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**Research Article**

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# Elastic Properties of the Centrilobular Emphysematous Space

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Abstract Bronchograms were performed using finely particulate lead on emphysematous lungs obtained at necropsy. X-ray films were taken of these lungs at distending pressures of 0, 5, 10, and 20 cm $H_2O$. The volumes of individual centrilobular emphysematous spaces were calculated at each distending pressure from measurements made on these bronchograms and pressure-volume curves were constructed for each space. The pressure-volume characteristics of seven normal lungs and one lung with centrilobular emphysema was also measured. The normal lungs, the lung with centrilobular emphysema, and the centrilobular emphysematous spaces were compared by expressing the volume of air contained in them at each distending pressure as a per cent of the volume contained at 20 cm $H_2O$ distending pressure. We conclude that centrilobular emphysematous spaces have a high residual volume, are less compliant than normal lung tissue, and are much less compliant than the emphysematous lungs which contain them. Furthermore, these spaces undergo little volume change in the tidal breathing range and probably add a relatively nondistensible series dead space to the surrounding lung parenchyma.

## INTRODUCTION

The description of centrilobular emphysema (CLE) by Gough and his associates (1, 2), and the realization that centrilobular emphysematous spaces could be seen on bronchograms (3) represent important advances in the morphologic description of emphysema. Although it is well known that emphysema decreases lung elasticity and it is generally assumed that this loss occurs in the areas of lung affected by the disease, there have been no studies of the elastic properties of specific emphysematous areas within a lung. The purpose of this investigation was to compare the elastic properties of normal lung tissue to those of centrilobular emphysematous spaces observed on bronchograms.

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## METHODS

Lungs from seven normal and four emphysematous cases were obtained from the autopsy service of the Royal Victoria Hospital. Finely particulate lead was insufflated into the emphysematous lungs to outline the bronchi and centrilobular spaces (4). X-ray films were taken at transpulmonary pressures of 20, 10, 5, and 0 cm of water on the deflation limb of the pressure-volume curve. These films were examined on a standard viewing box with a dissecting microscope and measurements were made with an eyepiece micrometer. The largest diameter of each space and the greatest diameter 90° to it were carefully marked on each film. These dimensions were measured by two observers and the volume of each space was calculated by taking the average of the two diameters and using the formula for the volume of a sphere. Errors due to magnification were assessed by blowing ball bearings into the bronchial tree of another lung and obtaining films and measurements in the same way. The size of the ball bearings was not known to the observers at the time of measurement.

Static pressure-volume curves were obtained on the normal lungs using a volume-displacement plethysmograph to measure lung volume, a Sanborn 267B transducer to measure transpulmonary pressure, a Tektronix storage oscilloscope, and a Sanborn 4-channel recorder to record the pressure and volume signals. The volume of the lungs (both tissue and air) at 0 cm $H_2O$ distending pressure was obtained by water displacement. The air was then evacuated from the lungs in a vacuum chamber and the tissue volume was obtained by water displacement of the gas-free specimen. The minimal gas volume (defined as the amount of gas in the lungs at zero transpulmonary pressure) was calculated by subtracting the tissue volume from the total volume at zero distending pressure. The gas volume at any distending pressure was found by adding the minimal gas volume to the volume measured by the plethysmograph. A distending pressure of 20 cm $H_2O$ was chosen as total lung capacity because of the marked tendency for air to leak from around the vasculature beyond this point. All lung volumes are expressed as a per cent of the value obtained at this pressure.

## RESULTS

An example of the quality of bronchographs obtained with this technique is shown in Fig. 1 where the variation in space size with distending pressure is shown. Although Fig. 1 demonstrates that the space is not absolutely spherical, it can be seen that the dimensions

changed uniformly so that the error introduced by the assumption of spherical space will not vary with distending pressure. Separate measurements of the spaces by the same observer agreed within 1% and measurements made by two observers were not significantly different when compared by the paired $t$ test ($P > 0.1$).

