Significance of the relationship between lung recoil and maximum expiratory flow[1]

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MEAD, JERE, JAMES M. TURNER, PETER T. MACKLEM, AND JOHN B. LITTLE. *Significance of the relationship between lung recoil and maximum expiratory flow.* J. Appl. Physiol. 22(1): 95–108. 1967.—During forced expirations lateral pressures at points within airways equal pleural pressure, and the pressure drop from alveoli to these points approximates the static recoil pressure of the lungs. We regard maximum expiratory flow as set by this pressure and the flow-resistance of the airways upstream from these points. The resistance of these segments has a frictional component which increases as lung volume decreases and an accelerative component which decreases as lung volume decreases. The two components show systematic changes with age in normal subjects which are interpreted as reflecting differential loss of parenchymal and airway recoil.

mechanics of breathing; dynamics of airways; airway resistance; airway conductance; aging in lungs; flow-volume curves

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IN THIS PAPER we develop a theoretical relationship between the static recoil of lungs and the maximum rate at which gas can be expelled from them. This relationship (the maximum flow-static recoil curve, MFSR) defines the resistance to gas flow offered by a particular segment of the bronchial tree, namely that running between the alveoli and points downstream where pressures at the inside wall of the airways equal pleural pressure. Changes in this resistance with changes in lung volume reflect the relative contributions of two components of the resistance: one, due to frictional losses, is small at high lung volumes and increases progressively as lung volume decreases; the other, due to convective acceleration of gas, mainly reflects the cross section of large airways and has its greatest effect at high lung volumes. We show that the relative magnitude of these components changes systematically with age in human subjects and we discuss the structural basis for these changes. We also relate our analysis to mechanisms limiting flow during forced expirations. We show that the configuration of maximum expiratory flow-volume curves, which we find to have greater detail than previously reported, can be accounted for by our theory. We begin by developing the central concept upon which our analysis is based.

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"EQUAL PRESSURE POINT" CONCEPT

Alveolar pressure, Palv, is the driving pressure which causes gas to flow through the airways. To a close approximation it exceeds the pleural pressure, Ppl, by an amount equal to the recoil pressure of the lungs, Pst(l). This may be expressed: Palv = Ppl + Pst(l). (Unless otherwise stated, all pressures are expressed relative to atmospheric.) Thus, the driving pressure may be thought of as being made up of two parts: one, Pst(l), is always positive in sign; the other, Ppl, is negative in sign for all inspirations and most expirations. During rapid expirations, however, it too is positive in sign. In this latter circumstance Palv is the sum of two components, Ppl and Pst(l), both of which are positive. Because Palv is the total pressure drop between the alveoli and atmosphere it follows that the pressure drop from the alveoli to some point within the airway must equal Pst(l). At this point the pressure at the inner wall must equal Ppl. The crux of our analysis is that we consider Pst(l) to be the driving pressure from the alveoli to this point, and Ppl to be the driving pressure from this point to atmosphere. We shall refer to the points where the pressure at the inner wall of the airways is equal to Ppl as equal pressure points (EPP).

What at first glance must seem an arbitrary division of a continuously changing pressure into two compartments becomes physically meaningful when we add the influence of pressure outside the airways. The pressure outside extrathoracic airways probably approximates atmospheric. The pressure outside intrathoracic but extrapulmonary airways—the trachea and the mainstem bronchi—is pleural pressure. The pressure outside pulmonary bronchi, which has generally been assumed to equal Ppl, has not been directly measured. Indirect measurements via neighboring blood vessels suggest that it may be systematically negative with respect to Ppl (12, 27).

Transmural pressure, Ptm, expresses pressure at the inside wall of a structure relative to that outside. Since, by definition, all pressures at inside walls upstream from EPP exceed Ppl, and since all pressures at outside walls are equal to or less than Ppl, it follows that all Ptm at points upstream from EPP are positive. All pressures at inside walls downstream from EPP must be less than Ppl. For extrathoracic airways Ptm downstream from EPP will be positive if inside pressures exceed atmospheric and negative if these pressures fall below atmospheric. For intrathoracic but extrapulmonary airways Ptm will be negative downstream from EPP. For intrapulmonary airways, if peribronchial pressures are negative with respect to Ppl, Ptm will be positive immediately downstream from EPP until points are reached where inside pressures have dropped by amounts equal to the difference between Ppl and peribronchial pressure. For points further downstream it will be negative.

From the foregoing it may be seen that EPP, whatever their location, divide the airways into upstream segments which have positive Ptm from downstream segments which may also have positive Ptm in portions of pulmonary and extrathoracic airways, but otherwise have negative Ptm. It follows that any compression of airways that occurs during forced expirations must take place downstream from EPP.

Location of EPP. While Ppl is subatmospheric there can be no EPP in airways—with the possible exception of the larynx where side pressures may be subatmospheric due to Bernouilli effects. Once Ppl increases to atmospheric, EPP are at the airway opening, and as Ppl increases still further they proceed upstream. How far do they go? We shall focus on events at the same lung volume so that the driving pressure for the segment upstream from EPP, namely the static recoil pressure, may be taken as constant. With driving pressure constant, flow through the upstream segment can increase only if the resistance of this segment decreases. One way for this to take place is for the EPP to move upstream, i.e., for the segment to shorten. We can assume, then, that EPP will continue to move upstream so long as flow increases. But it is well established that flow does not increase indefinitely as Ppl is increased. Isovolume pressure-flow curves (IVPF) introduced by Fry and co-workers (9) illustrate this. Some of these curves are presented in the following section (Figs. 1, 2, and 3). As Ppl increases flow increases with progressively smaller increments until a plateau is reached. With both flow and static recoil pressure fixed, the flow resistance of the upstream segment must be fixed and so must the location of EPP.

The sequence of events leading to fixation of EPP would be the following: When EPP reach the thoracic trachea a segment develops between the EPP and the thoracic outlet of the trachea in which Ptm is negative. For the intrathoracic trachea Ptm is zero at the EPP and, accordingly, all inside pressures downstream within the thorax are less than outside pressures. As Ppl increases and the EPP move upstream this compressed segment both lengthens and comes under a greater degree of compression. When the resistance of this compressed segment increases sufficiently rapidly with increasing Ppl to prevent further increase in flow, the EPP become fixed.

To summarize, at a given lung volume EPP appear first at the airway opening when Ppl is increased to atmospheric, move upstream along the airways, and become fixed when maximum flow is achieved. The fact that a plateau of flow is reached means that the EPP have progressed along intrathoracic airways to points when increases in compression of the intrathoracic airway downstream is sufficient to result in increases in downstream resistance which are directly proportional to Ppl.

Under conditions of maximal expiratory flow EPP divide the airways into upstream segments of fixed geometry (at a particular lung volume) and fixed driving pressure (Pst(l) at the volume in question) from downstream segments of variable geometry and variable driving pressure. Most of the remainder of this paper deals with the fixed segment upstream from EPP under conditions of maximal flow. Indeed, isolation of the comparatively simple events occurring in this segment from the more complicated ones downstream is the major purpose of the EPP concept. But first, we will use it to interpret isovolume pressure-flow curves in more detail.

Interpretation of IVPF curves in terms of the EPP concept. IVPF curves depict the relationship between pleural pressure and flow that exists at a particular lung volume. These curves were introduced by Fry et al. (8–10, 15) and used by them in a very fruitful way to analyze mechanisms limiting flow during forced expirations. We next show how these curves may be interpreted in terms of the EPP concept.

Just what IVPF curves are is most readily grasped by considering how they are obtained. To obtain them we estimated Ppl with esophageal balloons (25), volumes with a body plethysmograph (23), and flows with a pneumotachograph (6, 32). Subjects performed expired vital capacity maneuvers, slowly at first, and then more rapidly up to maximal levels. Volumes were expressed as percent of VC. Instantaneous values of esophageal pressure were plotted against simultaneous expiratory flows at the same lung volume each vital capacity maneuver yielding one point at a given volume. Lines of best fit, as determined by inspection, were drawn through the points. Figure 1 shows a typical set of points and the curve based on them. Figure 2 shows an average curve at 65 % VC based on measurements from eight healthy adult males.

