Time dependence of airways and lung parenchymal recoil hysteresis

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FAIRSHTER, R. D., R. B. BERRY, A. F. WILSON, AND J. E. LOWE. *Time dependence of airways and lung parenchymal recoil hysteresis.* J. Appl. Physiol. 61(1): 248–254, 1986.—Hysteresis of airways and lung parenchymal recoil was examined in normal subjects by measuring specific conductance (sGaw) and lung elastic recoil (Pst,L) before and 5, 10, 15, and 30 s after deep inspiration (DI). Routine lung function tests were normal before and after inhaled metaproterenol. sGaw increased significantly for 10 s after DI. Also, sGaw(DI) was > sGaw in 11 of 12, 8 of 12, 7 of 12, and 6 of 12 subjects at 5, 10, 15, and 30 s, respectively, after DI. The response of sGaw to DI and metaproterenol correlated significantly with each other ($r = 0.82$, $P < 0.001$). However, after metaproterenol, sGaw(DI) did not exceed sGaw. Pst,L decreased significantly for 15 s after DI, with the lowest measured Pst,L(DI) values occurring 5 s after DI ($P < 0.01$–0.001). Both sGaw(DI) and Pst,L(DI) values returned to base line (preinspiration) in a time-dependent exponential manner, with time constants of 9.2 ± 4.9 and 11.3 ± 6.1 s, respectively; these time constants were not significantly different from each other. We conclude that *1*) airways hysteresis is the predominant finding in normal subjects (even without prior pharmacological bronchoconstriction) before but not after metaproterenol; *2*) Pst,L decreases after DI and, in normal individuals, returns to base line in a time-dependent manner; and *3*) the time-dependent behavior of airways and lung parenchymal hysteresis have opposite (and unequal) effects on airway caliber.

airways hysteresis; lung elastic recoil; specific conductance

AIRWAYS HYSTERESIS can be defined as an increase in airway diameter at a particular lung volume following inspiration to and subsequent deflation from total lung capacity (TLC) (8, 9, 24, 30). Although some investigators found that normal airways do not exhibit hysteresis without prior pharmacological bronchoconstriction (4, 7, 14, 22), other studies have demonstrated that specific conductance (sGaw) and expiratory flow rates increased, whereas airways and total respiratory resistance decreased following a TLC volume history in normal individuals without pharmacologically constricted airways (2, 5, 8, 11, 18, 30).

Previous studies using maximal (MEFV) and partial expiratory flow-volume (PEFV) maneuvers as well as measurements of total respiratory resistance have shown that the effects of a TLC volume history decrease in normal subjects as a function of time after the deep breath (5, 11, 18). Other studies have demonstrated time dependence of sGaw results following methacholine-induced bronchoconstriction in subjects with normal pulmonary function (before bronchoprovocation) but histories of allergic rhinitis and rhinoconjunctivitis (9, 24). Studies of isolated airways have also demonstrated time dependence of airway hysteresis (25). Thus the effects of deep inspiration on airway caliber diminish with time after the deep breath.

Although airways hysteresis has been studied previously, further investigation seemed waranted, since differences (before and after a TLC volume history) in expiratory flow and in airway conductance may reflect other factors in addition to airways hysteresis; e.g., lung elastic recoil (Pst,L) exhibits hysteresis, diminishing after a TLC volume history (8). Time dependence of lung parenchymal recoil hysteresis would also influence studies of time dependence of airways hysteresis, since lung retractive forces influence airway size (17, 26, 29). In previous studies, time dependence of Pst,L following deep inspiration has not been examined in detail. Therefore, in the present study, we examined airways hysteresis and its time dependence by measuring sGaw before and 5, 10, 15, and 30 s after inspiration to TLC; Pst,L and its time dependence was measured at the same time intervals. Exponential equations were developed to characterize the time dependence of hysteresis of the airways and lung parenchymal recoil.

MATERIALS AND METHODS

Subjects. Twelve normal individuals (9 men, 3 women; age 29.8 ± 7.0 yr, mean ± SD) were studied; the studies were all performed without prior pharmacological increase in resting airway tone. All subjects were lifetime nonsmokers, and none had a history of atopic, cardiorespiratory, or other systemic disease. Informed consent was obtained from each subject.

