Practical importance of a preceding full inhalation or exhalation upon the measurement of airway resistance

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Summary
1. Airway resistance was measured close to functional residual capacity before and after a full inhalation of total lung capacity, as well as before and after a full exhalation to residual volume.
2. The effects of these volume manoeuvres upon airway resistance (and associated lung volume) were determined in four resting normal male subjects and in six normal men during experimentally induced bronchoconstriction after breathing an air/histamine mist from a Wright's nebulizer.
3. In four men the duration of the effect of a full inhalation upon airway resistance after induced bronchoconstriction was assessed separately.
4. Neither a full inhalation nor a full exhalation altered airway resistance under normal conditions. However, a full inhalation reduced airway resistance in the presence of bronchoconstriction and this effect lasted for a period of 45 s. Even with bronchoconstriction, a full exhalation had no effect on airway resistance.
5. Account must therefore be taken of the potential reduction in airway resistance which may result from a full inhalation, particularly when indirect measurements of airway function which involve a full inhalation, such as forced spirometry, are used to assess airway obstruction.

Key words: airway resistance, bronchomotor tone, lung volume, volume-pressure hysteresis.

Introduction
The airways share in lung expansion and, like the lungs, exhibit a volume-pressure hysteresis (Martin & Proctor, 1958). It appears likely that the volume-pressure hysteresis of the airways may differ from that of the airspaces (Froeb & Mead, 1968). This difference has importance in that the preceding volume history of the lung becomes a determinant of airway size. For example, if the hysteresis were greater for the airways than for airspaces, then airway size measured at the same lung volume would be greater after a full inhalation than after a full exhalation. The converse would be true if airway hysteresis were less than airspace hysteresis.

Many indirect measurements of airway size, for example, forced spirometry, involve both a full inhalation and exhalation. Such measurements may themselves influence airway size (Bouhuys, Hunt, Kim & Zapletal, 1969; Green & Mead, 1974). It is therefore important to know both the direction and magnitude of the effect of preceding lung volume history on airway size. Furthermore, understanding of the underlying mechanism is needed as the volume-history effect may mask or promote the action of bronchoactive drugs or disease on airways.

The current information is incomplete and conflicting. In normal subjects a full inhalation may cause a small increase in dead space, suggesting an increase in airway size (Froeb & Mead, 1968). Similarly a full inhalation may diminish airway resistance after experimentally induced bronchoconstriction (Nadel & Tierney, 1961). However, an increase in airway resistance, implying a reduction in airway size, has been observed in normal subjects after a full inhalation (Lloyd, 1965) and in asthmatic patients (Gayrard, Orehek, Grimaud & Charpin, 1975). A full exhalation may both reduce
and increase lower pulmonary resistance (measured from alveolus to trachea) (Vincent, Knudson, Leith, Macklem & Mead, 1970) and in asthmatic patients a smaller increase in airway resistance is observed after a full exhalation than after a full inhalation (Gayrard et al., 1975).

To clarify the manner in which preceding volume history affects airway size in normal subjects, we have compared the change in airway resistance after a full inhalation and after a full exhalation, both under resting conditions and after experimentally induced bronchoconstriction, by inhalation of air/histamine mist from a nebulizer. Separately the duration of the effect of a full inhalation after experimentally induced bronchoconstriction was measured.

**Materials and methods**

Inspiratory airway resistance and associated lung volume were measured by the whole-body plethysmographic method (Dubois, Botelho & Comroe, 1956). Signals representing box pressure, mouth pressure and airflow were displayed in pairs on an X–Y recorder. Vectors from the recorder were drawn by a single observer, who was unaware of the experimental protocols. A total of ten healthy and non-atopic male subjects was studied.

**Lung-volume history under resting conditions**

Four subjects were studied on two occasions on separate afternoons. In one, the subjects performed three measurements of airway resistance and associated lung volume at 10 s intervals, then took as rapidly and completely as possible a full inhalation, which was followed immediately on returning to functional residual capacity by nine further measurements again at 10 s intervals. This protocol was repeated four times. The other study was identical except for a full exhalation being performed instead of a full inhalation.

**Lung-volume history after bronchoconstriction**

Bronchoconstriction was induced in six subjects. Each inhaled for 2 min, firstly air and diluent as controls and then increasing doses of histamine hydrochloride solution from a Wright's nebulizer. At intervals of 8 min the following doses of histamine were successively inhaled: 0.59, 1.28, 1.97, 2.67, 2.89, 2.99, 3.36, 3.48, 3.76, 4.11, 4.45, 4.80 log µmol until airway resistance increased by 30%.

Each subject was again studied on two occasions on separate afternoons. Airway resistance and associated lung volume were measured three times in rapid succession after each treatment from the nebulizer. Then a full inhalation was made as rapidly as possible, followed within a few seconds of returning to functional capacity by three further measurements of resistance and volume. Thus, after each control and each dose of histamine, six measurements of airway resistance and associated lung volume were obtained. On the other afternoon, the same measurements were performed but a full exhalation was made instead of a full inhalation.

**Duration of the effect of a full inhalation**

Four subjects initially performed three measurements of airway resistance and associated lung volume, then inhaled the dose of histamine which had earlier caused a significant increase in airway resistance. A further three measurements were then made followed by a full inhalation after which on returning to functional residual capacity groups of three measurements were made at 15 s intervals.

In all the studies airways resistance and associated lung-volume measurements were subjected to analysis of variance. Where mean values were compared, for example values before and after full inhalation, multiple comparisons were used to provide P values of 0.05 for each comparison avoiding falsely positive results (Kirk, 1968).