We have pictured EPP as appearing at the airway opening as Ppl reaches atmospheric and moving upstream as Ppl exceeds atmospheric. Their arrival within the thoracic outlet should coincide with the onset of dynamic compression of the airways. We can gain some idea of the onset of dynamic compression by extending the flow-pressure relationship at low flows, where no dynamic compression has yet occurred, to higher flows, and noting at what point the experimental curve departs from this extension.

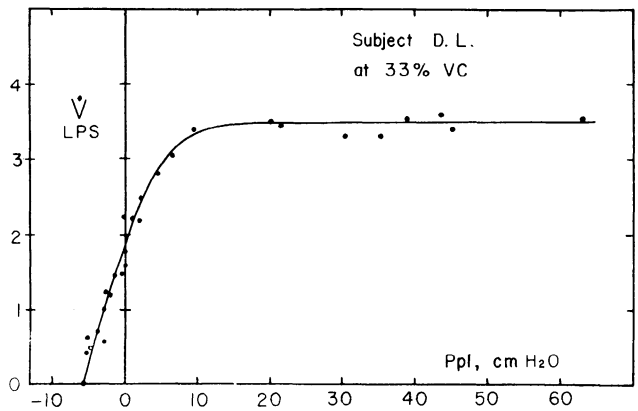


FIG. 1. Isovolume pressure-flow (IVPF) curve. The line was drawn by eye as the best fit to the points, each of which represents a separate expiration initiated from maximum inflation and measured at 33% VC.

The dashed line in Fig. 2 approximates the pressure-flow relationship that would obtain if no compression of the airways took place. It is based on an empirical expression Palv = K_1 (V) + K_2 $(\dot{V})^2$. This expression, which was introduced by Rohrer (30), has been shown to fit many pressure-flow relationships in the respiratory system. Curves were constructed which gave the best fit by eye to the experimental curves over a range of Ppl where no dynamic compression could take place, i.e., from Ppl = −Pst(l) to Ppl = 0. The dashed line corresponds to the average values for K_1 and K_2 for these curves. Dynamic compression as indicated by the deviation of the solid from the dashed line becomes apparent when Ppl is some 12 cm H_2O above atmospheric.

Our theory predicts that Ppl at the onset of dynamic compression should equal the pressure inside the trachea at its thoracic outlet. We now make a separate estimate of this pressure. The side pressure at the thoracic outlet, Pto, is approximated by the following: Pto = [K_a $(\dot{V})$ + K_b $(\dot{V})^2$]− K_c $(\dot{V})^2$. The terms in the bracket describe the pressure loss due to frictional flow resistance from the thoracic outlet to the atmosphere. The remaining term represents the Bernouilli effect and is the gain in side pressure between the thoracic outlet and the atmosphere due to convective deceleration of gas. The line Pto in Fig. 2 is based on values for K_a, K_b, and K_c of 0.3, 0.4, and 0.1, respectively. The first two values approximate published data (5, 16). The value for K_c assumes a blunt flow profile (17) and a cross section at the thoracic outlet of approximately 2.5 cm^2.

The curve for Pto should intersect that for Ppl at the point where dynamic compression begins, and this is seen to be the case. To a certain extent this close correspondence is fortuitous since Pto is an approximation. That it is not simply a matter of chance is suggested by the equally good correspondence seen at a different lung volume. Figure 3 includes similar curves in the same subjects at 35% VC. Pto is markedly curvilinear and its intersection with Ppl occurs at a considerably smaller value than at the higher volume but, again, the intersection corresponds closely with the onset of dynamic compression.

APPENDIX I presents further analyses of the curves in Fig. 2 in terms of changes in resistance of the segments upstream and downstream from EPP, at a given volume, as Ppl is increased.

Significance of "negative effort dependence" in IVPF curves. The IVPF curves shown up to this point have true flow plateaus: beyond certain levels of Ppl flow remains nearly constant. In their original curves, Hyatt et al. (15) represented flow as decreasing from maximal levels as Ppl increased. It has since been shown (18) that this result is, at least in part, an artefact related to the use of a spirometer at the mouth to indicate isovolume conditions. During forced expirations the gas in the lungs is compressed and lung volume decreases progressively below that indicated by the spirometer. In this case, reductions in flow are to be expected since as lung volume decreases maximum flow also decreases.

With a body plethysmograph all volume changes, including those related to gas compression, are sensed and IVPF curves usually show definite flow plateaus. In 4 out of 18 normal subjects, however, we did observe decreases in flow from maximal levels. We shall refer to these as instances of "negative effort dependence" in the sense that flow decreased as effort increased.

The implication of negative effort dependence to the movement of EPP allows us to predict how much flow may be reduced. Driving pressure for the upstream segment being fixed, any decreases in flow imply increases in the resistance of the upstream segment, and, hence, movements of EPP in the downstream direction. Since EPP could not pass back beyond the thoracic outlet and still allow dynamic compression of intrathoracic airways, a lower limit for the flow reduction can be set: it should not be possible for flow to decrease below levels seen in the rising phase of flow when EPP first reach the thoracic outlet. In the example shown in Fig. 4, flow appears to approach this theoretical minimum. In none of the four subjects exhibiting negative effort dependence did flows decrease more than would be predicted on these grounds.

Volume range over which maximum flow is independent of effort. Before presenting our analysis of the resistance upstream from EPP we need to define the volume range over which truly "effort-independent" flow maxima occur. Hyatt et al. (15) initially estimated the effort-independent portion of the MEFV curves to begin between 30 and 50% VC. This estimate was later increased to 60% VC (13). From Fig. 2 it is clear that true flow plateaus occur at least up to volumes of 65% VC. We have made no attempt to see the maximum volumes at which plateaus could be achieved, but in five subjects they were demonstrated at levels of 70% VC or higher. From these results and from some additional experiments described in APPENDIX II, we have concluded that the effort-independent range of maximum flow extends at least to 70% of VC.

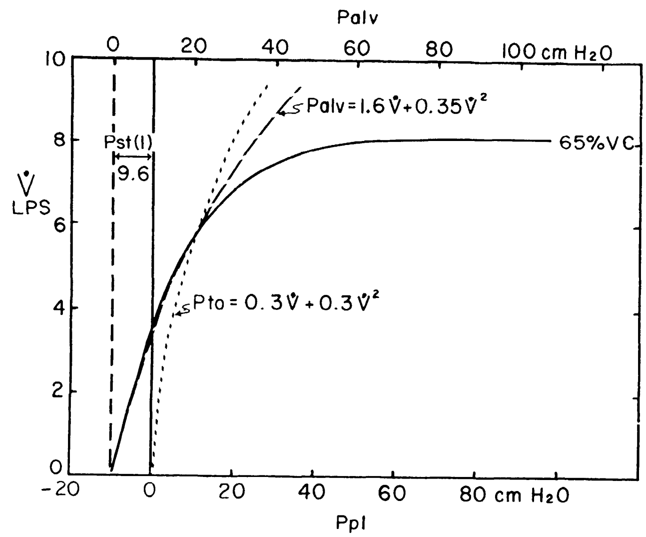


FIG. 2. Mean IVPF curve for six subjects at 65% VC.

ANALYSIS OF RESISTANCE OF THE UPSTREAM SEGMENT

To this point we have limited discussion to isovolume conditions. We now add the dimension of lung volume and restrict further analysis to the upstream segment.

Once maximum flow is achieved the resistance of the upstream segment at a given volume is fixed and is the ratio of Pst(l) to $\dot{V}_{max}$ at that volume. Since it is easy to obtain measurements of Pst(l) at any volume from static measurements (under static conditions Palv = 0 and Pst(l) = −Ppl) and of corresponding $\dot{V}_{max}$ from maximum expiratory flow volume (MEFV) curves, it is a relatively simple matter to describe how the resistance of the upstream segment changes with lung volume. In this section we prepare the way for interpreting such measurements.

The pressure drop along the upstream segment from alveoli to EPP will have two components: one, due to frictional losses from drag imparted by the airway walls and one due to convective acceleration of the flowing gas. (Hyatt and Wilcox (17) present a lucid account of convective acceleration and its significance in airway resistance.) The frictional component, Pfr, in turn, will have two components, depending on the nature of the gas flow. Where Reynold's numbers, Re, are less than 2,000, gas flow is probably laminar. Where they exceed 2,000, in particular if the passageways are irregular, gas flow is turbulent.

