ELASTIC PROPERTIES AND THE GEOMETRY OF THE LUNGS

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J Clin Invest. 1961;40(8):1515-1524. https://doi.org/10.1172/JCI104381.

ELASTIC PROPERTIES AND THE GEOMETRY OF THE LUNGS *

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(Submitted for publication August 8, 1960; accepted April 20, 1961)

The elastic properties of the lung are of primary importance to normal function. A definitive study of these properties entails the simultaneous measurement of pressure and volume under static conditions. A plot of the relationship between pressure and volume in the lungs results in a curve which is approximately linear in the middle part of the vital capacity. The retractive force in this limited part of the curve is a direct function of volume. Although elastic performance is a complex phenomenon, the balance of lung elastic behavior occurs without a delay in time and the majority of the elastic work done on the lung during inspiration can be recovered on expiration. Major contributions are made to the over-all elastic behavior of the lungs by surface phenomena and tissue factors. Factors of minor importance include the bronchial and bronchiolar smooth muscle and the amount of blood in the pulmonary vascular bed.

For many years the elastic properties of the lungs were attributed to elastic tissue fibers. Surface phenomena were not considered important until 1929 when von Neergaard (1) pointed out that the forces arising from the air liquid interfaces throughout the lung parenchyma could be eliminated by the complete replacement of the gas in the lungs with liquid. He demonstrated that pressure was less in the liquid-filled lung than in the air-filled lung at comparable volumes. He assumed an identical operation of tissue elastic factors in air- and liquid-filled lungs.

Radford (2) estimated the surface area of excised lungs, using the principles established by von Neergaard. The difference between air and saline pressure-volume curves during emptying was taken as a measure of the recoverable surface energy. The surface area of the lung was calculated from the recoverable energy. Surface tension was assumed to be 50 dynes per cm. Brown (3) repeated this work. He assumed a value for surface tension at maximal lung inflation. He then calculated a relative value for surface tension at successively lower levels of lung inflation by estimating the change in area associated with the change in volume. In his calculations Brown assumed that the spatial coordinates of all lung units decreased proportionately during deflation.

The purpose of the experiments to be presented was to elucidate further the factors involved in the elastic properties of the lung. The filling of the lungs with mercury metal was studied. It was possible to define the change in surface area of the lungs with accuracy because of the high surface tension of mercury. The equation utilized by Radford (2) was applied in this study:

$$\int_{V_0}^{V_1} P\,dV = \int_{A_0}^{A_1} \gamma\,dA \qquad [1]$$

where P is pressure, V is volume, γ is surface tension and A is area. The right-hand side of the equation was derived from the Helmholtz equation for the free energy of the surface. It was assumed that temperature was constant and that the quantity and composition of the associated bulk phases were independent of area.

Another approach to the problem was to eliminate the tissue elastic properties of the lungs. It was found that after sodium hydroxide extraction and treatment with elastase, the lung no longer exhibited elastic behavior when filled with saline. The pressure-volume measurements with air permitted a study of the geometry of these lung preparations.

MATERIAL AND METHODS

The experiments with mercury filling were carried out as follows. Adult mongrel dogs were given pentobarbital anesthesia (25 to 30 mg per kg of body weight). A Neophor valve was connected to a cuffed endotracheal

* Presented in part before meetings of the American Federation for Clinical Research in New Orleans, La., January 22, 1959 and in Atlantic City, N. J., May 1, 1960. Supported by a grant from the United States Public Health Service (H-4031).

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tube and the animal was ventilated with oxygen at an adjustable positive pressure; expiration was passive at ambient pressure. After opening the chest carefully to avoid injury to the lungs, the trachea was clamped. Virtually all of the gas was absorbed from the lungs prior to cardiac standstill (4). The gas-free lungs were excised and the pulmonary artery and left atrium ligated. A glass connector was secured in the trachea. The preparations were weighed and transferred to a bowl containing mercury metal and isotonic saline solution. Pressure was measured from the tracheal cannula with an open mercury manometer. The lungs were filled with mercury from a glass syringe through an arrangement of three-way stopcocks. The introduction and withdrawal of mercury were performed slowly allowing 3 minutes for equilibration at each volume increment. The pressure in the manometer was related to the surface of the mercury bath. Subpleural mercury spherules were measured with a stereomicroscope at various volumes of lung distention. Care was taken to avoid contact of the mercury-filled lung with the bottom of the bowl, since this elevated the manometer pressure. The lungs were filled to a volume of 500 to 735 ml. The filling and emptying was repeated three times in some of the preparations. At the end of each cycle the lungs were removed and weighed to determine the amount of trapped mercury. The pressure-volume relationships of some of the lungs were studied with saline filling. Preparations were also dried with air and examined microscopically.