Routine physiological measurements. Forced vital capacity (FVC) and its subdivisions were obtained by use of a 13.5-liter water-sealed spirometer (Warren E. Collins, Braintree, MA). Slow vital capacity (VC) and expiratory reserve volume (ERV) were also determined with this spirometer. Thoracic gas volume at functional residual capacity (FRC) and airways resistance (Raw) were obtained by body plethysmography (1). Raw was expressed as specific conductance ($sGaw = Raw^{-1} \cdot FRC^{-1}$). Residual volume (RV) was calculated by subtracting ERV from FRC. TLC was calculated by adding FVC or VC (whichever was larger) to RV. Single-breath diffusing

capacity for carbon monoxide (DL_{CO}) was measured by the method of Ogilvie et al. (23). Spirometric and lung volume measurements were repeated 10 min after four inspiratory capacity inhalations of 0.65 mg (total 2.6 mg) of metaproterenol from a metered-dose cannister.

Effect of volume history on sGaw. After subjects had avoided deep breaths for 3 min, sGaw was obtained in the usual fashion. To determine sGaw after a deep breath, the subjects inspired rapidly to TLC and then immediately exhaled back to a volume near FRC by relaxing with the glottis open; they then again began tidal breathing. Specific conductance after deep inspiration [sGaw(DI)] was measured at time intervals of 5, 10, 15, and 30 s after the TLC volume history. At each time period, multiple measurements were made and the results were averaged. The orders of the sGaw and sGaw(DI) studies were randomized; regardless of the order of these measurements, sGaw determinations were always preceded by 3 min of tidal breathing. Specific conductance measurements [sGaw, sGaw(DI)] were repeated after inhalation of 2.6 mg of metaproterenol.

Lung elastic recoil measurements. Pst,L were determined at FRC in six subjects by use of esophageal balloon technique (20). Differences between esophageal and mouth pressure were measured using a differential pressure transducer (Validyne) connected to a carrier demodulator. Results were recorded against time on an oscilloscope (DR-8, Electronics for Medicine, White Plains, NY). Simultaneous measurements of volume changes were made with a rolling-seal spirometer (Cardiopulmonary Instruments model 220, Houston, TX) that was connected to a different channel of the DR-8 oscilloscope. Pst,L was measured before as well as 5, 10, 15, and 30 s after a TLC volume history. The sequence of testing was as follows: after 3 min of tidal breathing without coughing or deep breaths (verified by observation of the subject and recording of the tidal breathing pattern using magnetometry), the subjects were connected to the spirometric circuit. Subjects were instructed carefully and repeatedly to avoid taking deep breaths while placing their mouths on the mouthpiece. After another brief period (~20 s) of tidal breathing, the airway was occluded at FRC and Pst,L was measured. The airway was then opened, and the subject inspired rapidly to TLC, immediately exhaled back to FRC by relaxing with the glottis open, and began tidal breathing again. Pst,L was then measured at the designated time intervals by occluding the airway again at FRC. Following this, the subjects reinspired to TLC and back to RV; this was to ensure the reproducibility of inspiration to TLC. The apparatus utilized and the pattern of breathing during these measurements are shown in Fig. 1; because of the visual display of the tidal breathing record, subjects could reproducibly return to FRC for Pst,L measurements. The large volume of the system prevented significant CO_2 buildup (as verified by measurements using a mass spectrometer). Multiple measurements of Pst,L before and after a deep breath were made in random order; the results at each time period were averaged. After metaproterenol, Pst,L was only measured prior to deep inspiration.

