Site of Airway Obstruction in Asthma as Determined by Measuring Maximal Expiratory Flow
Breathing Air and a Helium-Oxygen Mixture

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Abstract Because maximum expiratory flow-volume rates in normal subjects are dependent on gas density, the resistance between alveoli and the point at which dynamic compression begins (R*) is mostly due to convective acceleration and turbulence. We measured maximum expiratory flow-volume (MEFV) curves in asthmatics and chronic bronchitics breathing air and He-O₂. In the latter and in some asthmatics, MEFV curves did not change, indicating that R* is mostly due to laminar flow. Therefore, the point at which dynamic compression begins must be further upstream than in normal subjects and the site of obstruction must be in small airways. In other asthmatics, flow increased normally indicating obstruction in larger airways. The response to He-O₂ did not correlate with initial values of pulmonary resistance, the initial MEFV curves or the response to bronchodilators. We conclude that the site of airway obstruction varies among asthmatics and that the site of obstruction is not detectable by measurement of the usual parameters of lung mechanics.

Introduction

The site of airway obstruction in most patients with chronic obstructive lung disease is in airways less than 2-3 mm in diameter (1). Less is known about the site of airway obstruction in asthmatics. Bronchography indicates that central airways may be constricted (2-4) during an acute attack, while in remission there is evidence that considerable obstruction may affect peripheral airways (5-7).

Examination of the effects of altered gas density on the maximum expiratory flow-volume (MEFV) curve may be a simple way of defining the site of airway obstruction in asthmatics. According to Mead maximum expiratory flow rate at a particular lung volume is determined by the elastic recoil pressure of the lung at that volume and the resistance of the airways between the alveoli and the points where the lateral intraluminal pressure equals pleural pressure (equal pressure points, EPP). This resistance is defined as the upstream resistance (R*) (8). If EPP are in large airways most of R* will be due to convective acceleration and turbulence. Because pressure losses due to both of these are dependent on gas density, changes in gas density will alter R* and thus maximum expiratory flow. This is the case in normal subjects: EPP are in large airways at lung volumes above 40% vital capacity (VC) (9) and maximum expiratory flow rates over these lung volumes are density dependent (10-12). In the presence of airway obstruction in small airways, EPP will be further upstream (toward the alveoli) than in normal subjects and maximum expiratory flow will be less density dependent than normal to the extent that the resistance to laminar flow (which is independent of gas density) makes up a greater portion of the total resistance upstream from EPP. Obstruction in larger airways might have a lesser influence on the normal response to a change in gas density.

Previous studies in patients with airway obstruction reveal a marked variation in the changes in dynamic lung function that occur when gas density is altered (13-16). The variation is not obviously related to the residual capacity; MEFV, maximum expiratory flow-volume; Pₜₜ, pressure drop due to convective acceleration; Pₜₑ (1), elastic recoil pressure of the lung; R*, resistance due to convective acceleration; Rₑ, frictional resistance to airflow; Rₚ, pulmonary resistance; Rᵤ, upstream resistance; RV, residual volume; TLC, total lung capacity; VC, vital capacity; Vₓₓₓ, maximum expiratory flow at 50% vital capacity.

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Abbreviations used in this paper: Aₑₑₑ, cross-sectional area at EPP; EPP, equal pressure points; FRC, functional residual capacity; MEFV, maximum expiratory flow-volume; Pₜₜ, pressure drop due to convective acceleration; Pₜₑ (1), elastic recoil pressure of the lung; R*, resistance due to convective acceleration; Rₑ, frictional resistance to airflow; Rₚ, pulmonary resistance; Rᵤ, upstream resistance; RV, residual volume; TLC, total lung capacity; VC, vital capacity; Vₓₓₓ, maximum expiratory flow at 50% vital capacity.
TABLE I

Physical Characteristics and Lung Function of Patients Studied

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Irreversible airway obstruction
* 63.4 166 67 136 180 110 5.80

Normal
* 29.7 175 102 101 92 104 1.9

VC, vital capacity; FRC, functional residual capacity; TLC, total lung capacity; RV, residual volume; RL, pulmonary resistance.

* Mean values.

† Predicted values from Bates, Macklem, and Christie (25).

The severity of the airway obstruction or to the type of obstructive lung disease. Barnett (17) suggested that the site of airway obstruction may be an important determinant of the effects of gas density on dynamic lung function. The laws of aerodynamics as they apply to the airways support this suggestion and he showed that with...
tracheal obstruction, pulmonary resistance was density dependent but when obstruction was in peripheral airways the resistance was not density dependent (17).