A portion of the mercury-filled lung floated above the surface of the mercury reservoir. To correct the pressures in this part of the lung, the volume of exposed preparation was calculated by Archimedes' principle using densities of 1.005 for isotonic sodium chloride solution, 1.05 for lung tissue, and 13.6 for mercury. The area of contact between the lung and the mercury reservoir surface was estimated for various levels of lung distention. The mean transpulmonary pressure in the exposed part of the lungs was equivalent to the pressure at a level equal to one-half the exposed volume divided by the contact area. This correction was small at volumes of distention in excess of 300 ml in the dog lungs. The transpulmonary pressure in the submerged portion of the lung was equal to the difference between the mercury reservoir level and the height of mercury in the manometer. The corrected transpulmonary pressure at any given volume of distention can be expressed as: $(P_m V_i + P_e V_e)/100$ where P_m is the height of the mercury column in the manometer relative to the surface of the mercury reservoir, P_e is the mean transpulmonary pressure in the exposed part of the mercury-filled lung preparation, V_i is the volume percentage of the mercury-filled lung which is immersed, and V_e the volume percentage exposed. The size of the manometer rendered capillarity unimportant.

The interfacial tension between mercury and extracts of tracheobronchial mucus was measured with the drop weight method described by Bartell, Case and Brown (5). The mean results with aqueous and saline solution extracts against mercury were 9 per cent higher than those between mercury and distilled water. Because the intermolecular cohesive forces in mercury are high, the lung-lining layer must penetrate this phase only very slightly, if at all. Other data on the interfacial force area relationships of biological materials against mercury have not been found. As a conservative estimate the calculations in this report were made with an assumed lung mercury interfacial tension of 370 dynes per cm.

The experiments on extracted lungs were performed on dogs of similar body weight. Anesthesia and ventilation were carried out as described before. The lungs were exposed through an extensive transverse incision of the chest. Compliance was determined with a method described previously (6). The lungs were rendered free of gas and then excised. Blood was removed from the pulmonary vessels by perfusion with isotonic saline solution. The vessels were ligated. A glass cannula was tied into the trachea and the lungs were transferred to a vat containing 0.1 N sodium hydroxide solution. This solution was poured into the trachea under a pressure which never exceeded 10 cm of water. Fresh sodium hydroxide solution was replaced frequently over a period of 3 to 5 days with repeated filling of the lungs.

The lung preparations were rinsed with water followed by carbonate buffer at pH 8.8 (7). Crystalline elastase was dissolved in carbonate buffer (16 mg per L). The lung was filled with and immersed in this buffered enzyme solution. The preparation was incubated at 37° C for 18 to 24 hours at the end of which time the pH of the solution varied between 8.6 and 9.1. The lung preparations were drained of fluid and inflated with air. After determining that the preparations would hold air, pressure-volume relationships were measured with a stepwise inflation and deflation. In order to assess the flow-resistive characteristics of these preparations, the time course of passive collapse was also studied. Flow was recorded from a conventional pneumotachograph and pressure was measured with a strain gauge transducer. Surprisingly little air remained trapped within the lung preparations following passive deflation. This trapped gas was not measured but has been estimated as less than 30 ml.

The preparations were transferred to a vat containing a mixture of ethanol and ether (3:1 by volume). This solution was poured into the trachea. After 30 to 45 minutes in this bath they were drained of liquid and pressure-volume relationships were again measured with air inflation. Studies of passive collapse were repeated. Gas volumes reported are at an ambient temperature of 24 ± 2° C.