The pressure drop associated with each of these components depends on the geometry of the airways, the physical properties of the gas, and the magnitude of the flow. These are summarized in the following expressions:

$$\mathrm{Pla} \sim \frac{L}{D^4} \times \mu \times \dot{V}$$

$$\mathrm{Ptu} \sim \frac{L}{D^{4.75}} \times \mu^{0.25} \times \rho^{0.75} \times \dot{V}^{1.75}$$

$$\mathrm{Pca} \sim \frac{1}{(D_{EPP})^4} \times \rho \times \dot{V}^2$$

Where la = laminar, tu = turbulent, ca = convective acceleration, L = length, D = diameters, μ = gas viscosity, and ρ = gas density.

The first expression is based on the Hagen-Poiseulle formula. The second expression combines the empirical formulations of Darcy and of Blasius.[2] The third expression is based on the Bernouilli formula. Here we are concerned only with the influence of geometry and flow. Corresponding expression for the three components, expressed as resistances and with the physical properties of the gas ommitted are: Rla $\sim L/D^4$; Rtu $\sim (L/D^{4.75}) \times \dot{V}^{0.75}$; Rca $\sim (1/(D_{EPP})^4 \times \dot{V}$.

The total pressure drop from alveolus to EPP may be represented: Pst(l) = Pca + Pfr = Pca + Pla + Ptu. Similarly, the total resistance of the upstream segment may be represented as Rus = Rca + Rfr = Rca + Rla + Rtu.

Next, we predict how these components may be expected to change as lung volume changes. The pertinent geometry for the accelerative component is simply the cross section of the airways at EPP. If transmural pressures at EPP are zero, the cross section is that of the relaxed tracheobronchial tree and it should change with lung volume only to the extent that airway lengthening influences the relaxed cross section. Recent measurements of Hyatt and Flath (14) suggest that in the airways of canine lungs this influence is negligible. Since the points of fixation of EPP move upstream as lung volume decreases (see DISCUSSION) and since transmural pressures for intrapulmonary EPP may be positive, it is possible that the cross section at EPP actually increases with decreasing lung volume. On the other hand, if transmural pressures at EPP remain negligible even for intrapulmonary airways, their cross section should be largely independent of lung volume. This would be true because the total cross section of the relaxed tracheobronchial tree, of human lungs at least, remains nearly the same from the trachea to the level of bronchi of 2–3 mm internal diameter (30). We may anticipate, then, that the cross section at EPP under conditions of maximum flow should either remain unchanged or should increase as lung volume decreases. Since maximum flow decreases with lung volume and since the accelerative component of the resistance is flow dependent, we may predict that

[2] The following is Darcy's equation expressed in terms of pressure and flow:

$$P = \frac{F 16 L \dot{V}^2 \rho}{\pi^2 D^5 2g}$$

F is an empirical factor shown by Blasius to be approximated by the following for smooth-walled tubes:

$$F = \frac{0.316}{(\mathrm{Re})^{1/4}}$$

Reexpressed in terms of $\dot{V}$ is:

$$\frac{4\dot{V}\rho}{\pi D \mu}$$

Substituting Blasius' expression for F in Darcy's expression leads to the equation for Ptu in the text.

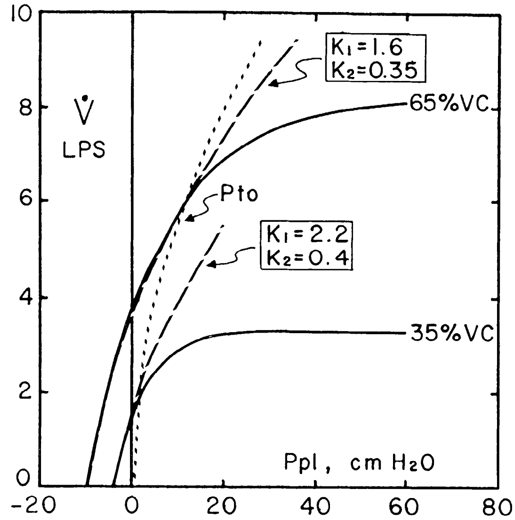


FIG. 3. Mean IVPF curves for six subjects at two lung volumes. The dashed line corresponds to line Palv and the dotted line to line Pto in Fig. 2.

the accelerative component of the resistance of the upstream segment will decrease as lung volume decreases.

The pertinent geometry for the frictional component includes the length and diameters of airways between EPP and alveoli. The length of this upstream segment will depend primarily on the position of the EPP at maximum flow and secondarily on the degree of extension of the tracheobronchial tree. As lung volume decreases all airways shorten and, furthermore, the fixation of EPP occurs at points progressively further upstream. Changes in diameter may be expected to have a greater influence on the resistance than changes in length. Over the volume range from 70 to 0 % VC lung gas volume is reduced about 66 % and airway diameters, which would be expected to vary approximately as the cube root of lung volume, would be reduced about 35 %. The associated increase in resistance would be approximately sixfold. A 35 % reduction in length, such as would occur if length and diameter changed equally, would decrease resistance by about one-third. The combined effect of reductions in length and diameter would then be approximately a fourfold increase in resistance. It seems doubtful that shortening of the upstream segment due to movements of the EPP at maximum flow would be so great as to reverse the tendency of the frictional component to increase as lung volume decreases. If we add now the influence of flow, we see that the frictional component would be unaffected by changes in flow if the flow is laminar, but would tend to decrease with lung volume if the flow is turbulent. Only in the instance of turbulent resistance would the geometric and flow effects be opposite.

Maximum flow-static recoil curves (MFSR)—Predicted configurations. The flow-pressure relationships of the upstream segment are represented by a graph of maximum expiratory flows against corresponding static recoil pressures. We will refer to these as MFSR curves. In Fig. 5 we show MFSR curves which would correspond to the predictions made in the last section if the components of upstream resistance existed in pure form. (The relationship between lung volume and Pst(l) is that of a young adult human lung.)

Figure 5*A* illustrates a purely accelerative resistance. The fine lines correspond to fixed cross sections at EPP. We have said that EPP move upstream as lung volume decreases and that cross sections at EPP may increase. The heavy line in Fig. 5*A* corresponds to this case. If the cross section at EPP remained fixed the MFSR curve would simply be one of the isocross-section lines.

Figure 5*B* illustrates a purely frictional resistance with laminar flow. The fine lines in this instance represent pressure-flow curves under conditions of constant lung volume. Here we assume resistance to be inversely proportional to volume expressed as percent VC. Accordingly, the slopes of the lines, which represent the reciprocal of resistance, namely, conductance, are directly proportional to volume. Pst(l) decreases with lung volume and the heavy line is the corresponding MFSR curve. It is seen to be curved in the opposite sense to that for a purely accelerative resistance.

Figure 5*C* corresponds to a purely frictional resistance but with turbulent flow. In this case pressure-flow curves at constant volume would be curvilinear. The curves are based on Rohrer's expression, $P = K_1(\dot{V}) + K_2(\dot{V})^2$. We assumed the ratio of K_1 to K_2 to equal 5, which is approximately true for the total airway. We also assumed K_1 and K_2 to be directly proportional to lung volume expressed as percent VC. The purpose of this example is not to give an accurate representation of the influence of turbulence but rather to show that the nonlinearity of pressure-flow curves which turbulence implies leads to a MFSR curve which combines the features of the purely accelerative and purely laminar frictional resistances. The MFSR curve would be curved in the same sense as for the laminar frictional resistance at low lung volumes but would tend toward the opposite curvature, namely, that seen for the purely accelerative resistance at high volumes.

To the extent that the accelerative or turbulent frictional resistance is important, we may expect that MFSR curves will be curvilinear in the sense shown in Fig. 5*A* and in the upper portion of Fig. 5*C*. To the extent that frictional resistance is important, we may expect curvature in the opposite sense at low volumes. It is also clear that an appropriate combination of these components might result in MFSR curves which would be nearly linear, in which case the resistance of the upstream segment would be substantially independent of lung volume.

