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Effect of lung inflation on bronchial length and diameter in excised lungs

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HUGHES, J. M. B., F. G. HOPPIN, JR., AND J. MEAD. *Effect of lung inflation on bronchial length and diameter in excised lungs.* J. Appl. Physiol. 32(1): 25–35. 1972.—Bronchi down to 1-mm internal diameter were outlined with tantalum dust in excised dog lungs. Stereoscopic X-ray pairs were taken at different lung volumes and transpulmonary pressures (Ptp), and bronchial lengths and diameters were computed from the films. At full inflation (Ptp 30 cm H_2O) bronchial segments ranged from 4.74 to 0.82 cm in length, and from 1.17 to 0.1 cm in diameter. As the lung was deflated from Ptp 30 to 1.0 cm H_2O, changes of bronchial length and in many cases diameter also (as a percentage of maximum) were proportional to changes in the cube root of absolute lung volume. No difference was found in the percentage changes for airways of different sizes. With regard to relative hysteresis, at the same lung volume but at Ptp's which differed by 1.0–7.0 cm H_2O due to an inflation or deflation volume history, all bronchial lengths and diameters were essentially similar. The changes of bronchial length and diameter were in many cases greater than would have been predicted from the behavior of airways dissected free from lung tissue, suggesting that bronchi in situ are exposed to distending forces in excess of transpulmonary pressure.

airways resistance; lung hysteresis; airway hysteresis; hysteresis of resistance; dead space; pulmonary mechanics; lung stress distribution

AIRWAYS RESISTANCE varies with change of lung volume (2), lung elastic recoil pressure (4), and previous volume history (34). For the most part, resistance alters in these situations because the length and cross section of the intrathoracic airways changes. Indirect estimates of changes of bronchial volume with changes of lung volume and lung volume history have been made from measurements of anatomic dead space by use of carbon dioxide (8, 34), but a more direct and selective method is bronchography.

In this study we outlined the airways in excised dog lungs with tantalum dust as described by Nadel et al. (27) and measured bronchial length and diameter at different absolute lung volumes. We were also interested in the relationship between bronchial diameter and transpulmonary pressure at the same lung volume, so that we could estimate the relative hysteresis of airways and air spaces. We found that measurements of bronchial length were unsatisfactory unless X-rays were taken in two planes. By taking X-ray pairs using a tube shift as for stereoscopic views we could display bronchi adequately in each view so that measurements of length could be made. A fuller description of this method is given elsewhere (12).

Measurements of bronchial diameter at different lung volumes and distending pressures have been made in man (7, 22, 24), anesthetized dogs (10, 18), and excised dog lungs (13, 15–17, 23), but in general bronchial length and diameter have not been related to absolute lung volume, and only in a study by Hyatt and his colleagues (15) was an assessment of airway hysteresis made. In the light of recent theories on the possible interdependence of air space and airway expansion (26), the relationship between lung volumes and bronchial volumes is of great interest. For example, although isolated bronchi of different sizes have markedly different distensibilities (25), interdependence theory predicts that local tissue stress would increase proportionately with individual bronchial elastance. Consequently differences in bronchial expansion in situ might be less than that seen in dissected airways. The two previous studies on the effect of lung parenchyma on bronchial caliber have given somewhat conflicting results (16, 23), indicating the need for further studies with simultaneous measurement of bronchial and lung volume.

METHODS

Mongrel dogs were anesthetized with barbiturate (Nembutal 50 mg/kg), given heparin (1,000 U/kg), and killed by exsanguination. The left lung was immediately removed and weighed; a cannula was tied into the left main bronchus and the lung placed horizontally on a Lucite plate which supported its weight. The airways were outlined with tantalum dust as shown in Fig. 1. Metallurgic tantalum powder (Norton & Co., Newton, Mass., or Fansteel Inc., North Chicago, Ill.) of nominal 1- or 5-μ particle size was vacuum dried before the study and placed in a 10-ml container (a nasal powder insufflator). It made no difference to the quality of the bronchogram whether the 5- or 1-μ powder was used. Puffs of dust were generated by intermittently occluding the flow of dry compressed air so that it flowed onto the dust through a needle. From the dust container a thin catheter (id 1.6 mm) passed through the bronchial cannula into the lung. The generating airflow was about 200 ml/sec: during the procedure the lung was inflated to a transpulmonary pressure (Ptp) of 20 cm H_2O with a blower pump. The catheter tip was moved around within the lung under fluoroscopic control until a satisfactory bronchogram was obtained. X-rays were then taken at different lung volumes and pressures using a 100-ml glass syringe to inflate the lung and a water manometer to measure airway pressure. The gas volume of the lung at

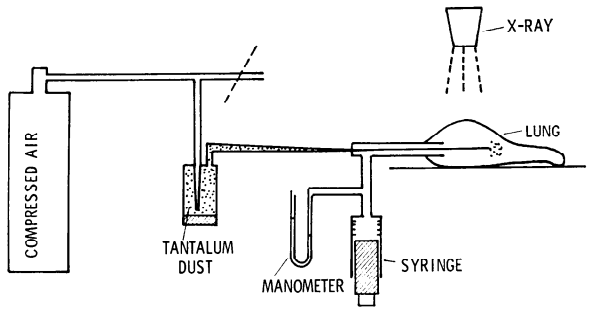


FIG. 1. Diagram of apparatus for outlining bronchi of excised lung with tantalum dust (see text). To obtain bronchograms at different lung volumes and transpulmonary pressures, catheter connected to the dust container was withdrawn, lung inflated from a syringe, and pressure measured with a water manometer.

Ptp 0 cm H_2O was measured at the beginning and end of the experiment by water displacement after subtraction of lung weight. All lung volumes were expressed in milliliters ATPS and refer to gas volumes only; corrections were made for gas compression because positive-pressure inflation was used.

After the measurement of volume by displacement, the lung was inflated with a syringe until the highest stable pressure was obtained. Satisfactory preparations were relatively gastight in that they were able to hold Ptp's ranging from 23 to 30 cm H_2O without change for at least 2 min. However because of slight air leaks at Ptp 30 cm H_2O lungs were then held at this pressure with a blower pump while radiographs were made. The assumption was made, and this was to some extent confirmed by repeating measurements of bronchial length and diameter, that lung gas volume remained constant at Ptp 30 cm H_2O. A connection was then made to the glass syringe and a measured quantity of air was immediately withdrawn and a further X-ray taken at Ptp 5 cm H_2O or similar pressure. More gas was withdrawn and then replaced so radiographs could be made at the same lung volume on inflation. Pressures remained steady (within ± 0.5 cm H_2O) at all lung volumes. Radiographs were exposed at 30 and 60 sec after reaching each lung volume. After reinflation to Ptp 30 cm H_2O further X-rays were taken at different pressures on deflation and reinflation. After a lateral film a final X-ray was exposed at Ptp 30 cm H_2O, gas was withdrawn and the residual air measured again.