Stimulated by Barnett's observations, we have studied the effects of 20% oxygen in helium on the MEFV curves and pulmonary resistance (R_l) in asthmatics. These effects were compared with those obtained in normal subjects and in patients with irreversible airways obstruction. The mixture's density is only 36% that of air but it is 12% more viscous.

METHODS

We studied 25 asthmatics with significant reversible airway obstruction who had been repeatedly studied in the routine laboratory. Most were symptomatic when we studied them and had a significant reduction in pulmonary resistance immediately following a bronchodilator aerosol (Table I). We also studied seven patients with irreversible airway obstruction. They had chronic bronchitis and dyspnea and showed little change in the degree of airway obstruction over several years. The control group were normal, nonsmoking subjects and included medical and laboratory staff.

While the subjects were breathing air we measured the subdivisions of lung volume, the static deflation pressure volume curve of the lung, pulmonary resistance at functional residual capacity (fRC), and the maximal expiratory flow-volume curves. Change in lung volume was measured by a Krogh spirometer attached to the body plethysmograph. Absolute lung volume was obtained by the gas compression technique based on Boyle's law (18). The static deflation pressure volume curve of the lung was obtained by plotting transpulmonary pressure (as assessed by the difference between mouth and esophageal pressure) during 1–2-sec periods of zero-airflow, against lung volume on deflation to residual volume (RV) after a full inspiration to total lung capacity (TLC). Esophageal pressure was measured by an esophageal balloon catheter (balloon length 10 cm, circumference 3.5 cm, volume 0.5 ml of air, catheter PE 200 tubing 60 cm long) coupled to a Sanborn 267B differential pressure transducer (Sanborn Div., Hewlett-Packard Co., Waltham, Mass.), the other side of which was connected via a catheter to the mouthpiece. Pulmonary resistance during inspiration (R_l) was taken as the ratio of the component of transpulmonary pressure in phase with inspiratory flow to flow during tidal breathing. Flow was measured by a Fleisch pneumotachograph coupled to a Sanborn 270 differential pressure transducer (Sanborn Div., Hewlett-Packard Co., Waltham, Mass.), the other side of which was connected via a catheter to the mouthpiece. Pulmonary resistance during expiration (R_e) was measured by attaching a transducer to the expiratory pressure line and passing the signal through a Tissot pressure transducer and a Sanborn 267B differential pressure transducer (Sanborn Div., Hewlett-Packard Co., Waltham, Mass.). Pressure transductions were calibrated with water manometers. The pneumotachograph was calibrated for air and for the He-O_2 by passing the gases through the pneumotachograph which was coupled by 2 inch diameter smooth bore tubing to a 120 liter Tissot spirometer. The pneumotachograph resistance was linear for both gases up to flow rates of 6 liters/sec.

RESULTS

Results obtained in the lung function tests for the three groups of subjects are given in Table I. The asthmatics were further subdivided into responders and nonresponders according to their change in maximum expiratory flow when they breathed He-O_2 (see below). Mean values only are reported for the normal subjects and those with irreversible airway obstruction. Among asthmatics R_l was increased in all but one subject (Lew) either at the initial study or at a subsequent study. R_e was markedly increased in several subjects.

MEFV curves. There was a substantial increase in maximum expiratory flow rates in all normal subjects breathing He-O_2 compared with the curves obtained when they were breathing air. The increase was in good agreement with the data of Wood and Bryan (10). Only one patient with irreversible airway obstruction increased his maximum expiratory flow rates. The others demonstrated no change. The asthmatic subjects fell into two groups. In twelve there was an increase in maximum expiratory flow rates comparable to the increase observed in normal subjects. In 13 there was little or no increase in maximum expiratory flow, the response to He-O_2 being similar to that observed in irreversible airway obstruction. Representative MEFV curves from each group are shown in Fig. 1. Those asthmatics in whom maximum expiratory flow at 50% vital capacity (Vmax50) increased less than 20% in He-O_2 were classified as nonresponders and those in whom Vmax50 increased by more than 20% were classified as responders. In normal subjects Vmax50 increased by a mean value of 48%±11.7 (SEM); in patients with irreversible airway obstruction Vmax50 increased by a mean value of 13.0%±32.6 (SEM). The large standard error in this group is due to one subject who increased Vmax50 by 85%. The others ranged between +12 and -13%. In responders Vmax50 increased by 53.5%±19.7 (SEM), and in nonresponders Vmax50 increased by 1.5%±5.25 (SEM). Among asthmatics there was no cor-
relation between the change in $V_{\text{max50}}$ and the severity of the obstruction as assessed either by the initial values for $V_{\text{max50}}$ or for pulmonary resistance, $R_L$ (Figs. 2 and 3).