The lung preparations were subsequently immersed in normal saline solution at 37° C. The pressure-volume relationships were determined during a stepwise distention with saline solution. Because some solution escaped during the procedure, it was necessary to estimate the final volume from the weight of the preparations. The intermediate volumes were calculated as though saline had escaped at a regular rate. It was demonstrated that saline escape occurred predominantly during filling, since the volume of distended preparations did not change appreciably over periods up to an hour. Thus,

TABLE I

Studies on mercury-filled dog lungs

Animal no.	Body wt	Wt of lungs*	Maximal volume†	Pressure at maximal volume	Pressure at 400 ml volume	On emptying from 400 ml volume: Work recovered‡	On emptying from 400 ml volume: Surface area	Pressure at 200 ml volume	Compliance	Volume of trapped mercury
	kg	*g*	*ml*	*mm Hg*	*mm Hg*	*10^6 ergs*	*m^2*	*mm Hg*	*ml/cm H_2O*	*ml*
1	8.9	108	500	106	82	24.2	6.54	51	6.1	27
2	10.2	167	500	96	78	24.2	6.54	47	5.1	15
3	6.4	107	600§	112	69					
			550	94	68	17.7	4.78	37	4.7	42
			592	103	68	18.6	5.03	38	5.7	61
4	7.3	104	735	84	45	10.7	2.89	34	6.8	82
5	5.7	109	500	95	74	22.0	5.95	45	5.5	21
			521	96	68	19.0	5.14	39	4.7	32
			532	98	67	16.9	4.57	36	5.1	49
6	10.9	137	600	93	68	21.2	5.73	44	6.8	29
			621	89	61	16.4	4.43	36	7.0	23
			625	90	62	18.2	4.92	37	6.3	43
Mean	8.2	122	573	96	67	19.0	5.14	40	5.8	38.5
SD‖	2.1	25			9	3.9	1.05	5	0.9	

* Includes both lungs and a segment of trachea. † Volumes refer to mercury contained in the lungs. ‡ As measured with a planimeter (see Figure 1). § The lungs were only partially emptied on this cycle. ‖ Standard deviation as $\sqrt{\frac{\Sigma(D^2)}{N-1}}$.

the pressures reported are reliable static measurements. Further, the contained saline could not be aspirated from the trachea so that data were obtained only during filling.

Finally, small sections of the preparations were fixed in formalin for histological examination with Verhoeff's elastic tissue stain. The balance of each preparation was stored at −4° C and subsequently analyzed for collagen and elastin with a modification of the procedure described by Lowry, Gilligan and Katersky (8). The modified method has been described previously (9) with the single exception that the initial overnight sodium hydroxide extraction was omitted, since the native lungs had been exposed to alkali.

RESULTS

Table I presents results of the mercury studies in detail. The mean transpulmonary pressure at maximal distention was 96 mm of mercury. Work recovered on emptying the mercury-filled lungs was calculated from a 400 ml contained volume (Figure 1). This volume was chosen arbitrarily to approximate the functional residual capacity, and the surface area of the lungs was calculated from this level of distention. The mean compliance of the mercury-emptying curves was approximately one-eighth that found in air-filled lungs. This indicates an eightfold increase in retractive force in the mercury-filled lung if the surface areas are assumed comparable with mercury and air filling at similar volumes of distention. Static measurements of pressure and volume with saline filling were similar before and after mercury filling. Gross and microscopic examination of air-dried specimens revealed no severe distortion of lung architecture after mercury filling.

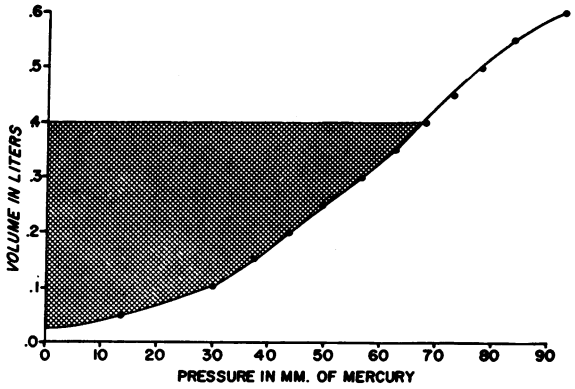

FIG. 1. STATIC PRESSURE-VOLUME CURVE OBTAINED ON EMPTYING THE MERCURY-FILLED LUNGS. The shaded area was measured with a planimeter to estimate recovered surface work. This recovered work was used in Equation 1 to calculate lung surface area.