X-Ray Measurements

X-rays were taken using nonscreen industrial film with settings kvp 60 and 25 ma. The exposure time was 0.2 sec. The width of the focal spot of the X-ray source was about 1.0 mm. The distance from focus to film was 100 cm and from focus to lung midpoint 90–94 cm. The height of the lung at full inflation (Ptp 30 cm H_2O) ranged from 6.7 to 8 cm. The radiographs were projected onto a wall or screen giving a 5–20 times magnification. Bronchial diameters at selected points in large, medium, and small airways were measured and expressed as a percentage of the diameter of that airway at maximal inflation. We neglected the changes in image magnification which occurred as an airway moved closer or farther from the X-ray focus as the lung expanded or contracted. From our stereo X-ray pairs (see below) we found on comparing the lung at Ptp 30 cm H_2O with Ptp 2 cm H_2O the maximum change of depth of an airway relative to the X-ray film was 2.5 cm. For an airway of 1-cm diameter this would introduce a relative error of 3.1%; part of the change in magnification which occurs with a change of depth is related to the width of the focal spot of the X-ray tube and is a fixed quantity. Therefore percentage errors for small airways will be greater. For airways of 2- and 1-mm diameter the relative error would be 5.5 and 8.5%, respectively. In fact, we mostly confined our measurements to airways greater than 2-mm diameter and only 13 of 77 airways measured (17%) had diameters of less than 2 mm. When the airway diameter is over twice the width of the focal spot, radiographic distortion arising from a change of depth of an airway relative to the film is small, and in comparisons made at the same volume it disappears.

Airway Length

Accurate measurements of bronchial length require X-rays to be taken in two different planes. The simplest solution geometrically would be to take frontal and lateral views to obtain the absolute X, Y, and Z coordinates. In practice airways which are well displayed on a frontal view are extremely crowded in a lateral and we found that we could not be sure of finding the same bronchial segment. By taking two frontal views using a tube shift as for stereoscopic X-ray pairs we were able to recognize the same bronchial segments easily and also compute their length. Stereo X-ray pairs have been used by radiologists for many years to locate the depth of foreign bodies in tissues, particularly the eye, and we have adapted these methods for measurements of the length of bronchial segments within the lung. The principle of the method is shown in Fig. 2. The line AB represents a bronchial segment whose length

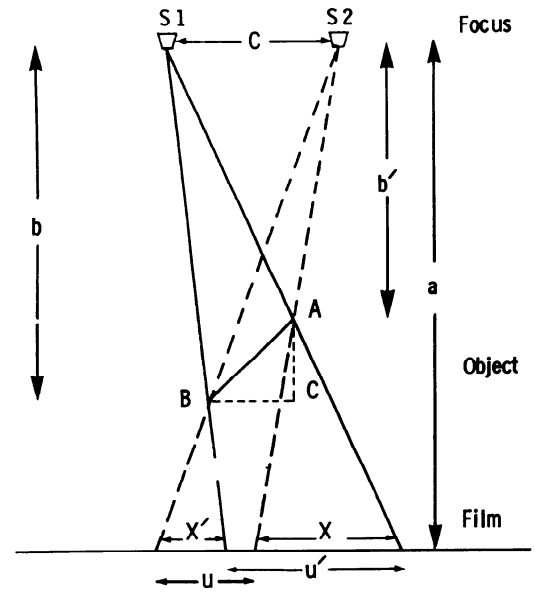


FIG. 2. Schematic diagram of method used for measuring bronchial length. u and u' are images of an airway of length AB X-rayed from tube focus positions, S_2 and S_1, respectively. From separation on the film of point B ($= x'$) and A ($= x$), distances b and b' can be calculated if X-ray focus shift, c, and focus-film distance, a, are also known. See text for explanation.

is to be determined. From position S_1 of the X-ray tube an image u' is produced on the X-ray film and from S_2 the image u. Because of the X-ray tube shift $S_1 - S_2$, the position of B of one end of the segment AB occurs as a double image on the film separated by the distance X'. Using the theory of similar triangles the depth of B from the X-ray focus (b) can be easily solved in terms of x', the image separation on the film, the X-ray tube separation c, and the distance from tube to film, a. The distance b' can be similarly calculated for point A and by subtraction the length AC obtained. BC is estimated from the mean of u and u' and AB is obtained by use of the Pythagorean theorem. In practice, as shown in Fig. 3, the bronchograms from each tube position are superimposed on a single film. An airway segment visible on both is located and the image separation of either measured (x and x') as well as the apparent length ($u + u'$).

Airways branching from the parent bronchus at approximately right angles made the best reference points, but the point at which a parent divided into two daughters was sometimes used. This method of assessing bronchial length (method A) is discussed more fully elsewhere (12) where the equation for bronchial length and its derivation is given. It is not absolutely accurate because $(u + u')/2$ only approximately represents the projection on the film of the distance BC. A theoretical study, supported by measurements made on wires of known length randomly oriented in space, showed that for deviations of point A of up to 8 cm, the maximum error will be 5%. The bronchial length equation used for this study was an early version of that eventually developed as method A (12), and no correction for magnification of u and u' was made. Thus a slightly less accurate estimation of the distance BC was obtained. Rather than recalculate all our results, we have compared the two methods on a selected group of measurements. In *lung 4* at Ptp 30, 5 (deflation), and 12 (inflation) cm H_2O the difference in mean length of airway segments comparing the two methods was 1.5, 0.9, and 0.3%, respectively. The largest difference for an individual segment was 4%.

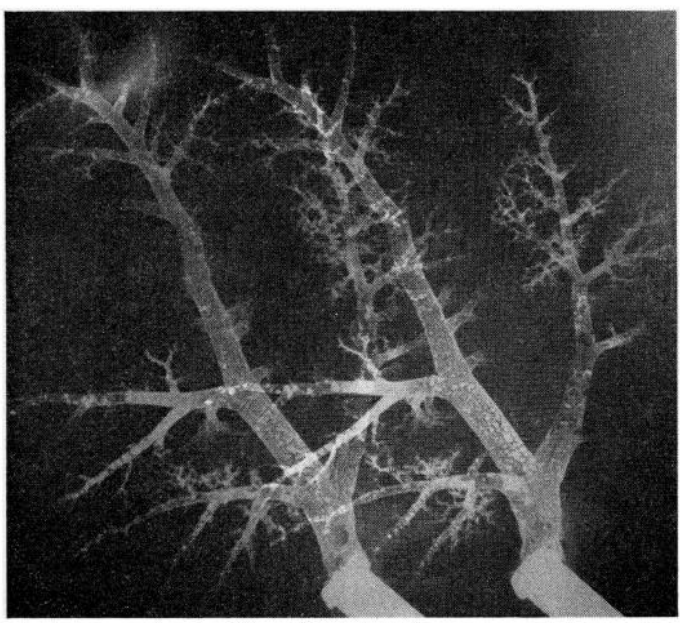


FIG. 3. Tantalum bronchogram of an excised lung inflated to Ptp 30 cm H_2O. Two exposures were taken with a tube shift and focus-film distance of 38 and 100 cm, respectively.

TABLE 1. *Lung weights and volumes*

Exp No.	Lung Wt, g	Volume, ml, at Ptp 30 cm H_2O		Vol/Vol Ptp 30 cm H_2O, %*		No. of Airways Measured
		Initial	Final	Ptp 10 cm H_2O	Ptp 5 cm H_2O	
1	56	853		79.8	51.2	16
2	60.5	841	866	85	62	20
4	70	901	903	80.6	53.5	18
5	50	631	642	81.5	50.5	13
6†	45		564	83	62	10

* On deflation from Ptp 30 cm H_2O. † Lower lobe only.