MAXIMUM FLOW-STATIC RECOIL CURVES IN MAN

In conjunction with a study of changes in static recoil of lungs with age in man, we obtained MEFV curves as well in an effort to relate individual differences in static recoil pressure to maximum flows. When we later developed the ideas presented here, we had data for about

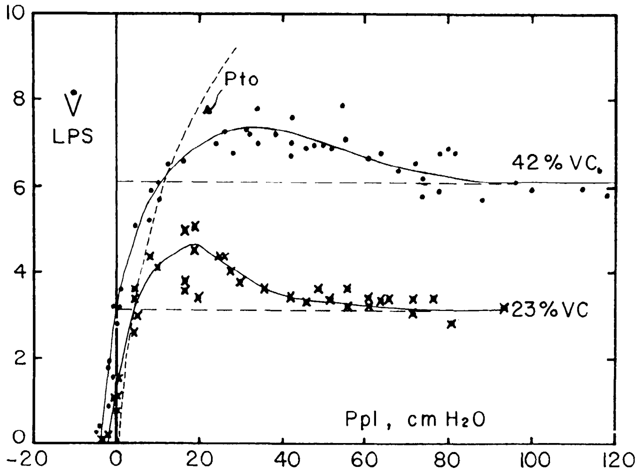


FIG. 4. IVPF curves at two lung volumes in a subject who exhibited reductions from maximum flow with increased expiratory effort. The individual points correspond to separate expirations, each begun from maximal inflation. Note that with increasing efforts, flows decrease to levels which correspond to ones that would obtain for EPP located near the thoracic outlet.

40 subjects ranging in age from 13 to 64 with which to describe the pressure-flow characteristics of the upstream segment.

The static recoil curves were obtained by the method described by Milic-Emili et al. (25). All measurements were made in the upright posture. Before each determination the subject inspired maximally three times in order to assure a constant volume history. He then inspired maximally and breathed out slowly into a spirometer. The tubes to the spirometer were occluded by means of a clamp at fixed volume increments—usually at 80, 60, 40, 20, 10, and 0% VC. Static transpulmonary pressure was measured as the difference between mouth and esophageal pressure during the periods of occlusion. Curves were constructed from mean values from at least three separate maneuvers.[3]

For the MEFV curves, subjects, seated in a body plethysmograph, inspired maximally three times and then breathed out as rapidly as possible from the maximal inspiratory level (TLC) to the maximal expiratory level (RV) through a calibrated flowmeter of either the Silverman (32) or Fleisch (6) type. Separate determinations of TLC were measured in all subjects by the method of DuBois et al. (4).

Figure 6 shows four typical sets of curves. Figures 7 and 9 include additional examples of MFSR curves. All MFSR curves were curvilinear in the sense predicted for accelerative resistance and/or turbulent frictional resistance at high lung volumes, and in the sense predicted for

[3] Particularly in younger individuals, esophageal pressures deviate in the positive direction at low lung volumes (25). We have assumed these deviations to be artefactual and have drawn straight lines from points estimated by inspection to be free of such artefacts (usually about 30–40% VC) through zero pressure at RV in order to approximate Pst(l) at intermediate volumes. These interpolations probably somewhat underestimate Pst(l).

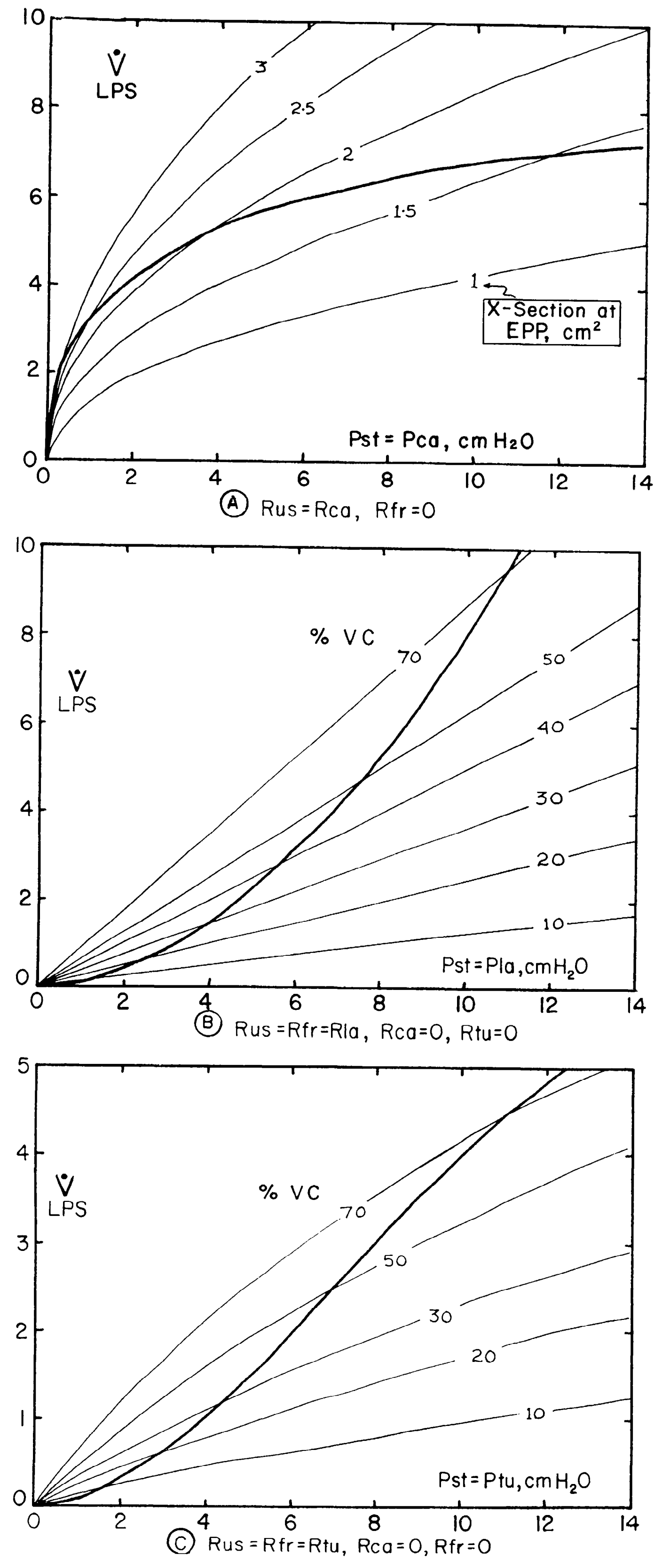


FIG. 5. Theoretical flow-pressure curves for the segment upstream from EPP. *A:* for purely accelerative resistance, *B:* for purely laminar frictional resistance, *C:* for purely turbulent frictional resistance.

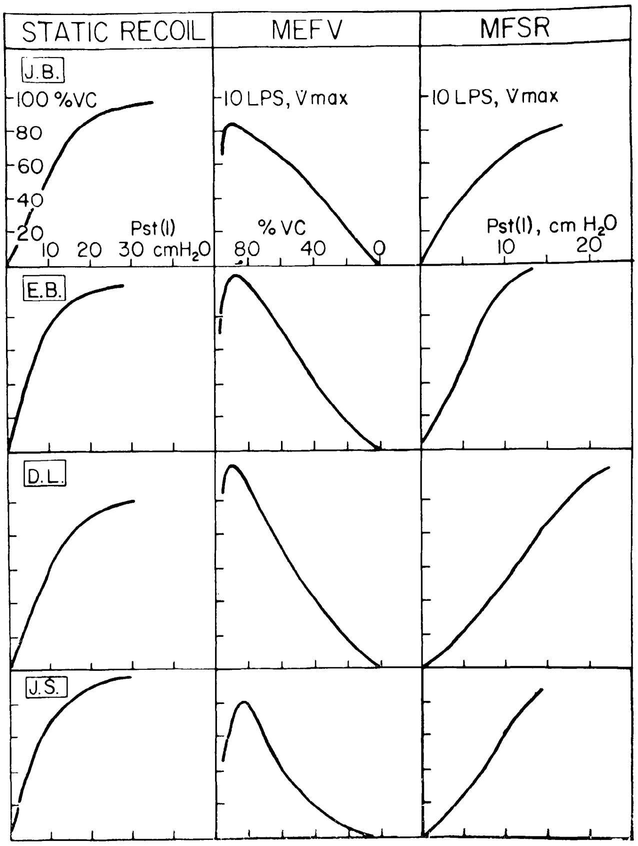


FIG. 6. Static recoil, maximum expiratory flow-volume (MEFV), and maximum flow-static recoil (MFSR) curves for four healthy male subjects.

frictional resistance at low lung volumes. In some instances the curves were nearly linear.