**Results**

**Full inhalation and exhalation on resting airway resistance**

All four subjects behaved similarly on each of their four 'runs', in that a full inhalation and full exhalation failed to significantly alter airway resistance (or the associated lung volume) when measured immediately after a full inhalation (or exhalation) or any of the subsequent measurements made at 10 s intervals \( P \leq 0.05 \).

**Full inhalation and exhalation after histamine**

A full inhalation reduced airway resistance consistently only in the presence of histamine-induced bronchoconstriction (Fig. 1). In subjects nos. 1 and 2, a full inhalation reduced and in subject no. 5 increased airway resistance in one of the two control measurements but these observations were
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FIG. 1. Airway resistance after control and each ‘dose’ of inhaled histamine (log μmol) for each of the six subjects. Mean values before (○) and after (●) a full inhalation are plotted. The arrows denote differences between mean values which were significantly different from zero (P < 0.05).

not confirmed in the second control measurement. The associated lung volume at which airway resistance was measured remained unchanged in all six subjects even after histamine or a full inhalation (P < 0.05).

On the other hand, a full exhalation failed to alter airway resistance even in the presence of bronchoconstriction (Fig. 2). Again the associated lung volume, at which airway resistance was measured, did not change (P < 0.05).

In summary, at the highest dose of histamine (range 2.89–3.36 log μmol) the average airway resistance for the six subjects as a percentage of control was 584.3% before and 236.3% after a full inhalation (average SE of difference 34.1%) and 395.1% before and 387.8% after a full exhalation (average SE of difference 43.0%).

**Duration of effect of a full inhalation after histamine**

Histamine-induced increase in airway resistance was diminished, by a full inhalation, for a period of 45 s (Fig. 3). All subjects behaved similarly and associated lung volume was not altered by either histamine or full inhalation.

**Discussion**

Airway calibre may be influenced by both bronchial smooth muscle tone and lung elastic recoil pressure (Vincent et al., 1970). Any difference between the volume-pressure hysteresis of the airways and airspaces is likely to be a result of bronchial smooth muscle tone. When smooth muscle tone is minimized by pretreatment of an
excised lung with EDTA then the difference between airway diameters on inflation, in contrast to deflation, is greatly diminished (Clay, Hughes & Jones, 1977) suggesting that in the complete absence of bronchomotor tone the airways expand (and deflate) in a comparable manner to airspaces. Failure to observe any change in airway resistance after a full inhalation or exhalation may imply that under resting conditions bronchial smooth muscle tone is absent (Nadal & Tierney, 1961). A more likely explanation for these observations, however, would be that the changes in airway size are small (Froeb & Mead, 1968; Vincent et al., 1970) and of short duration (Green & Mead, 1974), so escaping detection by the measurement of airway resistance, which is subject to random variation (Lord & Brooks, 1977) and takes a finite time to accomplish.

In contrast, after histamine-induced airway constriction a full inhalation did temporarily reduce airway resistance. This was presumably a result of a reduction in smooth muscle tone. But how does a full inhalation alter bronchomotor tone? It could be achieved simply by mechanical stretching of the airways analogous to the temporary reduction in smooth muscle tension observed in vitro after stretching preparations of guinea-pig taenia coli (Bulbring, 1955) and rabbit trachea (Hughes, May & Widdicombe, 1959). In both preparations application of histamine enhanced this effect presumably by increasing the smooth muscle tension before stretching. A full inhalation in vivo may additionally initiate reflex inhibition of airway tone, mediated by means of the vagus nerve (Bouhuys & Johnson, 1967).

Why does a full exhalation fail to alter airway resistance even in the presence of airways obstruction? Is it because a full exhalation leaves airway tone unchanged? After an exhalation to residual volume, bronchial smooth muscle tone may increase (Bouhuys & Johnson, 1967), but Wellman, Brown, Ingram, Mead & McFadden (1976) argued that changes in airway size due to alterations in airway tone are offset by the increase in lung elastic recoil pressure which follows a full exhalation. This complex interaction between bronchial smooth muscle tone and lung elastic recoil pressure in the determination of airway size could account for the failure to observe any change in airway resistance after a full exhalation.

Asthmatic individuals differ from normal subjects in their response to both a full inhalation and exhalation. Unlike the subjects in this study, those with asthma experience an increase in airway resistance after both an inhalation and exhalation (Gayrard et al., 1975; Fish, Peterman & Cugell, 1977). It is thought that the changes in airway size produced during a full inhalation or exhalation, by stimulating the hypersensitive bronchial irritant receptors of the asthmatic subject (Simonsson, Jacobs & Nadel, 1967), provoke reflex bronchoconstriction mediated by vagus nerve (Gayrard et al., 1975). These added reflex changes in airway size of asthmatic individuals presumably outweigh the normal changes which follow a full inhalation or exhalation.

In practical terms, under resting conditions in a non-asthmatic individual, a previous volume history of going to either total lung capacity or residual volume had little effect on airway resistance measured close to functional residual capacity. A full inhalation, after histamine-induced airways obstruction, resulted in a reduction of airway resistance ranging from 60 to 500%, an effect lasting for up to 45 s. No such change occurred after a full exhalation. Caution must be observed when assessing airways obstruction with measurements of airway function which involve a preceding full inhalation, as they may well in themselves reduce airway tone for a period longer than it takes to complete the measurement (Green & Mead, 1974). Small degrees of airways obstruction may therefore be obscured.

References


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