**Pulmonary resistance.** In normal subjects breathing He-O$_2$, pulmonary resistance fell to $77\% \pm 17.9$ (SEM) of the value breathing air; in patients with irreversible airway obstruction these measurements were made in only five of the seven subjects. In these subjects when breathing He-O$_2$, the resistance was $100\%$ of the value breathing air; in responders, pulmonary resistance fell to $73\% \pm 25.5$ (SEM) of the air value; in nonresponders it was $90\% \pm 22$ (SEM).

Although the change in pulmonary resistance with gas density was similar to the change in $V_{\text{max50}}$ when the groups were compared, there were several striking individual exceptions to this within each group accounting for the larger standard errors. There were three normal subjects in whom the $R_L$ when breathing He-O$_2$ was greater than $90\%$ of $R_L$ when breathing air but in whom $V_{\text{max50}}$ increased by $35$–$61\%$. By contrast, among the patients with irreversible airway obstruction there was one in whom $R_L$ when breathing He-O$_2$ was only $68\%$ of the $R_L$ when breathing air, whereas $V_{\text{max50}}$ increased only $7\%$ in response to He-O$_2$. These two patterns were reflected among the responders and nonresponders. In the former group, there were three subjects in whom there was either no change or a slight increase in $R_L$ when breathing He-O$_2$ but in whom $V_{\text{max50}}$ increased $34$–$80\%$. In the latter group, there were three subjects in whom $R_L$ on He-O$_2$ was $42$, $67$, and $73\%$ of the value on breathing air but in whom there was no change in $V_{\text{max50}}$. Among asthmatics there was no correlation between the severity of the obstruction as assessed either by the initial values of $V_{\text{max50}}$ or $R_L$ and the change in $R_L$ between air and He-O$_2$ (Figs. 4 and 5).

**Upstream resistance.** By plotting maximum expiratory flow against the static deflation elastic recoil pressure at equal lung volumes, the pressure-flow curve for the airways upstream from EPP is obtained (8). From these curves the relationship between lung volume and $R_{*s}$ may be obtained. This is plotted in Fig. 6 for the responders and the nonresponders. It appears that the shape of the $R_{*s}$ vs. VC curve is different between responders and nonresponders. In nine of the 12 responders, $R_{*s}$ decreased as lung volume decreased over at least part of the vital capacity range. The mean value for $R_{*s}$ was essen-

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**FIGURE 1** Representative maximum expiratory flow-volume curves for the four groups of subjects. ——— MEFV curves on air; —— MEFV curves on He-O$_2$; ····· predicted MEFV curves on He-O$_2$ from the data of Wood and Bryan assuming that $V_{\text{max}} \propto (\text{density})^{-0.5}$ (10). Values for pulmonary resistance ($R_L$) in cm H$_2$O/liters per sec breathing air and breathing He-O$_2$ are given for each case.

**FIGURE 2** Per cent increase in maximum flow at 50% VC ($V_{\text{max50}}$) induced by breathing He-O$_2$ (ordinate) plotted against the initial $V_{\text{max50}}$ breathing air (abscissa) in asthmatics.

**FIGURE 3** Per cent increase in $V_{\text{max50}}$ induced by breathing He-O$_2$ (ordinate) plotted against the initial pulmonary resistance ($R_L$) breathing air (abscissa) in asthmatics.
nally, in both groups the ratio of the maximum rate of expiratory flow to the initial value of the resistance was not altered. In only four of 11 nonresponders, $R_L$ decreased as volume decreased. In contrast to the responders, the mean $R_L$ increased by 5.5 cm H$_2$O/liters per sec/per cent VC between the highest lung volume at which $R_L$ was recorded and 50% VC in each subject.