Estimates of the cross section of major airways from MFSR curves. We have attempted to assess the relative importance of accelerative and frictional components of resistance of the upstream segment at high lung volumes along the following lines. If convective acceleration accounts for most of the pressure drop in the upstream segment at high lung volumes, it should be possible to estimate the cross section at EPP from MFSR curves. We have done this and compared such values with separate estimates based on measurements made on X-ray films. Although peak flow is probably effort dependent, its relative insensitivity to changes in external resistance (see APPENDIX II) suggests that dynamic compression has at least begun and that EPP have reached the intrathoracic trachea. On the other hand, Macklem and Wilson (20) have demonstrated that EPP at high lung volumes under conditions of truly effort-independent maxima do not proceed further than the lobar bronchi. This places EPP at peak flow somewhere between the thoracic outlet of the trachea and the lobar bronchi. Estimates of the cross section of these airways can be made from chest X-rays and the fact that the relaxed total cross section of the airways is similar for the first few generations (30).

Figure 7 illustrates how we used the pressure-flow relationships to make our estimates. The dashed lines are isopleths corresponding to known cross sections. The experimental curves tend toward the configuration of the isopleths at high lung volumes, i.e., at high Pst(l). We made visual estimates of the isopleths which most nearly corresponded to the experimental curves for 16 subjects. We also obtained posteroanterior (PA) and lateral chest films on these 16 subjects and measured the transverse and PA diameters of the shadows of tracheal gas in the immediate vicinity of the carina. The lateral films were slightly underexposed and the PA films overexposed, compared to usual chest X-ray technique, to best visualize the tracheal air shadow; in about one-half of the subjects, one or two additional films were required before satisfactory contrast was obtained. In one subject, one of the diameters could not be discerned and it was assumed that the diameter measured at a different level was the same. All films were exposed at RV so that transmural pressures were as near zero as possible. Corrections were applied to the measured diameters for magnification of the image due to the relative distances of the trachea and X-ray tube from the film. Cross-sectional areas were then calculated based on the assumption that the cross section was elliptical.

The results are presented in Fig. 8. On the average, the cross section at the EPP estimated from MFSR curves exceeded that of the trachea at the level of the carina as estimated by X-ray measurements by 16%. We have concluded from these measurements that at high lung volumes convective accelerative losses account for almost all of the flow resistance of the segment upstream from EPP.

MFSR curves in normal subjects of different ages. The 40 subjects for whom we had MFSR curves included 5 males under 20 and 5 over 45 years of age. Two additional age groups of 5 subjects each were selected from the remainder on the basis of lung size as judged by measurements of total lung capacity (TLC). In this selection we attempted to make the differences in average TLC among the groups as small as possible. Figure 9 presents the individual MFSR curves of the 20 subjects. From inspection there appear to be systematic changes with age in the configuration of MFSR curves. Figure 10 presents average static recoil, MEFV and MFSR curves for the four age groups. Volumes are expressed as percent TLC so that differences in residual volume, RV, may be shown. Flows are expressed in TLC per second rather than in LPS in order to adjust for differences in body (and, hence, lung) size.

Static recoil pressures at a given volume decrease markedly from the youngest to the next youngest group but without associated change in RV. The next older group exhibits further reduction in Pst(l) bus with an increase in RV. The oldest group shows no further reduction in Pst(l) but RV is increased.

Peak flows did not differ significantly between the groups but maximum flows appeared to fall off more rapidly with decreasing lung volume in the older subjects—resulting in increased curvilinearity of MEFV

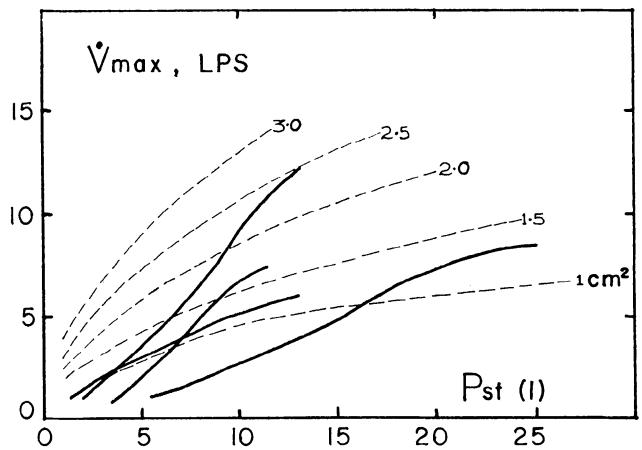


FIG. 7. Typical MFSR curves (solid lines) together with pressure-flow curves for accelerative resistance (dashed lines) corresponding to the cross sections at EPP as indicated. Note that the experimental curves appear to conform to the theoretical curves in their upper portions.

curves which became increasingly convex to the volume axis.

The flow resistance of the upstream segment is the ratio of Pst(l) to the corresponding $\dot{V}_{max}$. Average values for the different age groups are plotted against lung volume in Fig. 11 together with similar graphs for conductance of the upstream segment. (Conductance, G, is the reciprocal of resistance.) The latter is the more striking representation inasmuch as it reveals a nearly linear dependence of conductance at low lung volumes which extends progressively to higher volumes in the older subjects. At high lung volumes older subjects have higher conductances than younger ones. As lung volume decreases this relationship reverses.

We offer the following interpretation of these changes: Aging is accompanied by diminished elastic recoil of lungs resulting in decreased static recoil pressure at a given lung volume. It probably also is accompanied by increases in the resting length of virtually all elastic structures, including the walls of airways. With increasing age the relaxed cross section of airways increases while Pst(l) decreases. The time course of these opposing influences is such that $\dot{V}_{max}$ at high lung volumes shows little change.

At low lung volumes, where frictional resistance of the upstream segment dominates, the airways responsible for the resistance of the upstream segment are subjected to transmural pressures tending to expand them in proportion to Pst(l). Whether these airways increase or decrease in cross section with age depends on the balance of changes in elastic recoil between the airways and pulmonary parenchyma. For example, it is easy to picture a combination of diminished airway and parenchymal recoil which would result in no change in airway cross section at a given lung volume. One possible interpretation of the increase in resistance of the upstream segment with age at low lung volumes is that parenchymal recoil decreases with age more rapidly than airway recoil. This would result in a diminished cross section of airways at a given volume, and an increase in resistance of the upstream segment at low volumes.

The finding that conductance of the upstream segment decreases nearly linearly with lung volume in older subjects and appears to extrapolate to zero near RV suggests that airways upstream from EPP must approach total collapse at RV and that RV is set by properties of the lungs rather than of the chest wall in such individuals. Leith and Mead (unpublished observations) have obtained experimental evidence for this. They found that older normal subjects performing the VC maneuver remain on their MEFV curves as long as they continue their attempts to expire. In contrast, many young subjects remain on MEFV curves only transiently. In these, recoil of the chest wall appears to attenuate Ppl sufficiently to reduce it below levels needed to produce maximum flow. In the last portion of the VC in these individuals flow becomes effort dependent.

DISCUSSION

Direct observations of the location of EPP. Macklem and Wilson (20), by measuring lateral intrabronchial pressure in human subjects, have confirmed the theory of the development and movement of EPP during the course of an isovolume pressure-flow curve. Their diagrams show that EPP develop in the intrathoracic trachea when the pleural pressure has become sufficiently positive to overcome upper airway resistance, that they move upstream with increasing flow, and that they probably become fixed at $\dot{V}_{max}$. Over the middle half of the VC it was estimated that EPP stopped moving just beyond the level of the lobar bronchi. Below 25 % VC it was thought that EPP moved further upstream. Pride and Nadel (unpublished observations) have shown in living cats that EPP are at the level of the lobar bronchi at peak

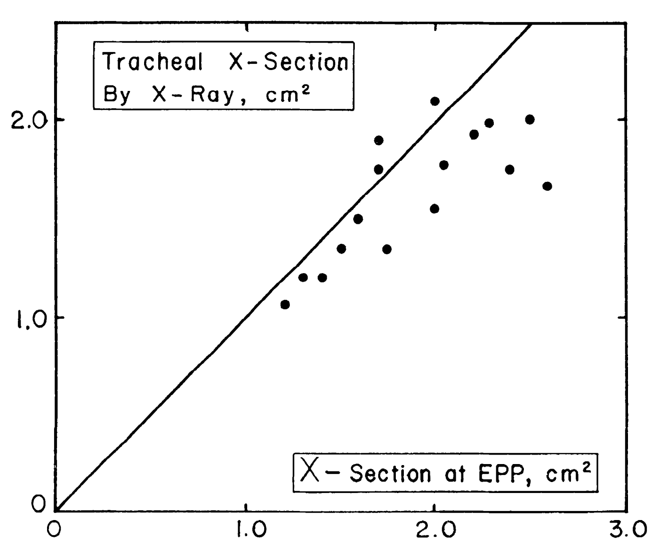


FIG. 8. Cross sections of the trachea estimated from chest films taken at residual volume plotted against cross sections at EPP estimated from MFSR curves.