RESULTS

Six excised left lungs were studied but one was rejected because of air leaks. Lung weights and volumes are shown in Table 1. The time from the initial to final measurement varied from 1 to 2 hr, but there was no substantial change in the lung volume at Ptp 30 cm H_2O during that time. Mean airway diameter at Ptp 30 cm H_2O at the beginning and end of the experiment differed on average by 2.3%. The static pressure-volume (P-V) relationships of the lungs on deflation were very similar in all preparations though the lung volume of *lungs 2* and *6* at Ptp 10 and 5 cm H_2O (as a percentage of the volume at Ptp 30 cm H_2O) were somewhat higher than the others. Table 1 also shows the number of airways measured in each lung. The largest airways measured in each preparation ranged from 11.7 mm in *lung 1* to 4.9 mm in *lung 6*, and the smallest from 1.9 mm in *lung 2* to 0.45 mm in *lung 1*, the latter being the only airway less than 1-mm diameter in this series.

Airway Diameter vs. Ptp

Figure 4 shows the relationship between transpulmonary pressure and airway diameter as the lungs were deflated from maximal volumes. For each lung the mean value and standard error of airways of all sizes has been plotted. In the range Ptp 12 to 1 cm H_2O change of airway diameter is fairly linear averaging 4.4% diameter change (as percent of maximum diameter) per cm H_2O. At higher Ptp airway diameter changed much less; the average diameter change in the range Ptp 30 to 11 cm H_2O is 0.45% per cm H_2O. These diameter changes are similar to those found previously in a smaller number of measurements in perfused dog lungs (13). On inflation we found that Ptp's some 2–7 cm H_2O greater were needed to achieve the same bronchial diameter, i.e., the pressure-diameter curve was shifted to the right. However, the relationship was not a simple one, depending very much on the previous lung volume history, and will be discussed in the section on hysteresis.

We did not find any significant differences in the percentage diameter changes of the larger as compared with the smaller bronchi. For each lung we calculated the percentage diameters of the 5 largest and the 5 smallest bronchi out of a total of 10–20 airways. Four to six comparisons were made in each lung at different transpulmo-

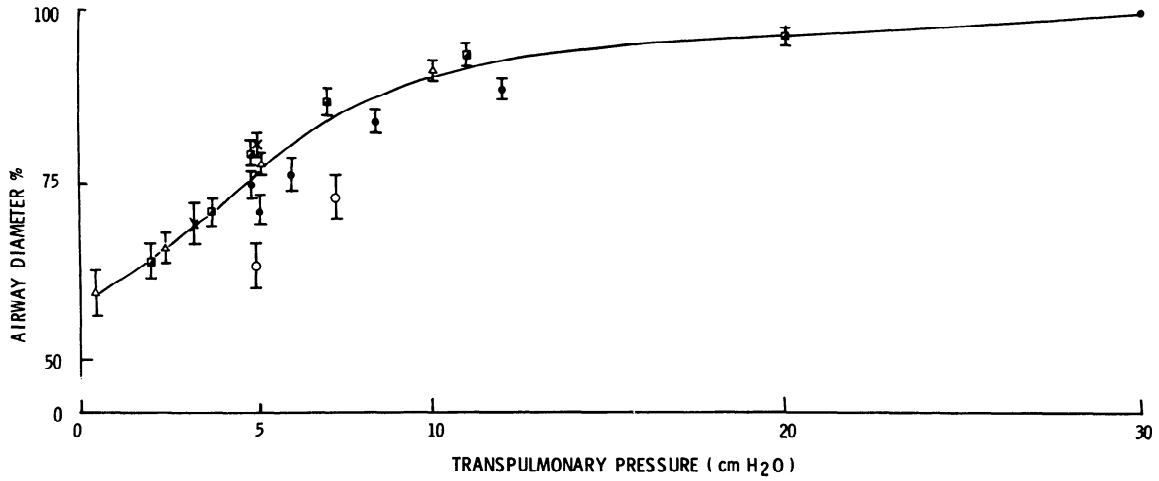


FIG. 4. Graph of transpulmonary pressure (Ptp) and airway diameter (as a percent of maximum) as lungs were deflated from maximal volumes (Ptp 30 cm H_2O). Each lung is represented by its symbol: (○) lung 1; (△) lung 2; (●) lung 4; (◪) lung 5; (×) lung 6: Vertical bars indicate one standard error of mean (SEM). Line connecting the points was drawn by eye.

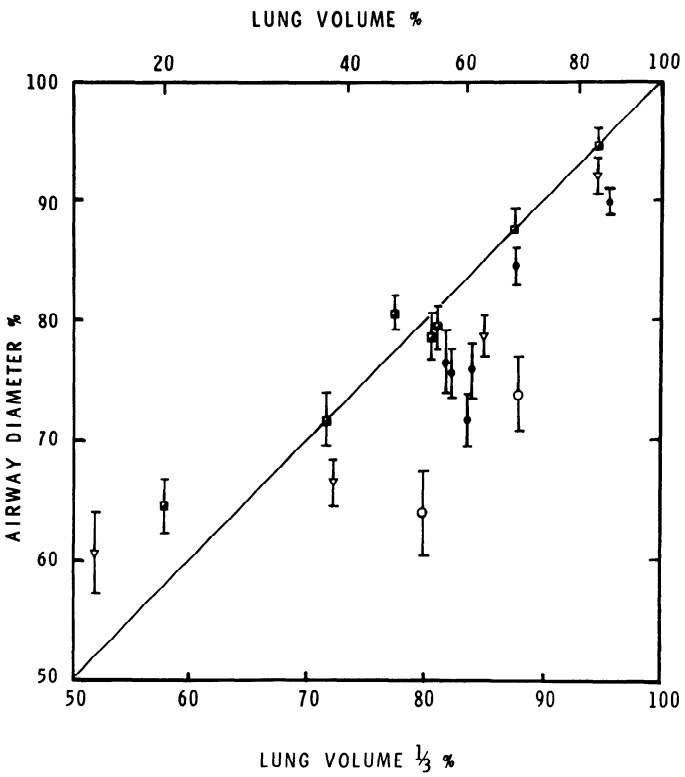


FIG. 5. Airway diameter as percent of maximum plotted against lung gas volume (*top abscissa*) and its cube root (*bottom abscissa*), both as percent of maximum. Continuous line is the line of identity with cube root of lung volume. Symbols and standard error of the mean as for Fig. 4.

nary pressures on inflation and deflation. In 26 comparisons the mean difference was 0.81%; in a t test on the samples the P value was 0.42, which is not significant. In any one comparison the largest difference was 10%.

Airway Diameter vs. Lung Volume

In Fig. 5 airway diameter is related to the cube root of lung gas volume. To the extent that excised lungs expand isotropically, the cube root of volume is the most appropriate linear function with which to compare length or diameter changes. As a guide, lung volume is plotted on the top abscissa. A fair correlation exists between percentage airway diameter and the cube root of lung volume. The maximum deviations occur in *experiment 1* (15 and 14%). (The results in *exp 1* for airway diameter in relation to lung volume and Ptp (Figs. 4, 5), differ from the other experiments; a final recheck of diameters at Ptp 30 cm H_2O was not made in this instance and it is possible that changes could have occurred during the experiment.)