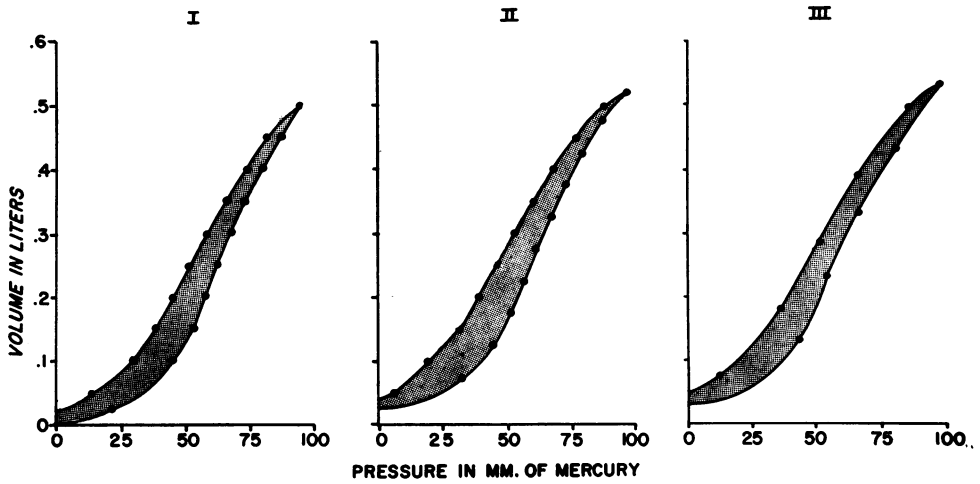

FIG. 2. SUCCESSIVE STATIC PRESSURE-VOLUME CURVES OBTAINED FROM A SINGLE PAIR OF LUNGS DEMONSTRATING THE REPRODUCIBILITY OF THE MEASUREMENTS. The shaded areas depict the differences observed between filling (lower curved line) and emptying (upper curved line) and referred to as hysteresis.

Emphasis has been placed on the measurements during emptying of the lung because only during this part of the cycle is it possible to recover work and hence, estimate lung surface area. Figure 2 represents data obtained on filling and emptying the lungs with mercury in Dog 5. The results shown are typical of those obtained in all animals. Hysteresis was regularly observed. It has been attributed to the irregular opening of terminal air spaces in various parts of the lung. This causes a discrepancy in the distribution of the contained volume on filling as opposed to that on emptying. Relative to the work recovered on emptying the lung, hysteresis was roughly similar in the mercury studies and in the elastase-treated lungs. Whether this hysteresis is related to the purely physical nature of the lining surface of the lungs or whether some chemical reaction might be involved is not entirely clear.

Measurements were made of the diameter of subpleural mercury spherules as observed in the exposed part of the mercury-filled lung. Physical limitations of the stereomicroscope required that these spherules be selected from a flat exposed surface. The results of these measurements are shown in Table II. It should not be inferred that these spherules were necessarily representative of all terminal air spaces. The largest spherules occurred at low volumes of distention while the smallest subpleural spherules were seen only with greater filling. It should be noted that these observations were made at levels of distention near the functional residual capacity and hence would not compare with fully expanded lung preparations.

Table III presents data on the experiments with alkaline extraction and elastase treatment of the lungs. Tissue elastic behavior has been assessed customarily in lungs filled with saline solution. Figure 3 presents such an assessment on a single pair of lungs from a dog. These results were typical of those obtained in several similar experiments. Curve I in Figure 3 presents static pressure-volume data obtained on emptying the lungs which were freshly excised, free of gas and filled with isotonic saline solution. Curve I thus represents the normal tissue elastic behavior in excised dog lungs. Curve II in Figure 3 was obtained in an identical manner after immersion for

TABLE II

Measurements of subpleural mercury spherules

Volume	No. of observations	Mean diameter	Range
ml		μ	μ
100	19	266	120–400
200	31	185	120–320
300	18	142	80–220
400	31	121	60–240
500	9	96	80–160

TABLE III

Studies on dog lungs extracted with alkali and exposed to elastase

Animal no.	Body wt	Compliance *in vivo* chest open	Measured with air on deflation following alkali and elastase: Rinsed with water	Rinsed with ethanol-ether	Pressure at 400 ml volume	On deflation from 400 ml volume: Work recovered	Surface area	Compliance under saline*	Elastin†
	kg	*ml/cm H_2O*	*ml/cm H_2O*	*ml/cm H_2O*	*cm H_2O*	*10^6 ergs*	*m^2*	*ml/cm H_2O*	%
7	9.5	40	25	62					
8	9.5	42	32	73	16.6	3.22	6.44	>1,000	1.9
9	10.2	52	38	123	12.5	2.69	5.38		
10	12.3	64	45	155	11.9	1.67	3.34		5.7
11	8.0	37	40	71	11.6	2.47	4.94	>1,000	
12	8.2	41	26	53				>1,500	
13	6.5	35	26	37	18.5	3.13	6.26	>1,500	4.1
14	10.5	61	55	118	11.0	2.58	5.16	>1,500	
Mean	9.3	46.5	36	86.5	13.7	2.63	5.25		3.7
SD‡	1.8	11	11	41	3.1	0.56	1.11		