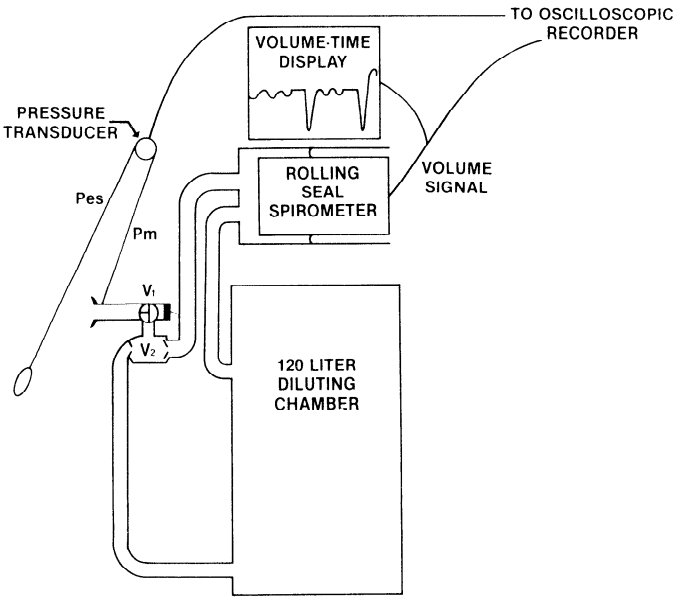

FIG. 1. Schematic representation of system used to measure time dependence of lung elastic recoil. Subjects breathed through a 2-way valve (V_1) connected to a Hans-Rudolph valve (V_2). Expiratory port of 2-way valve was occluded. Expiratory port of Hans-Rudolph valve was connected to a rolling-seal spirometer, which was connected to a 120-liter dilution chamber (a Tissot spirometer with the bell fixed at a volume of 120 liters). Volume signal from rolling-seal spirometer was displayed as a function of time on a physiological recorder to provide a visual display of breathing record for the subject. An example of a breathing record demonstrating airway occlusion before and 10 s after deep inspiration is shown. Volume signal from rolling-seal spirometer was also recorded on DR-8 oscilloscope as were differences between esophageal (Pes) and mouth pressure (Pm).

Statistics and data analysis. Spirometric results were compared with the predicted normal values of Morris et al. (21). Mean values, standard deviations, and standard errors of the mean were calculated by standard equations (15). Linear regression analysis was done by the least-squares method. The statistical significance of the relationships between sGaw and time and between Pst,L and time were analyzed using a computer program for the analysis of variance with repeated measures (BMDP2V). Subsequently, results at individual time periods were compared using a paired t test analysis. Other mean results (i.e., pre- and postbronchodilator) were compared using paired or nonpaired t test analyses as appropriate. $P \leq 0.05$ was considered statistically significant.

The relationships between lung recoil after inspiration and time were fit to the exponential equation

$$\text{Pst,L(DI)}_t = \text{Pst,L(DI)}_{max} - Ae^{-kt}$$

where Pst,L(DI)_t is elastic recoil at a specific time t, Pst,L(DI)_{max} represents the estimated asymptotic value, A is another constant describing the position of the curve, and k is a constant describing the shape of the curve. The derived relationship was extrapolated to $t = 0$ to estimate elastic recoil immediately after a deep breath [Pst,L(DI)_0]. The time constant of the exponential was calculated as the time where $\text{Pst,L(DI)}_t = \text{Pst,L(DI)}_0 + 0.63\ [\text{Pst,L(DI)}_{max} - \text{Pst,L(DI)}_0]$. The relationships between sGaw(DI) and time t were analyzed similarly

$$\text{sGaw(DI)}_t = \text{sGaw(DI)}_{min} + Be^{-it}$$

where $sGaw(DI)_{min}$ represents the asymptotic value and B and i are constants as described above. The derived relationship was extrapolated to obtain $sGaw(DI)_0$, and the time constant of the relationship was calculated. All curve fitting was performed using an iterative least mean squares regression (BMD-AR program) on a digital computer.

RESULTS

Routine pulmonary function tests. The results of routine pulmonary function tests are shown in Table 1. Pulmonary function was normal in all 12 subjects. Small but statistically significant increments in expiratory flow rates and VC were noted after metaproterenol.

Plethysmographic measurements. sGaw (measured without a preceding TLC volume history) averaged 0.237 $cm^{-1} \cdot s^{-1}$ before and 0.343 $cm^{-1} \cdot s^{-1}$ after metaproterenol ($P < 0.001$). Before metaproterenol, sGaw(DI) was higher than sGaw in 11 of 12, 8 of 12, 7 of 12, and 6 of 12 subjects at 5, 10, 15, and 30 s, respectively, after deep inspiration. For all time periods (before metaproterenol) after the TLC volume history, sGaw(DI) exceeded sGaw in 32 of 48 measurements, and the average value of sGaw(DI) was significantly higher than the average value of sGaw (0.259 vs. 0.237 $cm^{-1} \cdot s^{-1}$, $P < 0.005$).