Three nonresponders and five responders were studied on more than one occasion. Although the severity of their asthma was substantially different during the different studies, the pattern of response was always the same in that the responders remained responders and nonresponders remained nonresponders (Fig. 7). As the asthmatics as a group were selected on the basis of demonstrable improvement in their obstruction resulting from bronchodilator therapy, the responders and nonresponders could not be distinguished on this basis. Similarly, there did not appear to be any difference in the degree of wheezing between the two groups although this was specifically looked for.

DISCUSSION

It is apparent that the responders behaved in a qualitatively similar way to normal subjects when gas density was altered. Maximum expiratory flow rates increased and pulmonary resistance decreased. Furthermore, in both normals and responders there were the same paradoxical responses in which increased maximal expiratory flow rates were observed with little or no change in $R_L$. Finally, in both groups $R_L$ tends to increase at lung volumes above 50% VC (8).

The nonresponders behaved similarly to patients with irreversible airway obstruction when gas density was altered. Neither maximum expiratory flow nor $R_L$ was much changed. In both nonresponders and patients with irreversible obstruction paradoxical responses occurred in which there was no increase in maximum expiratory flow, but there was a substantial reduction in $R_L$. $R_L$ tended to decrease at lung volumes above 50% VC in the nonresponders.

The similarity between responders and normal subjects on one hand and between nonresponders and patients with irreversible airway obstruction on the other is circumstantial evidence that the mechanisms limiting maximum expiratory flow were also similar between normal subjects and responders and between patients with irreversible airways obstruction and nonresponders.

Maximum expiratory flow at any lung volume is equal to the ratio of lung elastic recoil at that volume, to the resistance of airways upstream from equal pressure points (8). This is expressed in the following relationship:

$$V_{\text{max}} = \frac{P_{\text{el}}(l)}{R_{us}},$$

where $P_{\text{el}}(l)$ is the elastic recoil at lung volume $l$ and $R_{us}$ is the resistance upstream from the point of equal pressure.
where $P^* (1)$ is the elastic recoil pressure of the lung at the particular lung volume. Because change in gas density does not influence the static pressure-volume relationships of the lung, any change in $V_{\text{max}}^*$ must be due to a change in $R_{\text{ca}}$. When $V_{\text{max}}^*$ did not change with gas density, $R_{\text{ca}}$ must have been independent of density.

$R_{\text{ca}}$ is the sum of two components, the frictional resistance to airflow ($R_{\text{fr}}$) and the resistance due to convective acceleration ($R_{\text{ac}}$) between alveoli and EPP. $R_{\text{ca}}$ is given by the following relationship:

$$ R_{\text{ca}} = \frac{P_{\text{ca}}}{\dot{V}_{\text{max}}} = \frac{K \cdot \rho \cdot \dot{V}_{\text{max}}}{2g \cdot \Lambda_{\text{app}}}, \quad (1) $$

where $P_{\text{ca}}$ is the pressure drop due to convective acceleration, $K$ is a constant relating to the velocity profile, $\rho$ is gas density, $g$ is the acceleration due to gravity, and $\Lambda_{\text{app}}$ is the cross-sectional area at EPP.

Rearranging,

$$ \dot{V}_{\text{max}} = \left( \frac{2g \cdot P_{\text{ca}}}{K \cdot \rho} \right)^{0.5} \cdot \Lambda_{\text{app}} \quad (2) $$

Thus if all other variables remain constant and $R_{\text{ac}} \gg R_{\text{fr}}$, $V_{\text{max}}^*$ is proportional to $\rho^{0.5}$. $R_{\text{fr}}$ is the sum of a laminar and turbulent component. If the turbulent component were much greater than the laminar component and $R_{\text{fr}} \gg R_{\text{ac}}$, then $V_{\text{max}}^*$ would be proportional to $\rho^{-0.5}$. If both the turbulent component of $R_{\text{fr}}$ and $R_{\text{ca}}$ contributed substantially to $R_{\text{ca}}$, $V_{\text{max}}^*$ would be proportional to gas density to a power ranging between $-0.5$ and $-0.43$. This would result in an increase of $56$--$70\%$ in $V_{\text{max}}^*$ on switching from air to He-O$_2$. The responders increased $V_{\text{max}}^*$ by $53.5\%$, indicating that the laminar component of $R_{\text{ca}}$ was relatively small and that most of the resistance upstream from EPP was either due to convective acceleration or turbulence or both.