In measurements of this type errors between the real diameter of an object and its shadow seen on X-ray are to be expected. The magnitude of these are shown in Table I where the measured diameter of the ball bearings is compared to their real diameter. At zero distending pressure this error ranges from 0.3 to 3.1% with an average of 1.22%, but at the highest distending pressure it increased 1.6–9.1%, average 4.5%. The error is not random and leads to an overestimate of the true dimensions and the overestimate increases with lung volume.

No systematic relationship could be demonstrated between the initial size of the space and its expansion. The spaces are grouped according to their initial volume in Fig. 2 which shows that most spaces changed little in size as the lung was inflated and that the spaces demonstrating the greatest increase in volume undergo the majority of this change between 0 and 10 cm $H_2O$ distending pressure. The per cent change in the size of the spaces is compared with the per cent change in size of the normal lungs in Table II. The initial volume of the spaces averaged 59% of the total volume and increased by only 26% of the total volume between 0 and 10 cm $H_2O$ distending pressure. The average initial volume of the normal lungs on the other hand was only 24% of the total volume and they increased by 64% of the total volume between 0 and 10 cm $H_2O$ distending pressure.

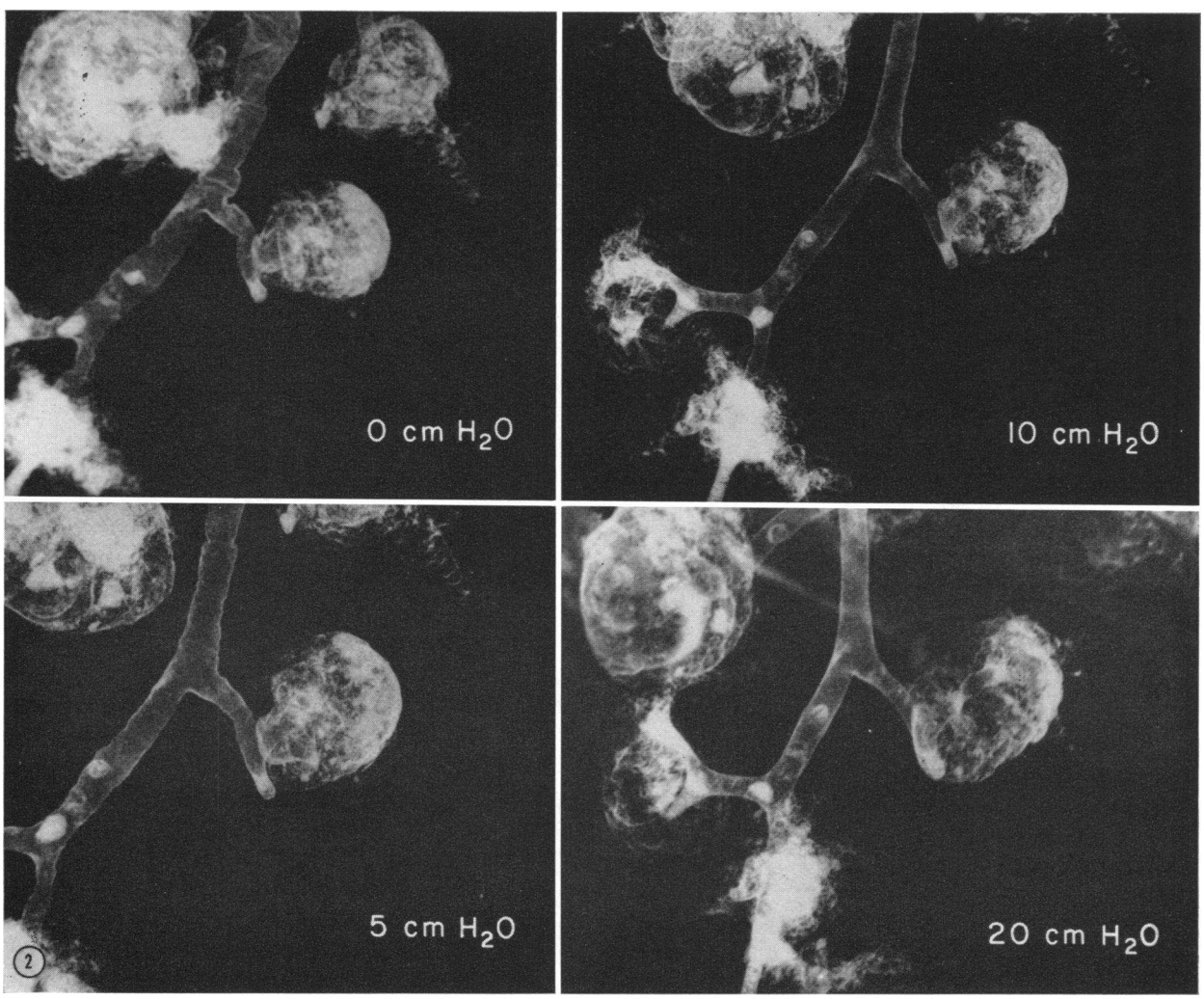


FIGURE 1 Demonstrates the change in appearance of a centrilobular emphysematous space at 0, 5, 10, and 20 cm $H_2O$ transpulmonary pressure. × 5.4.

Table III shows the distribution of the spaces in the four emphysematous lungs studied and the severity of the emphysema in these lungs.