Means ± SE for sGaw and sGaw(DI) are shown before and after deep inspiration in Fig. 2; the analysis of variance with repeated measures (ANOVA) indicated that the relationship between sGaw and time was statistically significant ($P < 0.001$). At 5 s, sGaw(DI) was significantly higher than all other sGaw or sGaw(DI) values ($P < 0.005$). In addition, at 10 s, sGaw(DI) was significantly higher than sGaw or sGaw(DI) at 30 s ($P < 0.05$). FRC averaged 2.64 ± 0.61 liters before and 2.70 ± 0.59 FRC to 2.66 ± 0.57 liters from 5 to 30 s after deep inspiration. Since FRC was very similar and not significantly different at any time interval before or after deep inspiration, the changes in sGaw were predominantly a reflection of changes in Raw.

After inhalation of bronchodilators, there was no hysteresis nor time dependence of sGaw (Fig. 2); values of sGaw(DI) did not differ significantly from each other or from postbronchodilator sGaw at any of the postbronchodilator time intervals studied. The improvement in sGaw after bronchodilator correlated significantly with the amount of increase in prebronchodilator sGaw 5 s after deep inspiration ($r = 0.82$, $P < 0.001$) (Fig. 3). Since all of the data points in Fig. 3 fall above the line of identity, it is evident that sGaw improved more after metaproterenol than after deep inspiration; however, it should be noted that sGaw results 5 s after deep inspiration underestimate the maximum effect of airways hysteresis (see below). After correction for the time dependence of prebronchodilator sGaw(DI) results (using the exponential analysis), sGaw still increased more after metaproterenol than after a deep breath, but the difference was not statistically significant ($P > 0.2$).

TABLE 1. *Pulmonary function before and after inhalation of bronchodilator*

	Prebronchodilator	Postbronchodilator
FEV_1, liters	3.73±0.64	3.89±0.73*
FEV_1, % predicted	104.2±10.9	108.3±11.1†
VC, liters	4.48±0.71	4.55±0.74†
VC, % predicted	103.1±9.4	104.7±9.5†
RV, liters	1.73±0.63	1.52±0.52
TLC, liters	6.21±1.11	6.05±0.97
D_{LCO}, $ml \cdot min^{-1} \cdot Torr^{-1}$	29.3±5.3	

Values are means ± SD. FEV_1, forced expiratory volum in 1 s; VC, vital capacity; RV, residual volume; TLC, total lung capacity; D_{LCO}, diffusing capacity for CO. * $P < 0.025$ compared with prebronchodilator values. † $P < 0.01$ compared with prebronchodilator values.