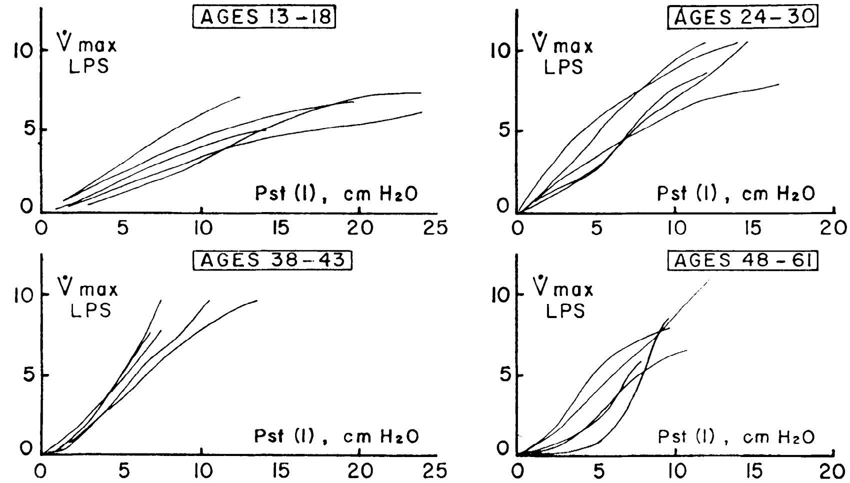


FIG. 9. MFSR curves for 20 subjects arranged in four age groups.

flow. Subsequently, Macklem and Mead (unpublished observations) have measured the location of EPP in living dogs. Their measurements confirm that at $\dot{V}_{max}$ EPP stop moving and stay at the same location despite further increases in Ppl. At high lung volumes the EPP were generally at the level of the lobar bronchi and moved upstream slightly as volume decreased to 40% of VC. Below 40% of VC, EPP moved upstream markedly. They also found retrograde movement of EPP in association with negative pressure dependence of flow in excised lungs.

Comparison of forced and relaxed expirations. Pierce (29) and also McIlroy et al. (22) have called attention to the fact that the time course for forced expirations is similar to that for relaxed expirations. McIlroy et al. pointed out that in both instances flow decreases nearly linearly with volume and the slopes of volume-flow plots are similar. These slopes have the units of time and approximate the mechanical time constants of the system. (The equation of motion of the passively expiring respiratory system is $V/C + R\dot{V} = 0$ which, rearranged to $V/\dot{V} = -RC$, defines the slope of the volume-flow relationship.) The observation that forced expirations appear to have time constants similar to those for relaxed expirations suggests the possibility of a similar mechanism. Our analysis leads to this conclusion. In the case of forced expirations the pertinent compliance is that of the lungs and the pertinent resistance that of the upstream segment which, in young individuals, is seen to be relatively independent of lung volume. The compliance of lungs is approximately twice that of the lungs and chest wall and the resistance of the upstream segment is about one-half that of the total respiratory system. Similar time constants for relaxed and forced expirations are to be expected on this basis.

Configuration of MEFV curves. Since their introduction by Hyatt et al. most analysis of MEFV curves has been focused on their lower portions. We find that the effort-independent part extends to higher volumes than has been generally recognized, and that this more extensive curve has three distinct segments: an uppermost one convex to the volume axis, a midportion concave to the volume axis, and a lowermost portion convex to the volume axis. According to our analysis the uppermost curvature reflects the curvilinearity of the static recoil curve at high lung volumes: Pst(l), the driving pressure for the upstream segment, falls off rapidly as lung volume decreases from high levels, and the reduction in flow reflects this. Indeed, if the resistance of the upstream segment were constant, MEFV curves would have precisely the same configuration as static recoil curves. The departures from such a configuration reflect at higher volumes the contribution of accelerative and turbulent frictional resistances, which tend to decrease with lung volume and, at low volumes, the frictional resistance of the upstream segment which increases with further decrease in lung volume.

The factors determining flow throughout the entirety of the forced expiratory vital capacity may be summarized as follows: in the rising phase of flow the driving pressure depends on the force developed by the expiratory muscles which, in turn, depends on their speed of contraction and velocity of shortening (1). This driving pressure is opposed by the total flow resistance of the respiratory system including the entire airway as well as that of the tissues of the lung and chest wall and any resistance of the measuring equipment. As flow rises EPP move rapidly upstream along the airways and become fixed at points in the neighborhood of the lobar bronchi. In normal individuals this occurs by the time 25–30% of the vital capacity has been expired. Beyond this point flow is independent of muscular effort as long as the effort is above certain levels. Flow may then be thought of as being determined by the static recoil pressure of the lung and the flow resistance of the airways between the alveoli and EPP. As we have stated, initially, that is at high lung volumes, this resistance is almost entirely accelerative, but as flow falls off and volume decreases the frictional resistance of the segment predominates. Finally, at least in young individuals, the rising opposition of the chest wall to further volume change opposes the falling static recoil of the lungs suffi-

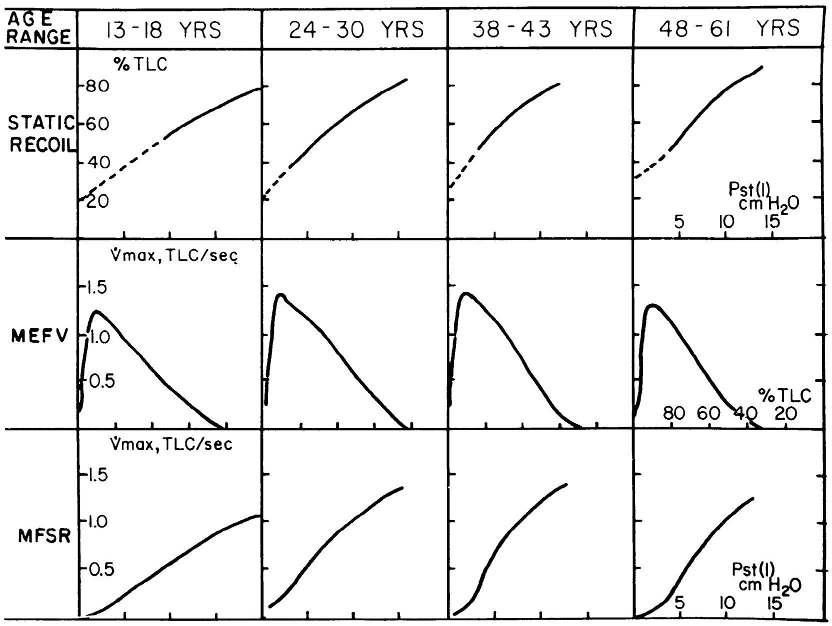


FIG. 10. Mean static recoil, MEFV, and MFSR curves for 20 normal subjects arranged in four age groups of 5 subjects each. The broken lines in the static-recoil curves are interpolated.[3] Maximum flows were divided by individual total lung capacities and expressed in TLC's per second to adjust for differences in lung size.

ciently to allow the EPP to move back up the tracheobronchial tree, and during the very last portion of the maneuver flow is again determined by effort.

When maximum expiratory efforts are initiated at TLC peak flows are attained at high lung volumes. These are commonly thought to be more effort dependent than maximum flows at lower volumes. But if EPP reach intrathoracic airways, which is probably the case in almost all instances, peak flows may be thought of as being limited by the cross section of the major airways and the static recoil of the lungs. When airway resistance is high, the frictional component of the resistance upstream from EPP must be appreciable even at high lung volumes and, in this case, peak flows would be sensitive to frictional resistances as well.