A comparison of the normal lungs, the centrilobular empyhsematous spaces, and one lung with centrilobular emphysema is shown in Fig. 3. This summarizes the data and shows that the lung with centrilobular emphysema had a higher residual volume and was more compliant than normal lungs, whereas centrilobular emphysematous spaces have a lower compliance and a higher residual volume than either normal lungs or the lung with centrilobular emphysema.

## DISCUSSION

The major source of error in experiments of this type arise from the fact that the volume of an object (i.e. CLE space) is estimated from its shadow on an X-ray. The measurements made on the X-ray were found to be reproducible by the same observer and there was no significant difference in measurement between two observers. The relationship of these measurements to the actual volume was another matter because the measurements of ball bearing dimensions (Table I) showed that the error depended on where the ball bearing was located

TABLE I

*Per Cent Error in the Assessment of the Known Diameter of 14 Ball Bearings in the Lung Subjected to Different Distending Pressures*

| Ball bearing No. | Distending pressure (cm $H_2O$) | | | |
|---|---|---|---|---|
| | 0 | 5 | 10 | 20 |
| 1 | 3.1 | 5.0 | 5.6 | 6.2 |
| 2 | 0.3 | 0.9 | 2.2 | 2.5 |
| 3 | 0.3 | 0.3 | 1.9 | 2.5 |
| 4 | 0.3 | 0.6 | 0.6 | 1.6 |
| 5 | 0.3 | 0.6 | 0.6 | 1.6 |
| 6 | 1.2 | 0.9 | 2.5 | 2.5 |
| 7 | 2.2 | 3.1 | 4.7 | 6.2 |
| 8 | 1.9 | 3.1 | 3.1 | 4.7 |
| 9 | 2.8 | 2.8 | 2.8 | 4.1 |
| 10 | 0.2 | 2.5 | 3.1 | 4.7 |
| 11 | 1.6 | 1.9 | 3.1 | 5.3 |
| 12 | 1.6 | 3.1 | 4.4 | 5.0 |
| 13 | 1.2 | 4.1 | 1.5 | 9.1 |
| 14 | 2.5 | 3.8 | 4.4 | 7.8 |
| Mean error in linear measurement | 1.2 | 2.3 | 2.9 | 4.6 |
| Mean error in volume measurement | 4.7 | 8.0 | 10.4 | 14.4 |