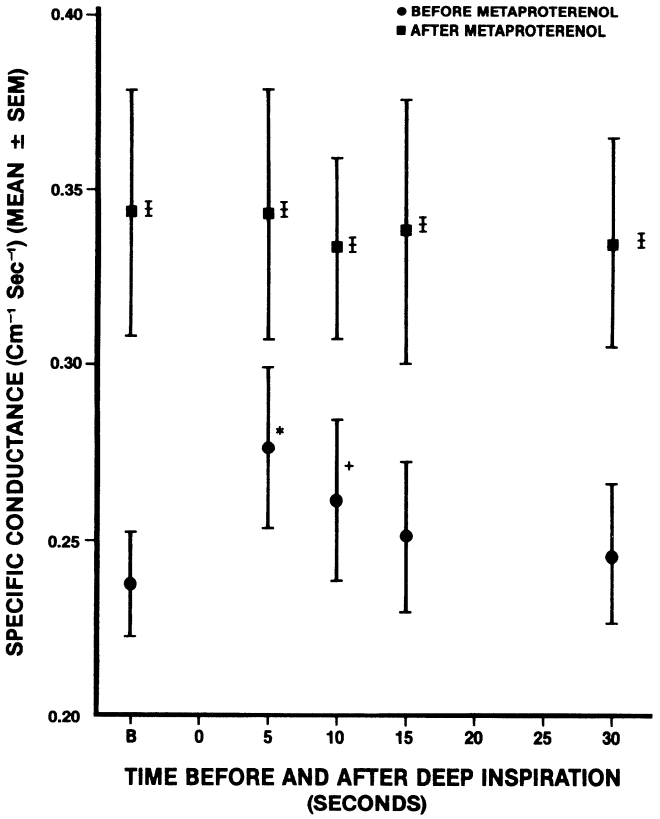

FIG. 2. Results of base-line (before deep inspiration) specific conductance (sGaw) and specific conductance after deep inspiration [sGaw(DI)] before and after inhalation of 2.6 mg of metaproterenol. * Before metaproterenol, sGaw(DI) at 5 s was significantly higher than sGaw or sGaw(DI) at any time period. + At 10 s, sGaw(DI) was significantly higher than sGaw or sGaw(DI) at 30 s. ‡ After metaproterenol, sGaw and sGaw(DI) were always significantly higher than corresponding before metaproterenol values; however, there were no significant differences between after metaproterenol values of sGaw and sGaw(DI) nor were there significant differences between sGaw(DI) values at 5, 10, 15, or 30 s.

Lung elastic recoil. As expected, Pst,L measurements demonstrated hysteresis of lung parenchymal recoil. Values of Pst,L after deep inspiration [Pst,L(DI)] were time dependent, increasing as a function of time after the TLC volume history (Fig. 4); the relationship between lung recoil and time was highly significant ($P < 0.0001$ by ANOVA). Before deep inspiration, Pst,L averaged 5.73 ± 2.76 cmH_2O (mean ± SD) and, at 5, 10, 15, and 30 s following the deep breath, Pst,L(DI) averaged 4.57 ± 2.48, 5.07 ± 2.75, 5.20 ± 2.19, and 5.57 ± 2.56 cmH_2O, respectively. Values of Pst,L(DI) were significantly reduced at 5, 10, and 15 s after deep inspiration ($P < 0.005$); Pst,L(DI) was less than the base-line values in

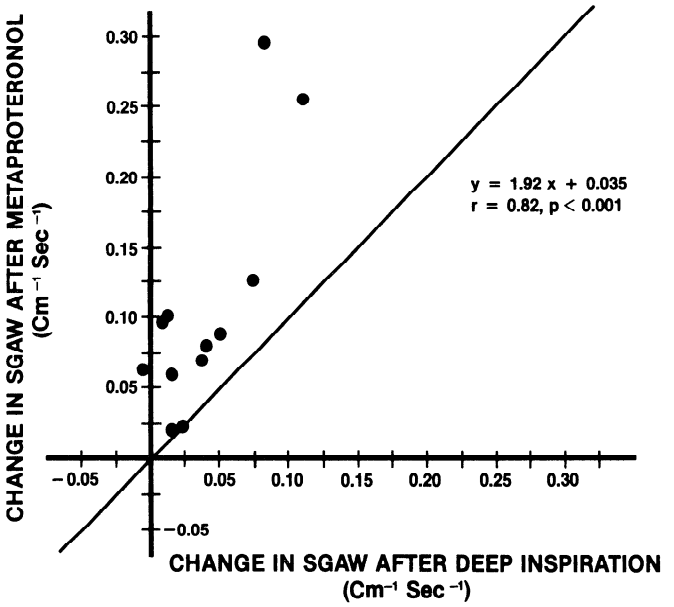

FIG. 3. Plot of changes in specific conductance (sGaw) after metaproterenol vs. changes in sGaw measured 5 s after deep inspiration. Changes correlated highly and significantly. Data points fall above line of identity, indicating that changes from metaproterenol exceeded changes caused by deep inspiration. Differences between response to metaproterenol and response to deep inspiration are influenced by time dependence of latter measurement (see text).

six of six subjects at all three time intervals. After inspiration to TLC, Pst,L(DI) was significantly lower at 5 s than at 10 or 15 s after the deep inspiration ($P < 0.01$). At 30 s after deep inspiration, Pst,L(DI) was slightly but not significantly reduced. At this time, Pst,L(DI) was still below the base-line (preinspiratory) value in four of six subjects. Following inhalation of metaproterenol, Pst,L diminished slightly, but not significantly, to 5.40 ± 2.85 cmH_2O.