Effect of Hysteresis

In comparisons made at the same lung volume on the inflation and deflation limbs of the lung P-V curve, bronchial diameters were not significantly different in spite of Ptp being 2–7 cm H_2O greater for the inflation measurement (Fig. 6). At isovolume the Ptp difference between deflation and inflation depended on volume history; the lower the lung volume prior to inflation the greater the Ptp difference and the wider the hysteresis loop. Advantage was taken of this property of lungs to compare bronchial diameters at constant lung volume at several Ptp's as shown in Fig. 7. Airway diameters are plotted on deflation at Ptp 5 cm H_2O and then at gradually increasing Ptp's on inflation. In contrast to the results shown in Fig. 4, there is now no significant change of airway diameter with changes of transpulmonary pressure. These results show how greatly volume history and lung volume modify the relationship between airway diameter and Ptp.

Effect of Time

Air-filled lungs show stress relaxation on inflation from low volumes and the reverse on deflation from high volumes (14); though the properties of the alveolar lining layer (surfactant) may be important in this regard, such a response to stretch and release is also a property common to most tissues containing muscle and elastic tissue (32). Rapid changes over 1–3 sec are usually followed by slower extension or shortening, lasting several minutes, which for length increases is termed "creep." In dissected bronchial

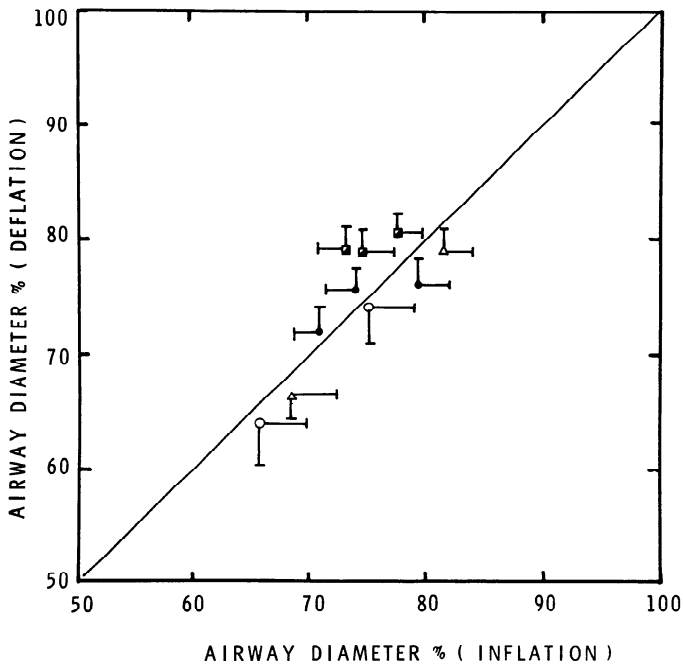


FIG. 6. Comparison of airway diameters as a percent of maximum at identical lung volumes following a deflation volume history (*ordinate*) and an inflation volume history (*abscissa*). Mean values are close to line of identity. Ptp difference between deflation and inflation ranged from 1 to 7.0 cm H_2O, and in absolute terms from Ptp 2.5 cm H_2O (deflation) to Ptp 14.5 cm H_2O (inflation). Symbols and standard error of the mean as for Fig. 4.

segments studied over periods of up to 45 min 80% of volume changes occurred within 30 sec of a step change in transmural pressure (25). The basic processes involved in this behavior of musculoelastic tissues are still poorly understood. Since we maintained a constant lung volume during our measurements, volume displacement within the lung from airways to parenchyma would also have been influenced by the relative rates of stress relaxation of parenchymal and bronchial tissue.

We usually took radiographs about 30 sec after reaching a certain lung volume, with the second exposure following the first by a similar time interval. Most of the time-dependent changes in bronchial caliber had by that time already occurred. Still it was possible that a late creep or, on deflation, a shortening of bronchial tissue could have occurred between the first and second exposure. It was in fact our practice to make all diameter measurements from the radiographic image from the same tube position regardless of whether that position had been used for the first or second exposure. In *experiment 5*, we compared airway diameters for each position of the stereo pair. The mean difference in 13 comparisons was only 1.08%. Nevertheless, a difference of 3.9% within one of the pairs prompted us to make serial measurements over longer periods of time in *lung 6* using a single exposure only. Figure 8 shows the change of airway diameter with time at constant lung volume. A significant change of Ptp at constant lung volume only occurred in the measurement on inflation where Ptp was initially 4.7 cm H_2O but fell to 4.3 cm H_2O at 40 sec and 3.7 cm H_2O at 100 sec. Significant reductions in diameter occur within the first 60 sec of achieving a volume with a deflation volume history, but there are no changes

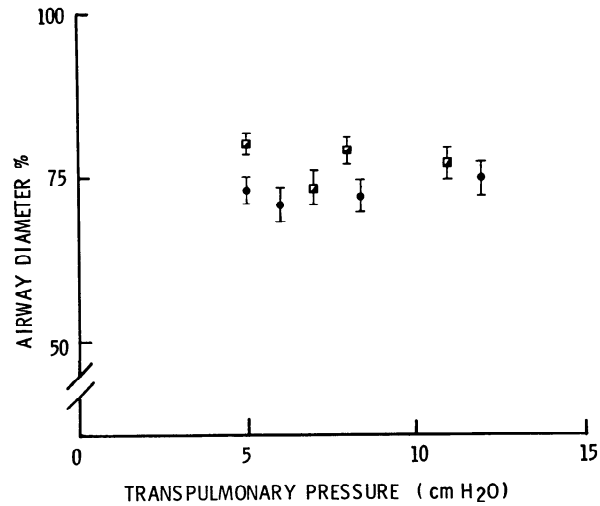
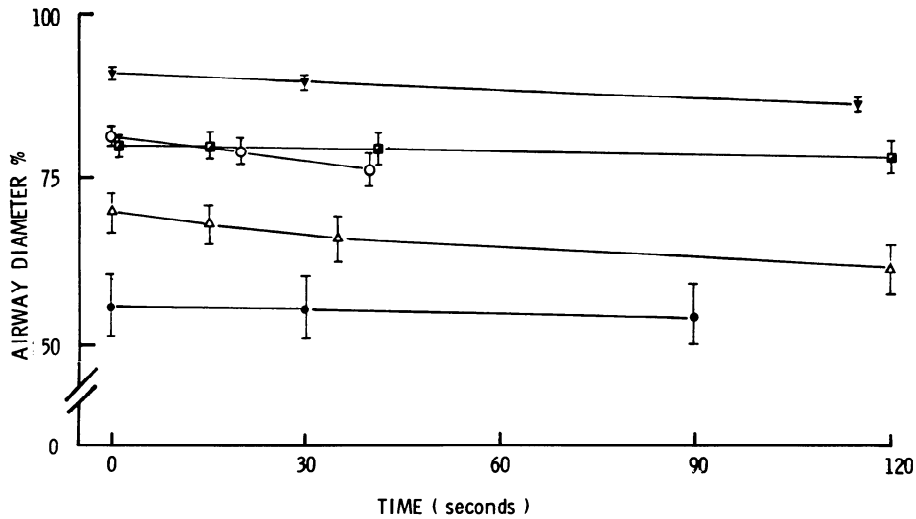


FIG. 7. Airway diameter as percent of maximum plotted against transpulmonary pressure (Ptp) at constant lung volume. Measurements at Ptp 5 cm H_2O were made following deflation from maximal lung volume, and the remainder on inflation from low lung volumes. Absolute lung volumes as percent of maximum ranged from 53.5–55% for lung 4 (●) and 50.5–52.5% for lung 5 (◪). Bars give 1 SEM.