* With saline solution following extraction with alkali and exposure to elastase; measurement completed on only 5 animals. † Expressed as percentage of normal assuming a ratio of collagen to elastin of 3; the analyses were done in groups. ‡ Standard deviation as $\sqrt{\frac{\Sigma(D^2)}{N-1}}$.

3 days at room temperature in 0.1 N sodium hydroxide solution. The same lungs were used in all curves of Figure 3. Any given volume of distention on curve II results in approximately one-half the pressure observed in freshly excised lungs (curve I). The lungs were treated with elastase in buffer for 24 hours and pressure-volume data were again obtained under saline immersion (curve III, Figure 3). These measurements were static but were made on filling, since saline could not be aspirated from the tracheal cannula. The resultant pressure in curve III is less than 10 per cent of that observed at comparable volumes of distention in the freshly excised lungs. The increasing slope of the pressure-volume diagram from curve I to II to III represents an increasing compliance of the saline-filled lung. More prolonged extraction in alkali or extraction in more concentrated (0.2 N) sodium hydroxide solution resulted in additional increases in saline compliance. Thus, the loss of elastic behavior by the lung tissue has not been considered a specific result of elastin hydrolysis. The changes observed with exposure to alkali are interpreted as evidence of a progressive loss of tissue organization.

The maximal increase in saline compliance occurred after treatment with elastase in buffer. For this reason the elastase-treated lungs have been considered as devoid of tissue elastic behavior. When such preparations were filled with air, the pressure-volume behavior was similar to that observed in native air-filled lungs. Figure 4 presents a typical static pressure-volume diagram on air inflation and deflation of an alkali- and elastase-treated dog lung preparation. The pressure-volume relationships in Figure 4 do not differ markedly from those measured *in vivo* with the

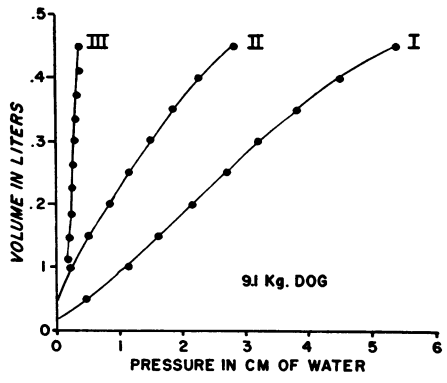

FIG. 3. STATIC PRESSURE-VOLUME CURVES WITH SALINE SOLUTION OBTAINED FROM A SINGLE PAIR OF DOG LUNGS. The curves are: I, before treatment; II, after exposure to sodium hydroxide; and III, after treatment with elastase. Curves I and II were obtained on emptying and curve III was obtained on filling the lungs with saline solution.

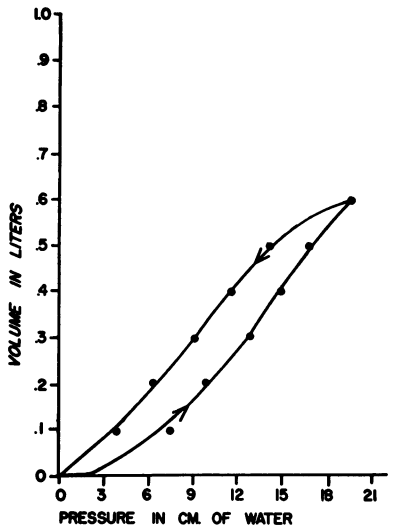

FIG. 4. TYPICAL STATIC PRESSURE-VOLUME DIAGRAM OBTAINED ON AIR INFLATION AND DEFLATION. The lungs had been exposed to sodium hydroxide and elastase solutions. A small volume of trapped air has been ignored (see text).