Exponential analysis. Changes in Pst,L(DI) and sGaw(DI) were accurately described by exponential equations (Fig. 4); in each individual subject, actually measured values of Pst,L(DI) and sGaw(DI) correlated highly with values calculated from the exponential functions for corresponding time intervals [average r for Pst,L(DI) = 0.91 ± 0.08, $P < 0.01$; average r for sGaw(DI) = 0.83 ± 0.14, $P < 0.01$). For all subjects together, mean calculated and measured values of each variable correlated very highly ($r = 0.996$ for Pst,L; $r = 0.98$ for sGaw) (Fig. 4). For all subjects, the equations for the exponential functions were

$$\text{Pst,L(DI)}_t = 5.62 - 2.08\ e^{-0.13t} \quad (1)$$

and

$$\text{sGaw(DI)}_t = 0.240 + 0.074\ e^{-0.136t} \quad (2)$$

The time constant for changes in Pst,L(DI) averaged 11.3 ± 6.1 s ($n = 6$). This did not differ significantly from the time constant for sGaw(DI), which averaged 9.2 ± 4.9 s ($n = 12$). In the six subjects who had both measurements, the time constants were very similar, suggesting that, within the same normal individual, airway and parenchymal recoil hysteresis have approximately the same time course. Extrapolation of *Eqs. 1* and *2* indicated that Pst,L(DI)_0 and sGaw(DI)_0 (if measurable) would average 3.64 ± 2.32 cmH_2O and 0.313 ± 0.087 $cm^{-1} \cdot s^{-1}$ (64 and 132% of their respective preinspiratory values).

DISCUSSION

The results of this study show that airways hysteresis was present in 11 of 12 normal subjects 5 s after deep inspiration. This result is different from results in previous studies that failed to demonstrate hysteresis unless bronchoconstriction had been induced (4, 7, 14, 22); the results are also different from another recent study showing hysteresis in normal nonprovoked airways (8) in that a much higher percentage of the subjects in the present study exhibited airways hysteresis. In fact, the present observations suggest that increased sGaw after a deep breath is the expected finding in normal persons. The differences between this and some of the previous studies are most likely due to the fact that we measured

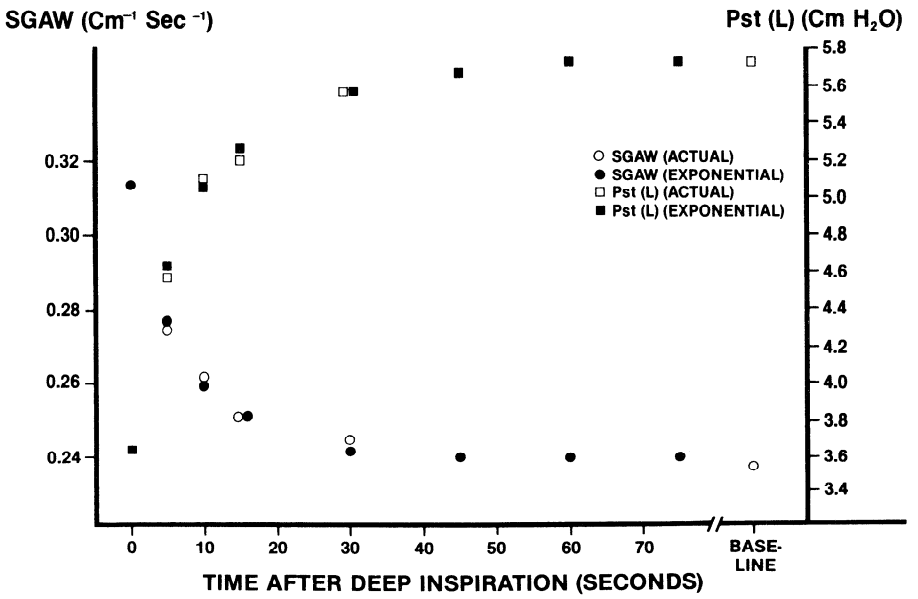

FIG. 4. Mean calculated values of specific conductance (sGaw) and lung elastic recoil (Pst,L) from exponential equations are displayed from 0 to 75 s after deep inspiration. For both relationships, asymptotes occur (at ~60 s for Pst,L and at 45 s for sGaw). Actually measured mean values of Pst,L and sGaw correlated highly with mean calculated values of same variable at 5, 10, 15, and 30 s ($r = 0.996$ and 0.98, respectively). Preinspiratory values of Pst,L and sGaw were very similar or identical to calculated asymptotic values. Extrapolation of exponential equations to *time 0* estimates maximum possible changes from airways and lung pressure-volume hysteresis.

sGaw(DI) earlier than others had done previously (8, 14, 22).

