lower zones. The true total volume of these zones is the product of their largest anteroposterior lateral and vertical dimensions and a constant which takes account of the zonal shape. If shape does not change with oedema, the percentage change in volume can be found from the change in the product of the three dimensions without considering shape. Similarly the percentage change in volume can be obtained from the product of representative fractions of the total linear dimensions. Use of an intrapulmonary marker has allowed us to compare the same portion of lung, before and after oedema, despite large changes in volume which greatly alter the relative positions of lung and rib cage. There are, however, several problems. (1) It may be incorrect to assume that no change in lung shape has occurred. (2) There are, possibly, measurement inaccuracies due to parallax if there is a change in alignment of the dog between the X-ray tube and the film. Malalignment, however, is obvious on the films and when seen, the films were rejected. (3) There are sampling errors because measurements depend on the availability of suitable bronchial landmarks. Volume loss does not appear to be evenly distributed throughout a zone, but is greatest in the most dependent parts. Generally we have attempted to measure changes as low down the lower zone as possible and therefore our measurements were biased in favour of the lowest part.

In our validation of the tantalum bronchography method we found a satisfactory correlation between radiographic and spirometric volume changes (Fig. 3). We suspect that the accuracy of regional volume-change measurements is higher than the comparison suggests. Owing to inhomogeneity of lung expansion from base to apex, total intrathoracic volume changes cannot be estimated accurately from three dimensions alone. Since inhomogeneity is likely to be less within regions of the lung, accuracy of regional volume measurements should be higher.

Volume loss correlated poorly with extravascular lung water, as we have shown before. The loss was much greater in volume-expanded dogs than with alloxan and was statistically insignificant in the latter group. We have previously found, with more florid alloxan oedema, that larger, statistically significant volume loss
occurs (Snashall et al., 1980). Volume loss was consistently due to reductions in the antero-posterior and vertical dimensions of the lower zones while lateral dimensions increased.

We can only speculate about the cause of the loss of volume. In volume-expanded dogs there is a great deal of accumulation of liquid beneath the diaphragm. At post-mortem examination these dogs frequently show ascites, retroperitoneal oedema, hepatic and splenic distension. The diaphragm will thus be elevated, with a reduction of vertical and antero-posterior dimensions in the lower zone. The increase of lateral dimension may also be due to abdominal distension since the upper abdomen is bounded on either side by the lower lateral ribs. It is also possible, however, that some of the lateral increase is due to tonic inspiratory activity, compensating for the decrease in lung volume (Sant’ Ambrogio & Widdicombe, 1965). Lung volume may also decrease due to an accumulation of water in airspaces leading to alveolar collapse or peripheral airways obstruction and atelectasis of distal airspaces. Although other workers have demonstrated increasedclosing volumes in oedema (Hughes & Rosenzweig, 1970), increased lung volume in oedema was never seen by us even at FRC. We assume that, in all cases, the regional closing volume was below FRC.

We have found an excellent relationship between physiological shunt and loss of lower-zone lung volume in oedema (Fig. 5) but a very poor relationship between lung water and shunt. These findings are reasonable since it is only when alveoli collapse that interference with gas exchange occurs. A great deal of oedema may accumulate in the extra-alveolar interstitium without interfering with gas exchange. The loss of lung volume indicates the degree of alveolar collapse and the magnitude of the shunt. Said et al. (1964) found that forcible inflation of oedematous lungs produced an immediate relief of hypoxia.

The close relation between volume and shunt suggests that there is little diversion of blood flow away from collapsed regions. Our regional perfusion studies have confirmed this in volume-expanded animals and agree with the findings of Muir, Hall, Despas & Hogg (1972). In our study, unlike that of Muir et al., there was no significant elevation of pulmonary vascular pressures at the time of the post-oedema flow measurement. A similar degree of oedema in alloxan-injected dogs caused no redistribution of blood flow. Although lung-volume loss may have caused the redistribution of perfusion in volume-expanded dogs, alternatively this may be due to changes in cardiac output, which probably increased after volume expansion and decreased after alloxan (Staub, Nagano & Pearce, 1967).

The limited extent of the blood-flow redistribution with oedema is particularly puzzling in the light of an incidental observation that we have made. After insufflation with tantalum powder it was noticed that several dogs became severely hypoxic. In four dogs in which physiological shunts were measured at this stage, $Q_{lu}$ ranged from 0-22 to 0-65 (mean 0-44 ± 0-15). However, in all cases these resolved spontaneously over 60–120 min during the baseline period. Although some of this resolution may have been due to relief of bronchial plugging by the tantalum, some was due to diversion of perfusion away from the right lung, as was demonstrated by the baseline microsphere study; the right lower lobe received 33% of total lung perfusion and the left lower lobe received 41%; this diversion continued after the production of oedema (right lower lobe 30%; left 41% of total perfusion).

Oedema was associated with a diversion of ventilation away from the lower parts of the lung and towards the apex. In volume-expanded dogs, lower-regional ventilation index (ventilation per unit lung volume) did not change with oedema. However, because lower-zone radiographic lung volume decreased (mean 27%) ventilation must have decreased to a similar extent. This implies that ventilation of uncollapsed units was little changed. In alloxan-injected dogs, the diversion of ventilation from the lower lobes in the absence of diversion of perfusion would seem to aggravate, rather than relieve, the tendency to hypoxia.

Large airways narrow considerably when pulmonary oedema is associated with a loss of lower-zone volume. Although it is not possible in our study to separate the effect of lung volume from that of oedema, the significant correlation between volume loss and airway narrowing (Fig. 7) suggests a causal relationship. The relationship between airway calibre and lung volume may have been altered by reduction of airway smooth-muscle tone due to atropine with which these dogs were premedicated. There seems to be no direct relationship between the increase of lung water and the decrease of either lung volume or airway diameter. All dogs showed some degree of peribronchial cuffing with oedema, but the size and extent of cuffing bore no relationship to the degree of narrowing. Upper-zone airways, which frequently showed peribronchial oedema cuffs, generally did not narrow with oedema even when this was associated with lower-zone volume loss.

Although airway resistance was not measured, we predict that changes in airway calibre of
this magnitude would have considerable effects on airflow resistance, particularly in the dependent lung zones. However, in open-chested dogs with pulmonary oedema, Hogg, Agarawal, Gardiner, Palmer & Maclem (1972) found little change in central airway (> 2 mm diameter) resistance, and peripheral airway (< 2 mm diameter) resistance increased. Since these lungs were hyperinflated to a pressure of 3 kPa before each resistance measurement, any oedema-induced loss of lung volume may have been overcome and changes in large airway size not observed.

Our observations may be relevant to the clinical presentation of pulmonary oedema. A loss of radiographic lung volume is frequently seen in man (Kreel & Sandin, 1977) and airway obstruction, manifest by wheezing or ventilatory failure (Avery, Samet & Sackner, 1970), is present in a minority of patients. There are likely to be multiple causes of narrowing of airways in clinical pulmonary oedema, but the possibility that lung-volume changes contribute is worthy of further investigation.

References