chest open. Air compliance *in vivo* was not significantly different from that found after alkali and elastase treatment (Table III). There was a difference in the amount of gas trapped on emptying, being much greater *in vivo* than in the alkali- and elastase-treated lungs. The striking feature is that the preparation shown in Figure 4 exhibited virtually no tissue elastic behavior when studied with saline filling. Figure 5 presents a pressure-volume curve obtained from static measurements of another air-filled dog lung preparation following treatment with alkali and elastase. Figure 5 also includes a pressure-volume diagram of an elastase-treated preparation after exposure to ethanol ether solution. It was estimated that this treatment should reduce the lung surface tension by one-half. The surface work recovered on deflation from a 400 ml volume was compared in the water-rinsed and ethanol ether-treated preparations. Ethanol ether treatment reduced the recovered surface work by 30 per cent in six preparations.

Histologic examination of the elastase-treated preparations revealed only scanty amounts of elastic tissue as compared with preparations treated similarly but without elastase. Moreover, chemical analyses revealed only 4 per cent of the expected normal amount of elastin. There is no doubt that elastic tissue fibers, as they usually exist in the lungs, were almost completely absent from these preparations. Compliance under saline was not found to change following 18 to 24 hours' incubation in carbonate buffer at pH 8.8 in the absence of elastase.

Passive collapse records with air, before and after elastase treatment, showed no appreciable differences. This indicates that the flow-resistive characteristics of the lung preparations were not greatly altered by treatment with elastase and implies that the geometry of the terminal air spaces was not severely disordered. Examination of elastase-treated preparations dried with air revealed architecture similar to that found in untreated lungs.

DISCUSSION

The studies with mercury metal are suitable for evaluation of the geometry of the terminal air spaces of the lung. This liquid has an extremely high surface tension and is essentially immiscible with the lining layer of the lungs. Thus the mercury-filled lung has an unusually large interfacial tension and produces a large retractive force on distention. The pressure on distention is sufficiently great that the small pressure observed in the saline-filled lung and attributed to tissue elastic performance becomes negligible. Interfacial tension has not been measured within the mercury-filled lung, but probably would approximate the interfacial tension of mercury measured against extracts of tracheobronchial mucus. Although the question is unsettled whether interfacial tension might vary with changes in interfacial area, a tension decrease of 40 dynes per cm would alter the present results by only 10 per cent. Thus the static pressure-volume characteristics of the mercury-filled lung appear to result from surface phenomena.

If it can be assumed that the pressure-volume relationships of the mercury-filled lung are a reflection of surface phenomena at the mercury lung interface, then the surface area of the lung can be readily calculated. The estimation of surface area is based on the familiar equation relating work to surface area (Equation 1). The pressure-volume curve on emptying is used in the calculation as the distention curves are modified by irregular filling in different portions of the lung. The method of estimating recoverable surface work is

TABLE IV

*Physical measurements of the surface area of the lungs of dogs**

Author	Year	Method	Surface area
			m^2
Radford (2)	1954	Air and saline emptying	0.5
Brown (3)	1957	Air and saline emptying	10.3
Present study		Mercury metal emptying	5.1
Present study		Air emptying of alkali- and elastase-treated lungs	5.2

* At 400 ml volume.

illustrated in Figure 1. The interfacial tension at the lung mercury junction was taken as constant at 370 dynes per cm. The mean values for surface area obtained in the dog lungs are compared with the results of other investigators in Table IV.

The alkali-extracted elastase-treated lung offers a similar opportunity to define the geometry of the lung. This lung preparation exhibits essentially no elastic properties when filled with saline. From this, it is reasonable to conclude that the pressure-volume characteristics with air are a reflection of the changing air fluid interfaces with inflation and deflation. If we assume a surface tension of 50 dynes per cm for the lungs washed with water, we can calculate the surface area and the ratio of area to volume at different levels of inflation, using Equation 1. While the value chosen for surface tension is not as secure as in the case with mercury, it appears reasonable. It is also necessary to assume that the surface tension does not vary with inflation and deflation of the lungs. The material described by Clements, Brown, and Johnson (10) may have been removed by sodium hydroxide extraction and repeated water rinsing. The mean value for surface area obtained from the elastase-treated lungs at a 400 ml inflation (5.2 m^2) agrees remarkably well with the data from the mercury-filled lung (5.1 m^2).