FIG; 8. Airway diameter in lung 6 as a percent of maximum plotted against time elapsed (in sec) from the moment the lung was held at a certain lung volume. Ptp and volume history (inflation or deflation) are indicated by symbols: ▼, ○, and △ represent Ptp 10, 5, and 3.3 cm H_2O (deflation), respectively, and ◪ and ● Ptp 10 and 4.7 cm H_2O (inflation). Bars are 1 SEM.

following an inflation volume history. It would appear that time-dependent changes of bronchial diameter are measurable and that our measurements made on deflation may have underestimated the instantaneous diameter by as much as 5%. It is also likely that the small differences in diameter between positions of the stereo pair in *lung 5* were due to time-dependent changes and not a consequence of noncircular airway cross section.

We have no information on whether bronchial diameter was influenced by the time taken for the lung to reach a given volume; the magnitude of stress relaxation in alveolar tissue strips increases with the rate of tissue extension (9) and it is probable that bronchial tissue behaves similarly.

Airway Length

Bronchial length was measured in *lungs 4* and *5*. Ten airway segments were measured in each lung. At Ptp 30 cm H_2O the length of the segments ranged from 4.74 to 0.82 cm; the mean length in *lung 4* was 1.38 cm ± 0.495 SD and in *lung 5*, 2.0 cm ± 1.215 SD. Average difference between the measured length of individual segments at Ptp 30 cm H_2O at the beginning and end of the experiment was 1.75% (range 0–8%). We compared our stereoscopic measurement of bronchial length with length measurements using a single exposure only. At Ptp 30 cm H_2O in *lung 5*, the mean airway length from single exposure measurements was 11% less than that measured with the stereo pairs; for individual segments the difference was as much as 27%. The segments encompassed a range of bronchial sizes from 8.0 to 0.9 mm in diameter. No difference in length behavior of bronchi of different sizes was found.

Bronchial length as a percent of maximum length is plotted against the cube root of lung volume in Fig. 9.

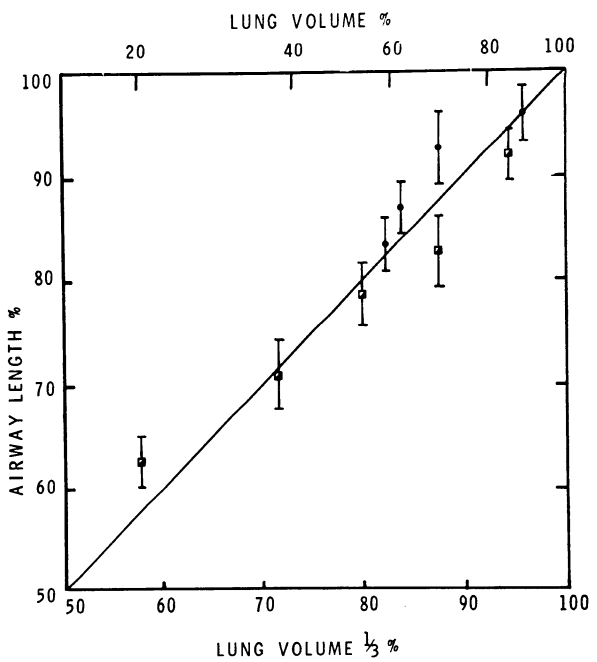


FIG. 9. Airway length as a percent of maximum plotted against lung gas volume (*top abscissa*) and its cube root (*bottom abscissa*), both as percent of maximum. Values fall close to line of identity with cube root of lung volume indicated by continuous line. Symbols as for Fig. 4. Mean values for 10 airway segments. Bars equal 1 SD.

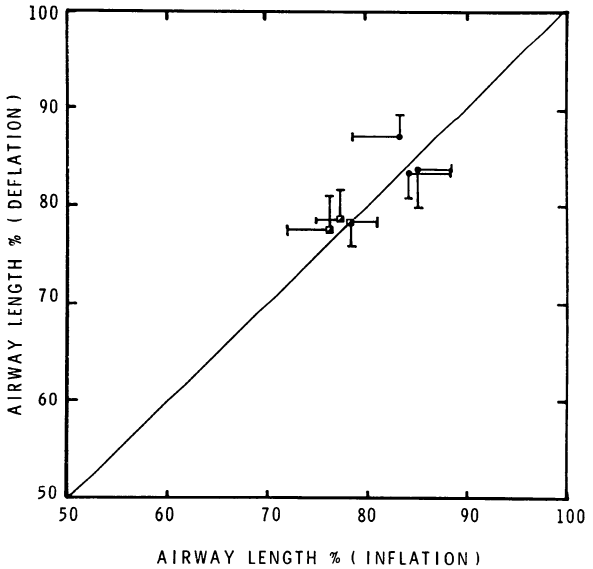


FIG. 10. Comparison of airway length as a percent of maximum at same lung volumes following a deflation volume history (*ordinate*) and an inflation volume history (*abscissa*). Points fall close to line of identity. Symbols and standard deviation as for Fig. 9.

The results are very close to the line of identity; the maximum deviation is only 5%. All measurements were made on deflation. At the same lung volume, airway length is essentially the same whether measured on inflation or deflation, as shown in Fig. 10.

DISCUSSION

In this discussion we relate our measurements to previous reports of bronchial length and diameter. From these considerations we draw some general conclusions about differences in behavior between airways in situ and when dissected free from lung tissue, which suggest that bronchi in situ are exposed to forces different from transpulmonary pressure. Finally, we consider these changes of bronchial diameter in excised lungs in relation to the effects of lung volume and tissue hysteresis on airway conductance measurements.

Airway Length

Macklin (22) first called attention to the alternate lengthening and shortening of the bronchial tree in inspiration and expiration, pointing out that, with a rigid bronchial tree, respiration would be impossible. In the time since Macklin's original observation, few measurements of bronchial length changes have actually been made. In previous reports (17, 18, 20), length changes in excised dog lungs have been measured from bronchograms taken in one plane only. Hyatt and his colleagues (17) reported that changes in bronchial length were accompanied by similar changes in the cube root of lung volume; their measurements were limited to the left upper lobe which in dogs is fairly flat, thus minimizing the foreshortening effect which otherwise may be considerable. Our technique of X-ray stereo pairs measures length changes more accurately and we have extended the observations of Hyatt et al. to lower lobes in dog lungs. In this study we show that there is

indeed a very close correlation over the range of lung volumes we have studied (above 20% of maximal gas volume) between changes of bronchial length and cube root of absolute lung volume. This finding is consistent with other observations in excised preparations which suggest that lungs over this volume range and in the absence of airspace or airway closure expand isotropically. For example, lung tissue strips from degassed cat lungs show similar stress-strain relationships regardless of orientation within the lung (31) and angles of bronchial branching remained the same as excised lungs are inflated (17). In addition we have found (Hoppin, Hughes, and Mead, unpublished data) that linear distance changes, calculated from surface markers, are similar in all directions and proportional to changes in the cube root of lung volume.