Prior to inhalation of metaproterenol, sGaw(DI) was higher than sGaw for 30 s, but the differences were only statistically significant for the first 10 s after inspiration to TLC. The average values of sGaw(DI) did decrease at each successive time interval, and there was a successive reduction at each time interval in the frequency with which sGaw(DI) exceeded base-line sGaw (see RESULTS). Thus the sGaw(DI) measurements were time dependent. In turn, this time dependence could be fit to an exponential function. In this regard, our results are consistent with the observations of Parham et al. (24) in individuals with rhinitis and airways hyperreactivity. On the other hand, the time constant of the exponential (9.2 s) was somewhat shorter than the time constant (11.7–11.8 s) observed in Parham et al.'s subjects (24). The reasons for this difference are probably due to *1*) differences in subject populations (normal vs. airway hyperreactivity) and 2) protocol differences (no bronchoprovocation vs. metacholine-induced bronchoconstriction). In addition, for purposes of the exponential analysis of sGaw, Parham et al. (24) required a 30% improvement in sGaw 7 s after lung inflation in their subjects; this requirement would tend to select a different population of subjects than would the sole requirement of our study (that subjects be normal individuals). Although time constants were not calculated for the normal individuals studied by Liu et al. (18), changes in total respiratory resistance after deep inspiration appear to follow a time course similar to that described in the present study.

In this study, the increment in sGaw after deep inspiration predicted the increment in sGaw following administration of metaproterenol ($r = 0.82$, $P < 0.001$; Fig. 3). In contrast to the before metaproterenol results, airways hysteresis (and therefore time dependence) was not present after inhalation of a β-agonist. By decreasing smooth muscle tone, metaproterenol apparently prevented any further bronchodilation from a deep breath.

Measurements of Pst,L indicated that our subjects also exhibited lung parenchymal recoil hysteresis prior to bronchodilator administration. Hysteresis of lung parenchymal recoil was not investigated after metaproterenol; however, the results of a previous study indicate that hysteresis of Pst,L, in contrast to airways hysteresis, is maintained after inhalation of metaproterenol (8). As was also true of airways hysteresis, the effects of deep inspiration on lung recoil diminished with time after a deep breath; Pst,L(DI) was significantly less than base line for 15 s, with the largest measured reduction in Pst,L(DI) occurring 5 s after inspiration to TLC. Analysis of the exponential function between Pst,L(DI) and time suggested that *1*) the return to base-line values of Pst,L had an average time constant of 11.3 s and *2*) Pst,L(DI) would reach its asymptotic value ~60 s after the TLC volume history.

There are relatively little previous data regarding the time dependence of Pst,L after deep inspiration. Green and Mead (11) indicated that Pst,L increased by 0.7 cmH_2O in the first 5 s following inspiration to TLC. Although it was not specified, Pst,L was presumably still lower at this time than were the preinspiratory Pst,L values. Lung recoil has also been shown to change with time during breath holding at lung volumes above and below FRC (19, 27); these changes in Pst,L during breath holding were attributed to stress adaptation. Marshall and Widdicombe (19) suggested that stress adaptation had a dual time course: a faster phase was completed during 6 s of breath holding, whereas, during tidal breathing at very high lung volumes, stress adaptation occurred for ~60 s. Sharp and associates (27) also studied the time course of stress adaptation during breath holding and found it to be complete in 7 s. Sharp et al. distinguished between stress adaptation, which they considered a change in Pst,L during breath holding, and pressure-volume hysteresis, which they considered the difference between Pst,L during inflation and deflation of the lung. In this study, the airway was occluded only briefly to measure Pst,L. Hence, stress adaptation during breath holding should not greatly influence our Pst,L results; this is especially true, since we measured Pst,L at FRC, a lung volume at which stress adaptation has minimal (27) or no effects (19).

There is a relationship between Pst,L and airway diameter (17, 26, 29). In an in vitro study, Hyatt and associates showed that airway diameter increased as did Pst,L. In normal humans (29), strapping the chest wall caused related increases in Pst,L and conductance. The relationship between Pst,L and airway diameter would influence the sGaw and sGaw(DI) results in this study. For example, following deep inspiration, time-dependent recovery of Pst,L(DI) would oppose the reduction in airway caliber due to time dependence of airways hysteresis (11). If lung volume changed after deep inspiration, distending pressure and airways size would also be affected. However, our studies indicated that FRC was very similar before and after deep inspiration in these normal individuals.