In both types of study the effects of surface phenomena have been exaggerated. This is true in the mercury-filled lung because of high interfacial tension and in the elastase-treated lung because of impaired tissue elastic performance. Neither preparation is exactly equivalent to the lungs during life. Abnormally large pressures existed across the mercury-filled lungs which must have imposed a strain on supporting structures such as the connective tissue fibers. The pressure exerted on the wall of any given air space depends on the major radii of curvature of the space and on the existing pressure within the lungs. With the smallest radius of curvature, one might expect negligible pressure on the wall. This occurs where the radius of curvature and the interfacial tension precisely satisfy the Laplace theorem. That is, $P = 2\gamma/r$, where P is pressure, γ is surface or interfacial tension and r is radius. Where the radius is greater there will be pressure transmitted to the wall and hence tension on the supporting framework of the lungs. The actual stress on the framework of the lung might lead to distortion or destruction of the normal lung structure. The elastase studies are open to the same criticism because the connective tissue has been altered. Several observations suggest that this error does not invalidate the present results. It was possible to fill and empty the lungs repeatedly without significantly altering the data obtained. This was

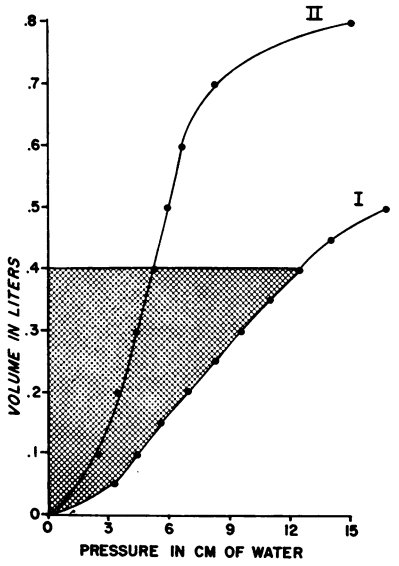

FIG. 5. STATIC PRESSURE-VOLUME CURVES WITH AIR OBTAINED ON EMPTYING AN ALKALI- AND ELASTASE-TREATED PREPARATION. The shaded area depicts the recovered surface work from 400 ml for curve I, after water rinse. Curve II was obtained following ethanol ether rinse to reduce the surface tension in the lungs. A small volume of trapped air has been ignored (see text).

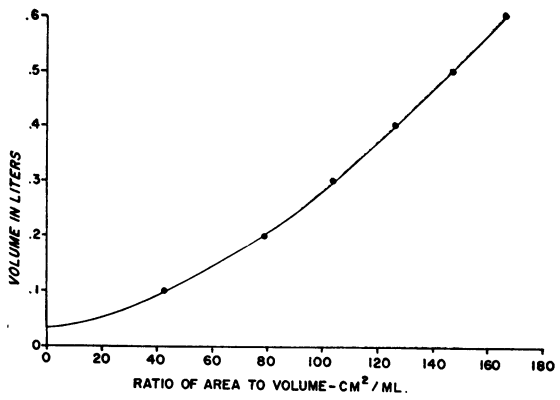

FIG. 6. A PLOT OF THE RELATIONSHIP BETWEEN VOLUME AND THE RATIO OF LUNG SURFACE AREA TO VOLUME, AS MEASURED WITH MERCURY METAL.

true in both types of study. Examination of specimens inflated and dried with air failed to reveal evidence of marked dilatation of the proximal air spaces. These examinations were performed following mercury filling and in preparations treated with elastase. It seems unlikely that the larger air spaces could withstand extreme overexpansion without rupture of the connective tissue fibers in their walls. Widespread rupture of these fibers should have been associated with changes in pressure-volume relationships and alterations in the appearance of air-dried inflated specimens. Finally, measurements of the size of subpleural mercury spherules are in general agreement with the measurements of Radford and McLaughlin (11) made on dog lungs during air inflation.

The elastase-treated lungs afford a striking example of the effects of surface phenomena. These lungs had virtually no tissue elastic behavior and yet retained normal relationships between pressure and volume on filling with air. Under these circumstances surface factors must have accounted for virtually all of the observed elastic behavior. This contrasts sharply with the findings in normal lungs. Tissue elastic performance measured by saline-emptying curves in excised lungs amounts to about one-half of total elastic behavior during inflation with air. The exact role of tissue elasticity, however, is far from clear. Interfacial tensions undoubtedly exist at cell boundaries and elsewhere in the alveolar wall. The importance of such interfaces has been discussed by Thompson (12) although they have not been evaluated in the lungs. Pressure-volume measurements of the lungs do not distinguish between the elastic behavior arising in tissue fibers and that resulting from such interfacial tensions. Although elastase treatment abolished tissue elastic performance as measured with saline distention, this in no way proves that the elastic fibers are solely responsible for these properties since the enzyme also probably destroys tissue boundaries and eliminates the effects of interfacial tensions. Thus, the precise role of the elastic fibers is not completely defined.