Hyatt and Flath (16) compared bronchial caliber in dog lungs in situ and dissected free from lung tissue. Over the same range of distending pressure they reported "a definite tendency for the lengths of the intact tree to exceed those of the dissected tree." There have been several reports that over a wide range of inflating pressures dissected bronchial segments undergo only modest changes of length. Increases of bronchial length at transmural pressures of 20–30 cm H_2O, as percent of those at zero transmural pressure, range from 15–17% (23, 25) to 30% (28), the latter being similar to our own observations in dissected bronchi. In contrast, bronchial segments when intact within the lung increase in length by 60% over the range Ptp 2–30 cm H_2O (Fig. 9).

Airway Diameter

Pressure-diameter relationships. Bronchial diameter changes in excised lungs of Boston mongrels (Fig. 4) are similar to those we have reported in a smaller series in perfused London greyhound lungs (13) though different in several respects from Hyatt and Flath's measurements (16). The essential difference is in the shape of the bronchial pressure-diameter curve. These authors (16) measured bronchial diameter on deflation after inflating excised dog lungs to Ptp 20 cm H_2O; nearly all the diameter changes occurred when Ptp was less than 5 cm H_2O with very little alteration between Ptp 12 cm H_2O and 5 cm H_2O. On the other hand, the overall percentage diameter changes (diameter at Ptp 12 cm H_2O as percent of Ptp 0 cm H_2O) were similar to ours. Recently, after premedicating dogs with 1.0 mg atropine which relaxes smooth muscle we have obtained (unpublished observations) bronchial pressure-diameter curves in excised lungs which approach those reported by Hyatt and Flath; although these authors did not give atropine, we believe differences in airway tone may explain these different experimental results. The scatter of our results for airway diameter is greater than that for airway length and it seems likely that variations in bronchomotor tone can lead to differences in bronchial diameter behavior even within an excised lung. In living dogs given atropine (data of Nadel quoted by Hyatt et al. (17)) a definite reduction of bronchial diameter (from 6 to 5.5 mm) occurred on deflation from Ptp 30 to 10 cm H_2O and a spectrum of bronchial pressure-diameter curves probably exists from that reported by Hyatt and Flath (16) to those in this study.

Another area in which different results have been obtained is in the behavior of bronchi of different sizes. We found similar percentage changes in bronchi ranging in diameter at Ptp 30 cm H_2O from 1.5 to 11 mm, in contrast to Hyatt et al. (17) who report similar absolute diameter changes over a wide range of distending pressures. Their measurements were made as lungs were inflated from Ptp 3 cm H_2O. On the other hand, the measurements made by Hyatt and Flath (16) on lung deflation show only small differences between percentage changes for different bronchial sizes; the diameter at Ptp 0 cm H_2O as a percentage of that at Ptp 12 cm H_2O (calculated from Fig. 4 in their paper) is 65% for airways less than 3.0-mm diameter (absolute change of about 1.25 mm) and 70% for airways greater than 3.0-mm diameter (absolute change 1.9 mm). Studies in man and animals have not shown any systematic differences in percentage diameter changes with lung inflation. Marshall and Holden (24) measured bronchial diameters at full inspiration (as a percent of diameter at functional residual capacity (FRC)) from bronchograms in normal subjects. They found a similar percentage increase in diameter (14–15%) for airways ranging in size (at FRC) between 1.7 and 7.0 mm, but a 28% change for airways less than 1.7 mm. However, we have some reservations about the accuracy of their technique for assessing diameter changes of airways less than 1.7-mm diameter; changes of depth of airways relative to the X-ray film with lung inflation and deflation result in larger errors for smaller airways (see METHODS) although this can be overcome by using a stereo-pair radiographic technique (12). Bronchi greater than 7.0-mm diameter showed smaller changes (5%), but since these were mainly extraparenchymal in site (trachea and main bronchi) radial stresses might have been less than for bronchi surrounded by lung tissue. Similar measurements made by Fraser (7) for intraparenchymal bronchi ranging in size from 5.9 to 2.7 mm showed percentage changes ranging from 26 to 33%. In only one of seven sites was a consistently larger change found (44% change for basal bronchus of lower lobe, diam 4.1 mm). Gayrard et al. (10) inflated anesthetized dogs from resting end expiration to positive airway pressure of 30 cm H_2O and found no consistent pattern in the percentage changes which, for bronchi from 2.0 to 8.9. mm, ranged from 15 to 27.6%.

Bronchial diameter and lung volume. Figure 5 shows the correlation between airway diameter and the cube root of lung volume. Though this relationship is not very precise in some preparations, in others the points fall close to the line of identity (*lungs 2* and *5*, for example). In other words, in those lungs where bronchial diameter and length changed proportionately with the cube root of lung volume the specific compliance of all bronchi was the same and equal to lung specific compliance. Such a situation is different from that seen in dissected bronchi. Specific compliance of bronchi 3–5 mm in diameter is about 50–60% of lung compliance (25, 28), but smaller airways (2-mm diam) are substantially more compliant (25) with values approaching that for lung tissue.

Airway Hysteresis

A method of comparing lung and bronchial static volume-pressure hysteresis is set out schematically in Fig. 11. If

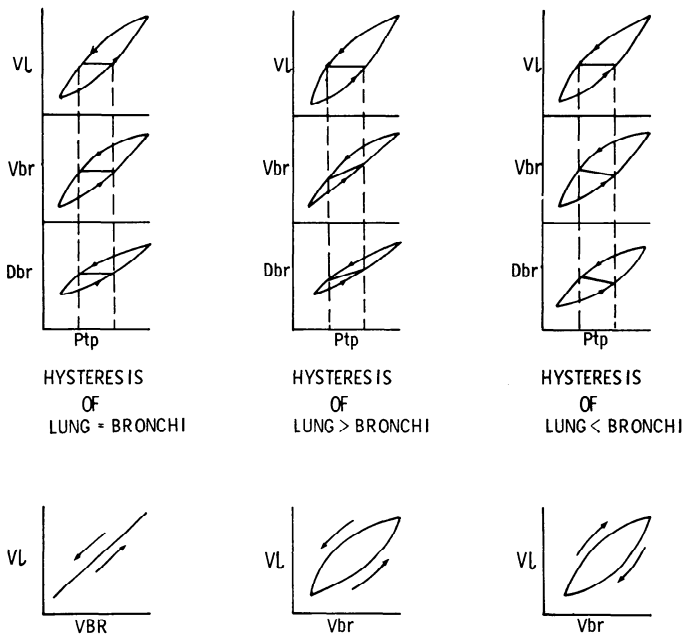


FIG. 11. Schematic diagram illustrating how relative volume changes of lung (VL) and bronchial (Vbr) volume-pressure systems, exposed to same pressure cycles, can be used to assess relative volume-pressure hysteresis. Dbr is bronchial diameter.