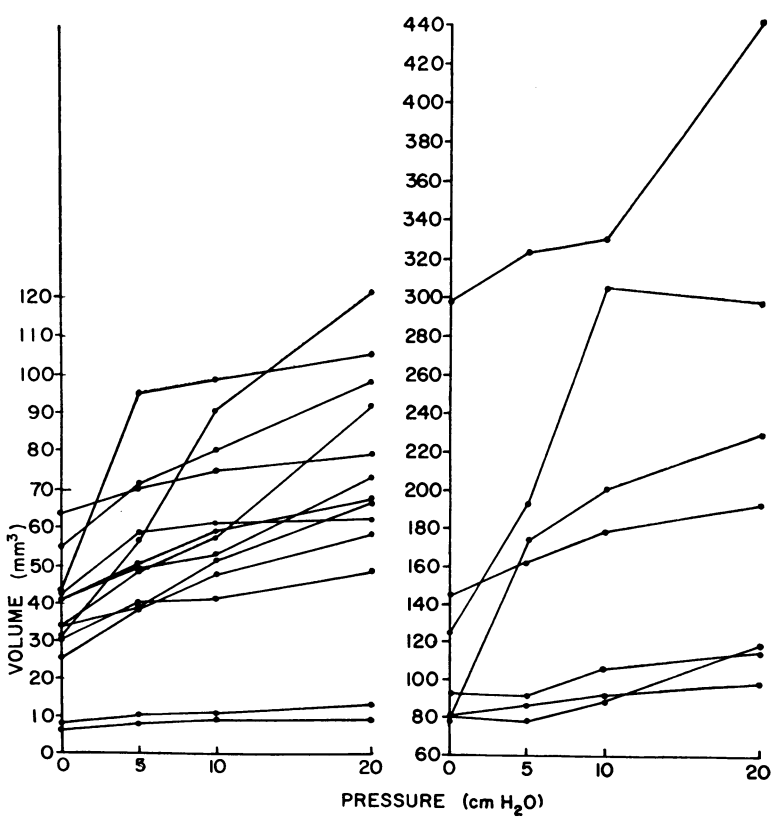


FIGURE 2 Change in volume of individual centrilobular spaces with distending pressure.

TABLE II

*Pressure-Volume Characteristics of Centrilobular Spaces and Normal Lungs*

| Space No. | Per cent of volume at 20 cm $H_2O$ transpulmonary pressure | | | | Gas volume at 20 cm $H_2O$ transpulmonary pressure, actual volume (ml) |
|---|---|---|---|---|---|
| | 0 | 5 | 10 | 20 | |
| 1 | 51 | 59 | 78 | 100 | 0.067 |
| 2 | 42 | 65 | 100 | 100 | 0.297 |
| 3 | 80 | 80 | 92 | 100 | 0.115 |
| 4 | 56 | 73 | 82 | 100 | 0.098 |
| 5 | 47 | 68 | 82 | 100 | 0.057 |
| 6 | 68 | 79 | 87 | 100 | 0.020 |
| 7 | 61 | 76 | 86 | 100 | 0.067 |
| 8 | 64 | 83 | 86 | 100 | 0.049 |
| 9 | 82 | 86 | 93 | 100 | 0.099 |
| 10 | 82 | 89 | 94 | 100 | 0.079 |
| 11 | 75 | 85 | 93 | 100 | 0.192 |
| 12 | 68 | 68 | 75 | 100 | 0.119 |
| 13 | 68 | 73 | 75 | 100 | 0.442 |
| 14 | 56 | 69 | 72 | 100 | 0.073 |
| 15 | 32 | 47 | 74 | 100 | 0.121 |
| 16 | 34 | 76 | 87 | 100 | 0.228 |
| 17 | 67 | 80 | 90 | 100 | 0.107 |
| 18 | 38 | 54 | 62 | 100 | 0.099 |
| 19 | 69 | 96 | 99 | 100 | 0.067 |
| | 59 ±7 | 74 ±5 | 85 ±4 | | 0.120 |
| Lung Side | | | | | |
| 1 L | 20 | 80 | 93 | 100 | 1650 |
| 2 R | 16 | 55 | 86 | 100 | 1050 |
| 3 L | 34 | 81 | 91 | 100 | 2210 |
| 4 L | 35 | 64 | 87 | 100 | 1930 |
| 5 R | 17 | 71 | 89 | 100 | 1720 |
| 6 R | 25 | 69 | 89 | 100 | 3630 |
| 7 L | 23 | 67 | 87 | 100 | 3330 |
| | 24 ±6 | 70 ±7 | 89 ±2 | | 2217 ±710 |