The lack of response to He-O$_2$ among the nonresponders indicates that $R_{\text{ca}}$ is not density dependent in this group. Thus, neither turbulence nor convective acceleration, nor even the density-dependent formation of parabolic velocity profile (20) contributes substantially to $R_{\text{ca}}$. Flow upstream from EPP must have been almost entirely fully developed laminar flow, in which for a given pressure drop, flow is inversely proportional to viscosity and independent of density. If the total $R_{\text{ca}}$ was composed of fully developed laminar flow we would have expected to see a $12\%$ fall in maximum expiratory flow rates because of the higher viscosity of the He-O$_2$ mixture. This was not observed. Schilder, Roberts, and Fry (11) observed a decrease in flow at very low lung volumes in normal subjects breathing He-O$_2$ as compared with air. This may have been present in our normal subjects as well, but because we were particularly interested in the effects at higher lung volumes we did not look for it and thus lacked sensitivity to detect small changes at low flow rates. On the other hand reference to Figs. 4 and 5 reveals that four nonresponders and one responder increased $R_{\text{ca}}$ by $10$--$20\%$ breathing He-O$_2$, which is consistent with pulmonary resistance being directly proportional to viscosity in these subjects.

The essential difference between the responders and the nonresponders then is a difference in the components of $R_{\text{ca}}$. $R_{\text{ca}}$ in responders is similar to that in normal subjects and at high lung volumes is principally made up of convective and turbulent components. In nonresponders $R_{\text{ca}}$ is similar to that in subjects with irreversible airway obstruction and is principally due to fully developed laminar flow.

Do known differences in airway dynamics between normal subjects and patients with irreversible airway obstruction shed light on the cause of the differences between responders and nonresponders? Because EPP are at the level of segmental or lobar bronchi, in normal lungs where the cross-sectional area at equal pressure points approximates to the trachea, $R_{\text{ca}}$ is the major component of $R_{\text{ca}}$ at high lung volumes (9, 21). The density-dependent component of $R_{\text{ca}}$ is presumably larger than it would be if EPP were further upstream, because $R_{\text{ca}}$ contains airways with higher Reynolds's numbers in which fully developed laminar flow would be the exception rather than the rule. This accounts for the density dependence of maximum expiratory flow in normal subjects (10, 12).

In patients with chronic bronchitis and emphysema, there is obstruction in peripheral airways smaller than 2 mm diameter (1). This results in an upstream move-
ment of EPP into airways where the total cross-sectional area at equal pressure points is presumably substantially increased. Because \( R_s \) is inversely proportional to the square of this cross-sectional area and because \( V_{max} \) is greatly reduced, one would predict that \( R_s \) would become small (see equation 1). In order for the density-dependent component of \( R_s \) to become small as well it would seem likely that the upstream motion of EPP would have to be quite considerable indeed, but one cannot state exactly how far. Thus, in order to account for density independence of maximum flow it is necessary to postulate peripheral airway obstruction with EPP situated where the total cross-sectional area at EPP is large and the flow upstream is laminar and fully developed. The upstream displacement of EPP is consistent with what is known about airway dynamics in irreversible airway obstruction (22).

We suggest that the nonresponders were similar to the patients with irreversible airway obstruction and that EPP were in airways where the total cross-sectional area was large and the flow upstream laminar. We suggest that this was due to obstruction in small airways.

The responders had a similar degree of airway obstruction as assessed by \( R_s \) and \( V_{max} \). In spite of this, we suggest that the site of obstruction was different and was located in larger airways so that EPP did not move so far upstream, with the result that the cross-section at EPP was sufficiently small so that \( R_s \) was a large component of \( R_s \) or the flow upstream was turbulent or both. Our data do not permit us to determine the exact location of EPP, but if \( R_s \) were substantial there may well have been bronchoconstriction at the site of EPP. We return to this point later.

If these considerations are correct, the site of obstruction in asthma is different in different individuals, being located in small airways in some and in larger airways in others. Because responders do not appear to become nonresponders and vice versa, it appears likely that the site remains fixed in any given asthmatic although a more prolonged longitudinal study would be necessary to make this statement unequivocally.

Our conclusions are consistent with the experimental evidence published by Barnett (17). He found that the resistance produced by obstruction in a large airway (the trachea) was decreased when He-O_2 was breathed compared with air, whereas when the obstruction was more peripheral, induced by histamine, the resistance was essentially independent of gas density. Vagal stimulation produced an intermediate response.