airways exhibit the same degree of hysteresis as the lung when subjected to the same pressure, relative bronchial volume changes will be directly proportional to lung volume changes and, as pointed out by Froeb and Mead (8), the volume changes of either one plotted against the other will fall along a single line independent of volume history. In the upper part of Fig. 11 the vertical broken lines represent two pressures on the inflation and deflation limbs of a volume-pressure curve at which lung volumes, because of hysteresis, are the same as indicated by the solid horizontal lines joining them. When lung and bronchial hysteresis are equal, bronchial volumes at these pressures (and at the same lung volume) will also be the same. Similar relationships will hold for other dimensions of airways (such as length and diameter) if they are linearly related to lung volume. When bronchial hysteresis is proportionately greater or less than lung hysteresis bronchial volumes and diameter will be different at inflation pressures at which lung volume is the same, as shown by the downward or upward sloping lines joining them. Under these circumstances the relationship between lung and bronchial volumes, shown in the lower part of Fig. 11, becomes dependent on volume history.

Figures 6, 7, and 10 show no difference between inflation and deflation diameters and length at the same lung volume but different Ptp. Thus airway hysteresis in our preparations was similar to lung hysteresis. In other studies (15), hysteresis of airway diameter also equaled lung hysteresis when lobes were taken to a minimum Ptp of 2 cm H_2O on deflation but was slightly greater than lung hysteresis when minimum Ptp was 0.5 cm H_2O. Our study, in which minimum Ptp was usually equal to or greater than 2 cm H_2O, is consistent with these findings.

Hysteresis may be an intrinsic property of tissue (or its surface lining); on the other hand an apparent hysteresis for airways may exist if bronchial distending pressure differs systematically from the pressure distending the lung. A large part of the hysteresis of air-filled lungs depends on surface forces of the alveolar air-liquid interface, and in particular the properties of the lining layer of surfactant (5). Although bronchioles may be lined with a similar substance (20), there is no evidence of surfactant in the larger bronchi measured in this study and in any case the radius of curvature is too large for surface forces to have much effect. On the other hand, hysteresis of smooth muscle is well known (32). Experiments on guinea pig taenia coli preparations show quite clearly that the tension developed by smooth muscle at the same length depends on its previous history (3); for example, the tension was up to 3 times greater as the preparation was stretched starting from a resting length compared with the tension at the same length following the stretch. Stretching smooth muscle causes depolarization and accelerates spike discharge thus increasing tension or, under isotonic conditions, shortening. Release causes hyperpolarization which slows spontaneous spike discharge and thus a lowering of tension or, under isotonic conditions, a lengthening. Nevertheless, it seems a little unlikely that the intrinsic hysteresis of airways would match that of lung tissue as closely as shown in Fig. 7, and the possibility that peribronchial pressure may depart significantly from pleural pressure will be discussed.

Mechanical interdependence of airways and air spaces. The striking experimental findings and conclusions from the data in this and previous studies are: *1*) at a given transpulmonary pressure airways in situ are longer than when excised and exposed to the same distending pressure; *2*) the expansion of airways of different sizes appears to be more uniform in situ than when excised; and *3*) airway expansion in situ appears to follow air-space expansion quite closely in that bronchial and lung hysteresis tend to be similar.

These observations suggest that lung tissue exerts an influence on airways which tends to make them conform to the surrounding parenchyma. A possible mechanism for this is suggested in a recent analysis of stress distribution in lungs, in which Mead et al. (26) related the forces from surrounding tissues to the areas on which they operate. Where nonuniformities of expansion exist, they postulated that local distending pressure would differ systematically from transpulmonary pressure and in the direction to reduce the nonuniformity. To the extent that bronchi were more or less distensible than surrounding lung, the stress at the outer surface of the limiting membrane of the bronchus should differ from that elsewhere so that peribronchial pressure would be different from pleural pressure. Mead et al. analyzed these relationships for a bronchus in situ (Fig. 6 of ref 26), and while peribronchial pressure from theory became more subatmospheric than pleural pressure the effect on bronchial volume was rather small. To some extent this was a function of the shape of the bronchial compliance curve which was chosen, in which dissected bronchi reached maximum diameter at 6 cm H_2O. For example, other pressure-diameter studies of dissected bronchial segments suggest that bronchial tissue has not reached its limit of expansion at transmural pressures of 14 cm H_2O in one study (15) and 30–40 cm H_2O in another (23).

In Fig. 12, we have extended this analysis to show how in theory lung hysteresis might modify bronchial hysteresis. Lung and bronchial volumes are expressed relative to the undistended state. The lung curve is a volume-pressure relationship calculated from the preparations in this study. The isolated bronchus curve in Fig. 12*A* comes from measurements of bronchial volume by Martin and Proctor taking average values for bronchi 2 mm and 5 mm diameter and about 2 cm in length (Figs. 3, 4 of ref 25) (Note that Mead et al. (26) derived excised bronchial volumes from pressure-diameter data (16) and the assumption that bronchial lengths changed with pressure as the cube root of lung volume at the same pressure.) From these two curves the in situ bronchus curve was derived on the assumption that the effective distending pressure at the surface of the bronchus varied as $Ppl_0 \times (V_0/V)^{1/2}$ (26) where Ppl_0 represents the pleural pressure and V_0 the volume of the hypothetical bronchus before the volume change was initiated. This expression, as used by Mead et al., refers to the case of a cylinder of fixed length. The isolated bronchus in Fig. 12*A* shows a greater relative hysteresis than the lung in that for two points of equal lung volume on the deflation and inflation limbs of the pressure-volume curve it has a smaller volume on the inflation side than it does on the deflation limb. For the bronchus in situ these differences in bronchial volume become less, showing that interdependence results in bronchial hysteresis approaching more nearly the hysteresis of the lung. In Fig. 12*B* we have shown a hypothetical bronchus with no hysteresis in the isolated state, by taking a line midway between the deflation and inflation limbs of the isolated bronchus in Fig. 12*A*. Again the influence of lung parenchyma is to bring the hysteresis of the bronchus in situ slightly closer to that of lung tissue. In Fig. 12*A* at equal lung volumes the in situ bronchus shows volume differences of 0.25 compared with 0.55 in the isolated state, and in Fig. 12*B* a difference of 2.3 compared with 2.7.

This example of the effect of interdependence on bronchial hysteresis is a conservative one on several counts. It assumes no change in tension as the radial tissue elements distort from their geometry in the homogeneous state. To the extent that bronchial volumes changed proportionately less than air-space volumes local distortions and increase of forces in tissue elements will occur. Second, this analysis does not take account of additional longitudinal forces acting on bronchi in situ. For instance, the change of length over the pressure range 0–30 cm H_2O from Martin and Proctor's data (25), from which we took the curve for the isolated bronchus, was only about 15% whereas we find in situ bronchi over this pressure range increase their resting length by 60%.