in the lung. Those located at a distance from the film had greater errors due to magnification than those located closer to the film. As inflating the lung increases all of the object film distances, the errors in linear measurement increased on the average from 1.2% at 0 distending pressure to 4.6% at a distending pressure of 20 cm $H_2O$. When this error in linear measurement is converted to the error in measurement of the volume of a sphere the mean error increased from 4.7% at 0 distending pressure to 14.4% at a distending pressure of 20 cm $H_2O$. As we are comparing the same spaces at different distending pressures the errors due to magnification result in an overestimate of CLE space volume which increases with lung volume and makes the centrilobular spaces appear to be more compliant than they really are.

In spite of this error we found the CLE spaces to be less compliant than normal lung tissue. Presumably the

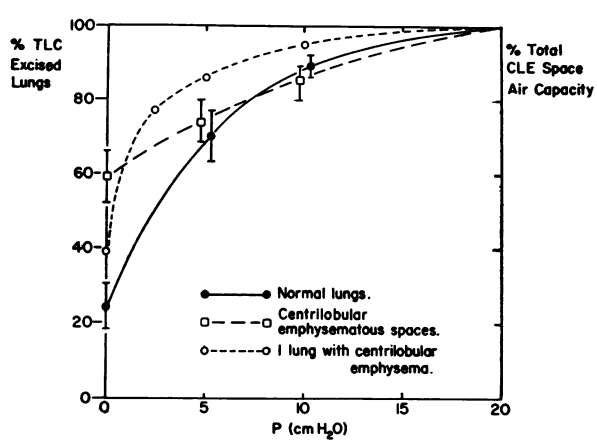


FIGURE 3 Comparison of the pressure-volume characteristics of centrilobular emphysematous spaces. Normal lungs and one of the lungs (case 1, Table III) with centrilobular emphysema. TLC = total lung capacity.

TABLE III

*Demonstration of the Severity of Emphysema in the Four Cases from Which the Measurements on the Centrilobular Emphysematous Spaces were Obtained and the Distribution of These Spaces in the Lungs*

| Case No. | Space No., see Table II | Severity of emphysema | | | |
|---|---|---|---|---|---|
| | | Lm | $ISA_5$ | Point count | Subjective index |
| 1 | 1–8 | 124 | 82 | 41 | 16 |
| 2 | 9–13 | 154 | 59 | 95.3 | 18 |
| 3 | 13–17 | 146 | 66 | 87.3 | 17 |
| 4 | 17–19 | 106 | 113 | 60.9 | 14 |

Lm = mean linear intercept and is expressed as a per cent of the predicted value; $ISA_5$ = the internal surface area of the lung at a volume of 5 liters; point count: modification of Dunnill's method of quantitating emphysema and expresses the percent of the parenchyma involved in the disease; subjective index: grades emphysema on a 0–30 scale on the basis of both extent and severity of the disease. These methods of measuring emphysema are fully discussed in reference 5.

CLE spaces are even less compliant than we measured them to be, whereas the lung with centrilobular emphysema was more compliant than normal lungs.

It is important to note that the centrilobular spaces have been compared to emphysematous and normal lungs and not the structures which have been destroyed by emphysema. It is theoretically possible that if the respiratory bronchioles and alveolar ducts were rigid tubes, then destruction could cause an increase in compliance of the lung while the centrilobular space was only slightly less rigid than normal. However, since Storey and Staub (6) have shown that the alveolar ducts and alveoli expand equally when the lung is inflated and Macklin (7) thought that the ducts actually expanded more than the alveoli this explanation seems untenable. Therefore, we conclude that the centrilobular space is much less compliant than the structures which were destroyed to form it.