Application of the EPP concept to abnormal lungs. In our analysis we have treated the lungs as a unit. This approximation loses some of its usefulness in diseased lungs where nonuniformity may become the dominant feature. When this is the case some pathways will empty faster than others. These rapid compartments will contribute more to the MEFV curve early in the expiration—that is, at high lung volumes, whereas the flows obtained at lower volumes will be more influenced by the emptying rates of the slower units. Turner and Mead (unpublished observations) have shown that this is an additional cause for convexity toward the volume axis of the MEFV curve. In addition, they have predicted that when nonuniformities occur maximum expiratory flows should exhibit "time dependence" as well as volume dependence. That is, they predicted that the value of $\dot{V}_{max}$ at any given lung volume would depend in part on the time taken to arrive at that particular volume. They have obtained experimental evidence of such time dependence, both in older normal subjects and in patients with obstructive lung disease. Tests of ventilatory capacity in such instances may be more influenced by this additional dimension than they are by the factors listed in the previous section.

Comparison with other theories of maximum expiratory flow. Fry (8) was the first to attempt a rigorous explanation of the mechanisms limiting expiratory flow. He has applied aerodynamic theory to events occurring along the whole airway and has developed the concept of the "flow-limiting segments." These segments were the first to narrow sufficiently to limit flow. Analysis is complicated due to the difficulties in accurately characterizing events occurring along the whole compressed segment.

Permutt and co-workers (26) have made extensive and valuable use of a simple mechanical analogue, the Starling resistor, to explain the dynamics of flow through collapsible tubes. They point out that when the pressure at the outlet of the tube is less than the pressure surrounding it, flow becomes dependent on the difference between driving and surrounding pressure and independent of the difference between driving and outlet pressure. In applying these concepts to the lungs, it is seen that surrounding pressure is Ppl, driving pressure is Palv, and outlet pressure is atmospheric. Once $\dot{V}_{max}$ is reached we have shown that flow is dependent on the difference between driving and surrounding pressure, i.e., Pst(l) and independent of the total pressure drop from alveolus to atmosphere. This is closely analogous to the behavior of the Starling resistor. The major difference between it and the lung is that in the latter at any given volume, flow continues to increase even though Ppl rises considerably above atmospheric. As discussed previously, this is in part due to the pressure required to move EPP to the thoracic outlet and in part because a finite pressure is required to increase the resistance of the compressed seg-

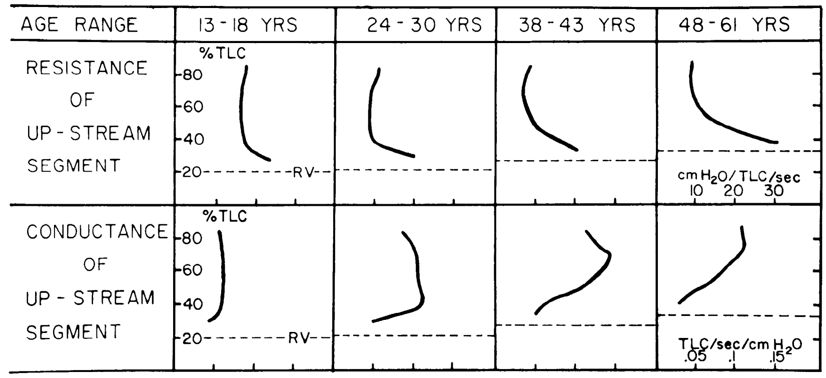


FIG. 11. Average relationships between resistance or conductance of the upstream segment and lung volume in the four age groups.

ment sufficiently to limit flow. It is in attempting to explain these differences that our concepts diverge from Permutt's.

Permutt (personal communication) suggests that, at a given volume, flow continues to increase until the transmural pressure across the wall at some point along the airway reaches a critical value Ptm′, which is sufficient to limit flow. Ptm′ is equal to the transmural pressure required to close the airway under static conditions when no air is flowing. He states that all events downstream from Ptm′ would be irrelevant and have no effect on flow. This permits him to restrict his analysis only to the segment upstream from Ptm′ which he regards as a fixed resistor with a fixed driving pressure. Although this approach avoids the complexities of analyzing the variables with which Fry must contend, it still requires consideration of events in the compressed segment. In the normal lung, at least, the pressure required to close the airway, Ptm′, must lie downstream from EPP.

Our concepts, which make no attempt to explain the exact mechanisms by which flow is limited and, therefore, in no way conflict with the views of Fry or Permutt, ignore the compressed segment and thereby simplify the analysis still further. We have divided the lungs into two separate physical parts which are in series. The analysis of one part is complicated (downstream from EPP) but the analysis of the other (upstream from EPP) is straightforward. Because they are in series, flow through the whole system may be described if we know the factors governing flow through either of the parts. The factors governing flow through the upstream segment (i.e., Pst (l) and the resistance of small airways) are parameters long known to be important in pulmonary mechanics and easily measured. Although elastic recoil has been recognized to be a factor governing maximum flow its role has been thought to be indirect through its influence on airway caliber (2). We assign it a direct role in which it is the driving pressure-producing flow through the upstream segment. Similarly we assign a direct role to the upstream conductance so that $\dot{V}_{max}$ is directly proportional to both of these parameters.

Furthermore, pathophysiological changes occurring with disease primarily affect the upstream segment. Reductions in $\dot{V}_{max}$ are directly proportional to reductions in both the pressure due to elastic recoil and the conductance of the smaller airways. As either of these parameters approaches zero, $\dot{V}_{max}$ also, approaches zero. Changes in the downstream segment, in which an increase in compressibility is the only clinically relevent example, will have a much more limited influence on $\dot{V}_{max}$. The extreme instance would be a trachea so collapsible that flow limitation took place as soon as EPP reached the thoracic outlet. $\dot{V}_{max}$ would then be that observed at the crossover of curves Pto and P in Figs. 2 and 3. Increased collapsibility at any other level could have only a smaller, not greater, effect. We conclude that changes upstream from the flow-limiting segment account for most of the limitation of expiratory flow seen in pulmonary disease. We also conclude that surgical intervention with the aim of rendering the walls of the airways more rigid can result in only a limited increase in $\dot{V}_{max}$ (11).

Relevance of the EPP concept to the cough mechanism. In healthy individuals the only circumstance in which the mechanisms discussed in this article come into play naturally is during coughing; thus their principal pertinence is to expectoration rather than ventilation. Dynamic compression of the intrathoracic airways is undoubtedly an essential part of an effective cough since it makes possible the high kinetic energy of the air stream required to move material at the airway wall (3, 20, 31, 33). It is possible that instability leading to rapid oscillations of the wall serve to concentrate the energy further but, whatever the precise nature of the mechanism, it is apparent that a cough would be largely ineffective in airways that did not undergo compression. Seen from this point of view, the position of EPP takes on added significance: cough is only effective at points downstream from them. In healthy individuals, EPP are in relatively large airways at high lung volumes and move upstream as lung volume decreases. In these, the cough should be effective at different levels of the tracheobronchial tree depending on the lung volume at which the cough is produced. A series of coughs without intervening inspirations would tend to clear progressively "deeper" portions of the airways.