Greater airway lengths in situ mean that airways are subjected to longitudinal stresses in excess of transpulmonary pressure. One way in which this might occur is through shear stress at the outside wall from tissue attachments; quite modest degrees of distortion, leading to changes in the angle of attack of radial elements, could in theory lead to substantial increases in longitudinal forces. Increases in longitudinal tension for more central airways might also result from distortions of side bronchi and their peripheral ramifications. The extent of this longitudinal stabilization is being measured in our present research; it appears that the lung tissue forces which oppose changes of bronchial length at constant lung volume are considerable. Experimental evidence that forces additional to lung distending pressure (Ptp) affect bronchial diameter in situ is somewhat contradictory. Hyatt and Flath's results (16) suggested that bronchial and lung distending pressures were probably the same, but the shape of the pressure-diameter curve of the isolated bronchus may have obscured an effect of interdependence (26). Marshall (23) on the other hand compared bronchial diameter at the same intrabronchial pressure (10 cm H_2O) in partially atelectatic and inflated

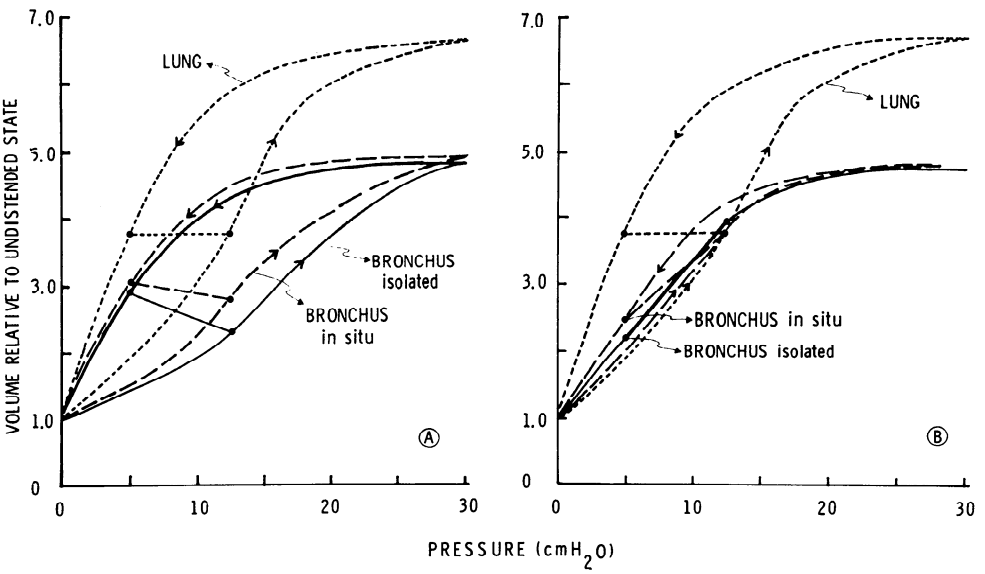


FIG. 12. Pressure-volume relationships on deflation and inflation comparing hysteresis of lung and bronchus, dissected free from lung tissue (isolated) and intact within the lung (in situ). In situ bronchial curve has been derived after the method of Mead et al. (26), taking into account relative distensibilities of lung and isolated bronchus and changes of surface area. In *A*, isolated bronchus has relatively greater hysteresis than lung, whereas *B* illustrates an isolated bronchial curve without hysteresis. Note that at equal lung volumes on deflation and inflation, in situ bronchial volumes are more nearly equal in *A* and *B* than isolated bronchial volumes, showing that in theory the effect of lung tissue will be to bring in situ bronchial hysteresis closer to lung hysteresis.

excised lobes and found the average diameter in the atelectatic lobes as a percent of resting diameter was 130% compared with 217% in the inflated lobe. Dissected bronchi at a similar intrabronchial pressure also had smaller diameters than when in situ in lobes inflated to the same pressure. In the case of pulmonary blood vessels, Howell, Permutt and co-workers (11, 30) have shown that under certain experimental conditions intravascular pressures changed more during lung inflation than could be accounted for if perivascular pressures equaled pleural pressure.

Relation of bronchial caliber changes to airway conductance. Measurements of total airways resistance in man have shown a linear relationship between conductance (the reciprocal of resistance) and lung volume (2), and it has been inferred that as the size of the lungs increases the size of the airways increases proportionately. Measurements of lower airway resistance (from alveolus to trachea) in normal subjects with and without atropine administration also show a fairly linear increase of conductance with increase in lung volume (34), though the relationship is not so linear as with measurements of total airway conductance, and some subjects showed a decrease of conductance at high lung volume. In living dogs (not given atropine) conductance was linearly related to volume at lung volumes less than 50% of vital capacity (VC), but again an increase in resistance was seen at higher volumes (19). Other studies in living dogs show that the linear relationship between lower pulmonary conductance and volume can continue up to 80% VC (21). Pedley et al. (29) have developed a theory for predicting the energy dissipation and associated pressure drop for flow in systems of branched tubes; with a realistic model of lung anatomy and the assumption that airway caliber changes were proportional to lung volume, they found good agreement between predicted conductances at different lung volumes and the measurements of Vincent et al. (34).

In spite of the fact that the intact human lung with uninterrupted blood and nerve supply must differ substantially from a uniformly expanded excised dog lung with minimal bronchomotor tone, it was intriguing to find that the intraparenchymal airways in some of our excised lung preparations changed length and diameter proportionately with lung volume, as originally suggested to explain airway resistance changes in human subjects. There are still several experimental findings at variance with this simple model of proportional bronchial and lung volume tissue changes. For example, neither theory (29) nor our own measurements of airway caliber can explain the decreases of lower pulmonary conductances at high lung volume, though recently Gayrard et al. (10) have shown that tracheal diameter decreases with positive pressure inflation in anesthetized dogs. After vagotomy, dog lungs did not show any changes of conductance with lung volume change until low volumes (20% VC) were reached (20); surprisingly the caliber changes in excised lungs in this study would be more consistent with the conductance-volume relationship found before vagotomy.

Hysteresis of conductance. If measurements are restricted to inflation or deflation, conductance can be directly related to elastic recoil pressure. For example, at mid-lung volume after inflation from residual volume increases of elastic pressure produced by chest strapping lead to a rise in conductance (4). Recently it has been shown that the relationship between conductance and lung recoil pressure or lung volume depends also on volume history (34). Vincent et al. found lower pulmonary resistance considerably increased at the same lung volume after inflation from residual volume than after deflation from total lung capacity, although lung recoil pressure was some 4–5 cm H_2O greater in the former instance. These results suggest that airway hysteresis in terms of length and diameter change was greater than lung hysteresis. After atropine the differences in resistance were much less, although the differences in lung recoil pressure remained about the same. In this instance airway hysteresis must have been approximately equal to lung tissue hysteresis. Thus, if bronchomotor tone is diminished by the administration of atropine the relative volume changes of airways and air spaces in human and excised dog lungs is similar. This comparison only refers to those airways, which in human lungs contribute most of the lower pulmonary resistance, and to intraparenchymal bronchi down to a diameter of about 2 mm in the dog lungs we have studied. The relatively greater airway hysteresis found in normal subjects not given atropine is in agreement with measurements showing dead-space hysteresis to be slightly greater than lung hysteresis (8).

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