Bates and Christie (8) postulated that $\dot{V}a/\dot{Q}$ abnormalities surrounding the centrilobular spaces might result in severe defects in gas exchange in this condition. The concept that patients with centrilobular emphysema have defects in gas exchange out of proportion to the amount of lung tissue that is destroyed has been supported by Dunnill (9) who found that the volume of centrilobular emphysema in five patients dying of the disease was small and that a large volume of normal parenchyma remained. Staub (10) has suggested that if the spaces were hypercompliant they would receive a larger proportion of each tidal breath than the well perfused normal lung and that this would affect gas exchange. This means that if a patient increased minute ventilation he would increase the ventilation of CLE spaces but not necessarily increase the ventilation to normal lung regions. The centrilobular spaces would then represent a parallel or alveolar dead space with a high $\dot{V}a/\dot{Q}$ that would increase with tidal volume, whereas the $\dot{V}a/\dot{Q}$ of the normal parenchyma would be low and there would be an adverse effect on gas exchange.

Our data suggest that on the contrary the centrilobular spaces have a decreased compliance so that increasing tidal volume would not increase their contribution to the dead space. This means that the VD/VT ratio should decrease with increasing tidal volume and (if poorly perfused) the CLE spaces would make up part of the series or anatomic dead space of the lung.

Although there has been no comprehensive morphologic study of the airways leading to centrilobular emphysematous spaces, the airways leading to spaces which Leopold and Gough (2) studied by serial sections were always patent and often completely unobstructed. Because our bronchograms showed that airways surrounding the centrilobular spaces were often plugged (Fig. 1) we have recently speculated (11) that the CLE spaces may function as antechambers which fill and empty directly from the atmosphere and collaterally from surrounding normal parenchyma with obstructed airways. Our present study lends support to the concept as we have shown that these spaces are nearly fully inflated at low distending pressures so that collateral ventilation can take place easily. If this hypothesis is correct, the centrilobular lesions themselves would not greatly affect gas exchange, but if the volume of lung ventilated via collateral channels was large, gas exchange would be impaired on this account.[1]

The description of the elastic properties of elastin and collagen has led to theoretical considerations concerning the role of tissue forces in the lung, which are of importance to the interpretation of our data. Elastin is a highly extensible substance with length-tension curves that are very nearly linear up to 70% extension beyond its resting length while collagen is virtually inextensible beyond its resting length (12). The suggestion that these two structures make up single units in parallel has been used by Setnikar (13) to describe the pressure-volume behavior of the lung and by Burton (14) to describe similar behavior in blood vessels. If they are arranged as units in parallel so that during the initial stretch of the unit the collagen fiber remains at less than its resting length the unit will exhibit the

[1] Brown, R., A. Woolcock, N. Vincent, and P. T. Macklem. Physiologic effects of experimental airway obstruction. *J. Appl. Physiol.* In press.

length tension characteristics of the elastic fiber. When the unit is further stretched however, the collagen fiber will come into play so that the unit becomes nonextensible.

At the present state of our knowledge it is impossible to assign specific elastic properties to each of the variety of individual structures which make up the lung. However, it is possible to explain our data by using a model similar to the one suggested by Setnikar. This model would have two types of elastic element. Type A would behave like elastin and have uniform elastic properties through its entire length whereas the other, type B, would behave like collagen and would be easily stretched initially but would become much stiffer as it was stretched beyond its resting length. Their combined effect during inflation is shown in Fig. 4. It is important to note that we do not assign a type of behavior to a particular lung structure but merely suggest that the structures in a given lung lobule could be classified in one or the other of the elastic types. Now if in centrilobular emphysema the structures which behave like elastin are slowly destroyed we would expect the lobule to gradually become more compliant so that it would eventually exhibit the pressure-volume characteristics of a lobule constructed from the collagen-like type B fibers. Under these conditions the lobule would fill rapidly at relatively low distending pressures and its volume would change little as the distending pressure was further increased.