Quantitative estimates of the effects of changes in Pst,L(DI) on sGaw(DI) would be very difficult, since it would require extrapolation from different experimental circumstances. In the study of Hyatt et al. (17), changes in airway caliber due to increased Pst,L were small. However, relatively small changes in airway size would cause much larger changes in sGaw, since conductance varies directly with the fourth power of the radius of the airway. In this study, the largest measured increase in sGaw(DI) occurred simultaneously with the maximal decrease in Pst,L(DI). Thus, consistent with other studies (10), changes in airway size due to airways hysteresis appeared to predominate over changes due to lung parenchymal recoil hysteresis.

Airway caliber is the result of a balance between opposing radial stresses (26). Intrabronchial pressure and local lung parenchymal recoil (which varies similarly but not identically with overall Pst,L) act to increase airway size, whereas airway smooth muscle tone and wall elasticity are inwardly directed stresses which decrease airways size (25, 26). Other forces such as cartilage elastic recoil would also influence the size of some of the airways. In the current study, our sGaw results clearly indicate that the balance between the opposing forces was altered

in favor of increased airway size after a TLC volume history. With regard to the site of this effect, sGaw values are thought to primarily reflect the caliber of the large airways in normal persons (5, 16); however, changes in both large and peripheral airway size may well have occurred following deep inspiration. There is in vitro and in vivo evidence from other studies that both large and peripheral airways are influenced by lung volume history (3, 7, 10, 25, 30).

In an in vitro study, Sasaki and Hoppin (25) showed that hysteresis was present in airways constricted with carbachol; in contrast, hysteresis was markedly reduced in bronchodilator-treated airways. In this and previous in vivo studies (8), airways hysteresis was blocked by administration of bronchodilators. Accordingly, consistent with in vitro data (25), airway smooth muscle tone is probably the most important factor in the hysteresis. Resting airway tone is thought to be predominantly vagal in normal subjects (5, 14); however, in some studies (4, 6), airways hysteresis persisted (although it was attenuated) following muscarinic blockade. In normal individuals, treatment with cyclooxygenase modulators did not influence airways hysteresis (8).

Because hysteresis can be demonstrated by stretching isolated tracheal muscle (12, 25), it seems likely that hysteresis is, at least in part, an intrinsic property of airway smooth muscle. Sasaki and Hoppin (25) have suggested that cross bridges between the contractile elements of airways smooth muscle lengthen at a certain level of stretch, thereby resulting in increased airway size. Sasaki and Hoppin (25) also demonstrated that hysteresis of isolated airway smooth muscle is time dependent; thus, during volume cycling, the amount of tracheal hysteresis varied at different frequencies of cycling. Similarly, the amount of length-tension hysteresis of isolated, contracted tracheal muscle also depended on the frequency of cycling (25). Sasaki and Hoppin attributed the frequency dependence of tracheal muscle hysteresis to a slow rate of smooth muscle contraction relative to the rate of change in muscle length. Tracheal muscle has been shown to have a relatively slow maximum velocity of contraction compared with skeletal and cardiac muscle (28).

The above observations are pertinent to the findings in this study. During tidal breathing, forces stretching the airways are small; consequently, cross bridges might have formed between the contractile elements, thereby causing a certain level of sustained bronchomotor tone. Subsequently, inspiration to TLC stretched the airways, presumably lengthening the cross bridges and reducing bronchomotor tone. Although the forces stretching the airways decreased with the subsequent expiration to FRC, bronchomotor tone would remain reduced because of the slow velocity of contraction of airway smooth muscle. Given sufficient time, cross bridges would again form and the preinspiratory level of bronchomotor tone would eventually be reestablished. This time-dependent process would be reflected by a progressive return of sGaw toward base-line values as time after deep inspiration increased (Fig. 4).

In conclusion, the results of this study show that airways hysteresis is usually present in normal nonprovoked airways (if measured early enough) and that the hysteresis displays time-dependent behavior; neither characteristic is present after inhalation of 2.6 mg of metaproterenol. Lung parenchymal recoil hysteresis is also time dependent in normal subjects. Changes in specific conductance after deep inspiration probably represent a balance between two opposing forces (airways and parenchymal hysteresis) with the effects of airways hysteresis appearing to predominate.

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