How can our conclusions and Barnett’s observations be reconciled with the paradoxical responses that we observed? Among the responders and the normal subjects there were individuals in whom \( R_s \) did not change, but in whom there were substantial increases in maximal expiratory flow. During the measurements of \( R_s \) the subjects were breathing quietly. Resistance due to convective acceleration is not a component of \( R_s \). Thus any response to He-O_2 must have been due to density dependence of the frictional resistance of the airways. If the frictional resistance was principally due to laminar flow, very little density dependence would be apparent. During forced expirations, however, \( R_s \) does contribute to \( R_s \) and is directly proportional to density (equation 1). The paradoxical finding that \( V_{max} \) increased while \( R_s \) remained unchanged may be explained if \( R_s \) was a major component of \( R_s \) but in the absence of dynamic compression during the measurement of \( R_s \) (to which \( R_s \) does not contribute) flow was essentially laminar through those airways with the highest resistance. If this were the case it seems likely that the cross-sectional area at the site of EPP, where the transmural pressure across these airways is presumably close to zero, would have to be substantially less than it is during quiet breathing when these airways are distended. This might well be consistent with an increase in bronchomotor tone at this site.

The other paradoxical response (a decrease in \( R_s \) without substantial change in \( V_{max} \)) also requires explanation. An increase in the tone of large airways makes them less compressible but increases their resistance to airflow (23). During quiet breathing at a given flow rate, this would increase the Reynolds’s numbers, and the degree of turbulence within them, which would render the frictional resistance more density dependent. Because they are less compressible, however, EPP would move further upstream so that \( R_s \) would not contain the frictional resistance of these airways. Thus, the paradoxical change in \( R_s \) without much change in \( V_{max} \) would be explained if EPP were located upstream from narrowed airways whose frictional resistance was density dependent and contributed substantially to \( R_s \) but not at all to \( R_{fr} \).

A curious finding among most responders, similar to that in normal subjects was, that \( R_s \) increased as lung volume increased above 50% VC (Fig. 6). In normal subjects this has been attributed to changes in \( R_{fr} \) with lung volume. As volume decreases, EPP move upstream so that the cross-sectional area at EPP increases. Furthermore, as volume decreases \( V_{max} \) decreases. Both of these will result in a decrease in \( R_s \) as volume decreases (equation 1). If a similar mechanism were operating in the responders to account for the change in \( R_s \) with volume, the contribution of \( R_s \) to \( R_s \) would have to be large. Because \( V_{max} \) was markedly reduced, the cross-section at EPP would also have to be reduced in order for \( R_s \) to be large. Mead, Turner, Macklem, and Little plotted \( V_{max} \) against \( P_{fr}(1) \) at the same lung volumes to obtain pressure-flow curve of the airways upstream from EPP. They also plotted isopleths of \( R_s \) using different
assumed values for the cross-section at EPP. They found that the curve relating maximal flow to static recoil became asymptotic to the one or other of the Rₘₚ isopleths. They suggested that if Rₘₚ >> Rₑ, the isopleth to which the curve became asymptotic would give the cross-sectional area at EPP in each subject. Cross-sectional areas so determined correlated well with the cross-sectional area of the trachea in their subjects (8).

Similar curves in the responders are shown in Fig. 8. If the decrease in Rₑ with an increase in volume is due to the same mechanism as in normals, the cross-sectional area at EPP would in most cases fall between 1.0 and 0.25 cm². In normal subjects the cross-section at EPP ranged between 1.1 and 2.7 cm² (8). Thus in responders the cross-section at EPP would have to be substantially smaller than the diameter of the trachea, but this is feasible given an increase in bronchomotor tone.

The alternative explanation for the change in Rₑ with volume is a fall in Rₑ as volume decreases. This could in part be due to the decrease in flow if Rₑ was turbulent but it does not seem likely that this could account for all of the change. It has recently been shown that airway resistance increases in humans and dogs at high lung volumes, although the mechanism for this is obscure (24). If this were present in asthma to a greater degree than normal then this could account for the change in Rₑ. If so one might expect to see similar curves in nonresponders, but this was not the case (Fig. 6). For this reason we favor the explanation that the cross-sectional area at EPP in asthmatics who respond to He-₉₆ is substantially smaller than the trachea, that this reduction is due to bronchospasm and that it results in a resistance to convective acceleration that is a major component of the upstream resistance even though flow rates are markedly reduced.

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REFERENCES