The size of the air sacs also has importance. Any regularly shaped geometric figure has a unique ratio of surface to volume at every different size. An increase in the radius of curvature leads to a decrease in this ratio. In considering the entire lungs, the ratio of surface to volume must reflect the mean size of the spaces in the lungs. Figure 6 presents the ratio of surface to volume calculated on emptying the mercury-filled dog lungs. It is of interest that this ratio decreases as the volume diminishes. The elastase-treated lungs gave similar results. This can only be interpreted to indicate that the mean radius of curvature of the air spaces increased as volume was removed from the lungs. This must have resulted from the closure of some of the smaller air spaces. In the mercury-filled lungs, this was documented by the measurements of subpleural mercury spherules at various levels of distention. Radford and McLaughlin (11, 13) obtained results similar to these on air inflation and deflation after surface-active solutions had been introduced into the terminal air spaces of the lungs of rats. Their observations on the alveolar behavior of freshly excised lungs, however, indicated rather marked discrepancies between inflation and deflation.

Several observations suggest that the lungs are lined by a fluid layer with intense surface activity. Macklin (14) has discussed this in detail, citing the report of Terry (15), who in 1926 observed a clear free fluid in the alveoli during life. Macklin visualized this material as facilitating the removal of inhaled particles and suggested that the fluid was produced by the granular pneumonocytes. Pattle (16) noted an unusual stability in the foam of pulmonary edema fluid and in fluid expressed from the cut surface of fresh lung tissue. He con-

cluded that the stability of the foam was due to an insoluble surface layer of protein that arose from the lungs. Clements (17) described the surface characteristics of extracts of lungs and tracheobronchial mucus. This material exhibited marked hysteresis on expansion and compression when studied as an adsorbed film in a surface balance. Similar effects were not observed with extracts of defibrinated blood plasma. Chase (18) studied lung tissue which had been rapidly frozen and demonstrated a homogeneous film on the surface of the alveoli in electron photomicrographs. This material was positive with the periodic acid-Schiff stain. The chemical nature of this material has not been clarified, although it is thought to be a polysaccharide protein complex. Clements, Brown, and Johnson (10) have pointed out that the material observed in the film balance could extend the range of stable volume behavior for individual alveoli and permit the coexistence of alveolar spaces of widely varying sizes in the lungs. They describe this material as having "antiatelectasis" properties. There seems little room for doubt about the existence of an alveolar lining layer which has intense surface activity.

Such are the factors which govern the elastic behavior of the lungs. Information about these factors gained in diverse ways can not be transferred directly to the conditions which exist during life. Thus, the central problem now concerns the relative importance of the various factors already discussed. In our opinion, the size of the air cells is critical in providing a properly curved surface to produce the retractive force necessary to expel air from the lungs. The material lining the lungs may delay the closure of small air spaces with minor changes in pressure and thus lessen the work required to fill the lungs on tidal breathing. The connective tissue framework of the lungs may not participate at all in lung elastic behavior at small volumes of distention. At large volumes, however, these fibers supply the strength necessary to retain the structure of the lungs and thus avoid permanent deformity. Additional studies will be required to determine whether these views are correct.

SUMMARY

1. The elastic properties of dog lungs were studied with mercury filling and after treatment with elastase. The effects of surface phenomena were dominant in both of these experiments.

2. Estimates of lung surface area from measurements of recovered surface work were in agreement by these two methods.

3. In the mercury studies, the over-all ratio of surface to volume decreased and the size of subpleural mercury spherules increased as the lung was emptied; the reverse occurred on filling.

4. The studies with elastase-treated lungs served to show that elastic fibers are not essential for normal elastic performance on inflation with air.

5. Those factors important to the normal pressure-volume characteristics of the lungs were considered in some detail. We believe the size of the terminal air spaces is the single most important consideration.

ACKNOWLEDGMENT

The authors are deeply indebted to Dr. Richard V. Ebert for valuable advice and constant encouragement.

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