The data which we have summarized in Fig. 3 is consistent with the above analysis providing we assume that airway closure traps gas in the lung so that a transpulmonary pressure of zero, the pressure in the lung parenchyma, and in particular in the centrilobular spaces, is slightly greater than zero. This would have little affect on normal parenchyma but it would keep the centrilobular spaces nearly fully inflated because they would exhibit the pressure-volume characteristics of the collagen-like type B fibers. When the whole lung was inflated these spaces would undergo little further increase in size but the lung containing them would be hypercompliant if lung regions not involved by fully developed centrilobular emphysema had a milder form of the disease. This concept was supported by the examination of the lung in which we measured both the elastic properties of the CLE spaces and the pressure-volume curve of the whole lung because it was easy to demonstrate mild emphysema in the parenchyma not involved by centrilobular spaces (Fig. 5).

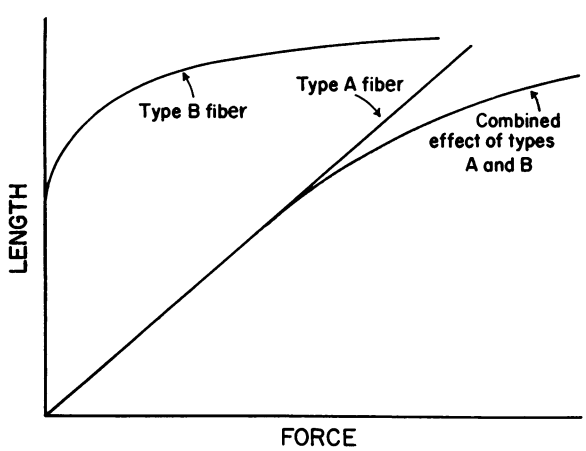


FIGURE 4 Length tension characteristic of elastin-like type A fibers and collagen-like type B fibers and their combined effect based on data from reference 12.

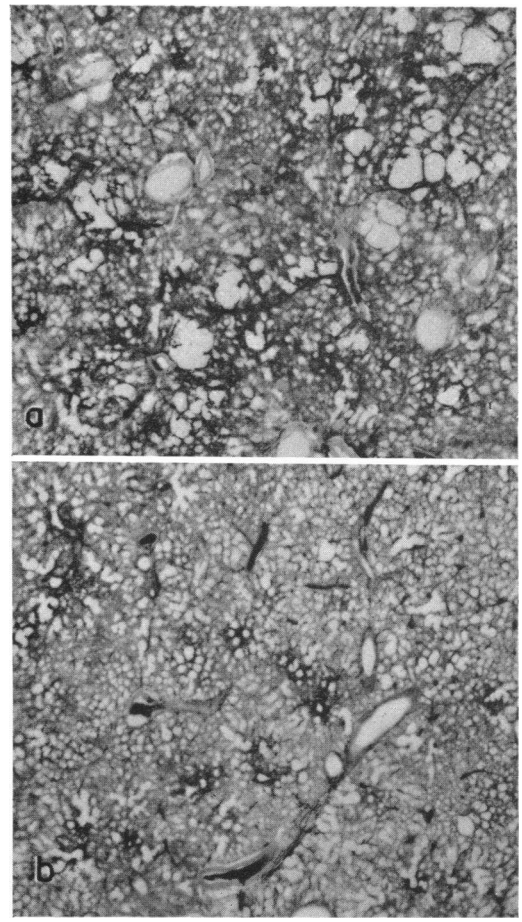


FIGURE 5 Photographs of a paper mounted section from a lung, (case 1, Table III) with centrilobular emphysema where a pressure-volume curve was obtained (Fig. 3). (*a*) demonstrates centrilobular emphysema found in the upper lobe; (*b*) demonstrates mild panlobular emphysema found in the lower lobe and thoughout much of the remaining lung. × 1.3.

## ACKNOWLEDGMENTS

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