It is probably true that an effective cough is an important homeostatic mechanism and that abnormalities

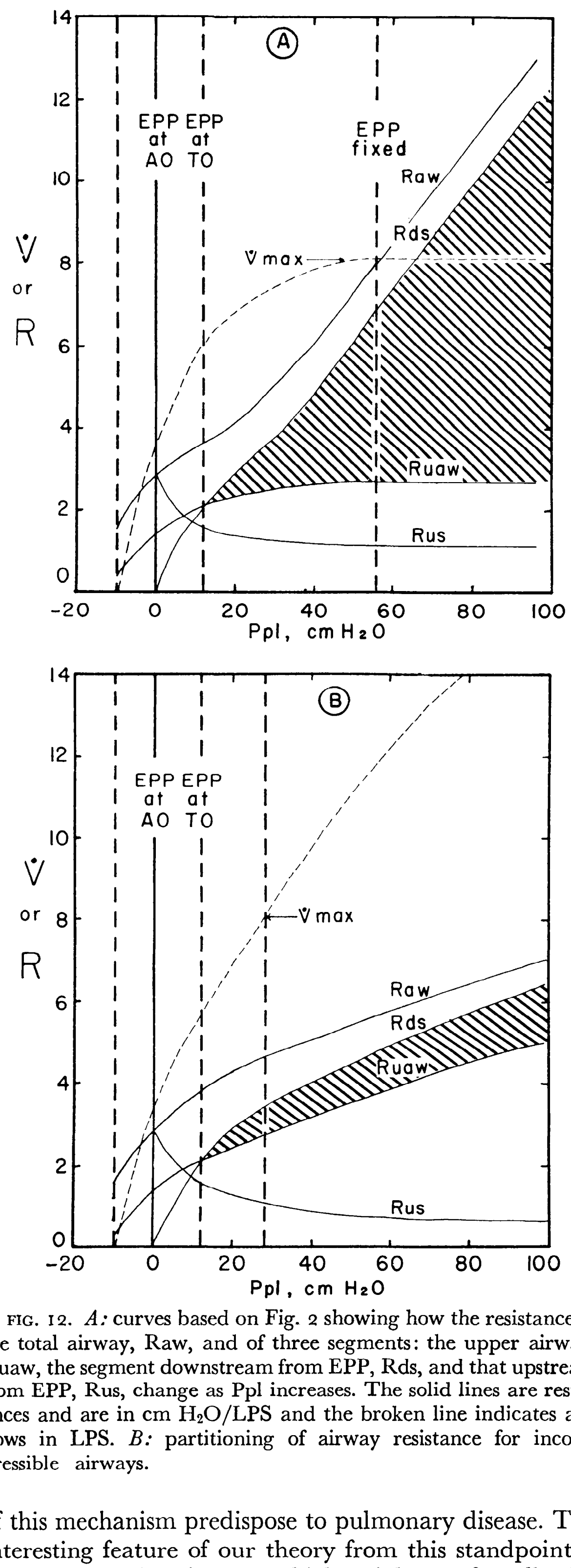


FIG. 12. *A:* curves based on Fig. 2 showing how the resistance of the total airway, Raw, and of three segments: the upper airway, Ruaw, the segment downstream from EPP, Rds, and that upstream from EPP, Rus, change as Ppl increases. The solid lines are resistances and are in cm H_2O/LPS and the broken line indicates airflows in LPS. *B:* partitioning of airway resistance for incompressible airways.

of this mechanism predispose to pulmonary disease. The interesting feature of our theory from this standpoint is that changes in airways which might profoundly influence the cough mechanism could well have an undetectable influence on ventilatory performance. This statement is a corollary of our earlier conclusion that increased collapsibility of airways per se would be expected to have comparatively little influence on maximum flow, but this same increase in collapsibility would profoundly effect movements of EPP and, hence, the extent of dynamic compression. For example, abnormally high compliance of major airways could render coughs totally ineffective for all intrapulmonary airways and, at the same time, have only a modest influence on maximum flow. These abnormalities have been described in patients with bronchiectasis (9) and in patients with bronchitis and emphysema (19). In the former group, indeed, ventilatory performance is usually well maintained but bronchial pressure measurements and bronchography during coughing and forced expiration revealed that bronchiectatic sacs generally underwent no compression and the pressures within them remained high due to the collapse of lobar bronchi (7). The patients with bronchitis and emphysema also had collapsing lobar bronchi during forced expiration which, in some patients, prevented compression of airways upstream over the whole vital capacity. In these patients EPP presumably never went beyond the lobar bronchi, rendering cough almost totally ineffective in ridding the smaller airways of their secretions (19).

APPENDIX I

Use of isovolume pressure-flow (IVPF) curves to partition airway resistance. In this appendix we use IVPF curves to partition changes in airway resistance between the segments upstream and downstream from EPP. The driving pressure from alveolus to atmosphere, Palv, is approximated by Ppl + Pst(l), which is seen in the example of Fig. 2 to equal the horizontal distance between the ordinate at Ppl − 9.6 cm H_2O and the experimental curve. The driving pressure for the upstream segment is Pst(l) which, in this instance, is 9.6 cm H_2O; that for the downstream segment is Ppl which is the horizontal distance between the ordinate at Ppl = 0 and the experimental curve. The driving pressure from the thoracic outlet of the trachea to the atmosphere, i.e., for the extrathoracic or upper airways, is the horizontal distance from the line Pto to the ordinate at Ppl = 0.

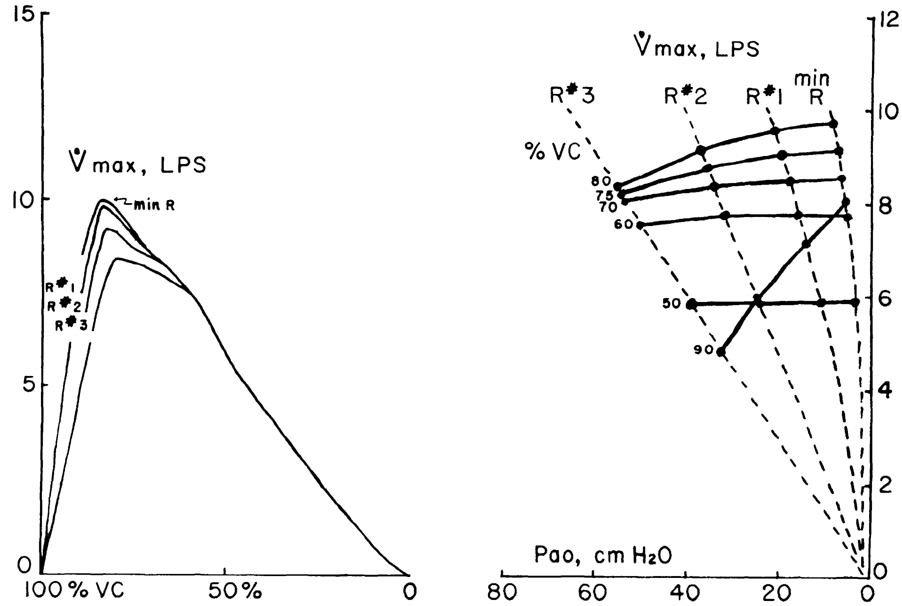
The resistance of the airways and their various segments is expressed as the ratio of corresponding driving pressures to flow, flow being the same for all segments. Figure 12*A* shows total airway resistance, Raw, upper airway resistance, Ruaw, and the resistances upstream and downstream from EPP, Rus and Rds, respectively, all plotted against Ppl. Resistances upstream and downstream from EPP are defined only for Ppl greater to or equal to 0.

Figure 12*B* shows these resistances for rigid airways and is based on the dashed line in Fig. 2. It is shown to clarify the contribution of dynamic compression.

The two representations are identical until EPP reach the thoracic outlet of the trachea. Thereafter, Raw increases more in Fig. 12*A* than in Fig. 12*B* due to compression of the segment between the EPP and the thoracic outlet. Indeed, a point is reached beyond which Raw and Rds increase in direct proportion to their driving pressures; from that point on, flow remains fixed and independent of further increases in Ppl. With flow fixed the EPP have reached their furthermost points upstream.

By comparing Fig. 12*A* and *B* we gain some idea as to the extent of dynamic compression and also of the degree of compression required to prevent further increase in flow. The dashed ordinate in Fig. 12*B* intersects the flow curve at $\dot{V}_{max}$. At this flow EPP would be at the same location as during dynamic compression at maximum flow. Comparison of the resistance upstream with that downstream from EPP in the uncompressed state in Fig. 12*B* gives a rough idea of how far EPP progress. At $\dot{V}_{max}$ total intrathoracic airway resistance (Raw-Ruaw) in the uncompressed state is about

FIG. 13. *A:* average MEFV curves in normal subjects expiring through different resistances. *B:* maximum flow plotted against mouth pressure, Pao, for different resistances and at different lung volumes expressed as % VC.



2. Intrathoracic resistance downstream from EPP (Rds-Ruaw) is about 0.7 so that EPP are approximately one-third of the way along the total intrathoracic resistance in the uncompressed state at a maximum flow at this lung volume. (At 35% VC EPP were about half way along the total intrathoracic resistance.)

Comparison of the resistance of the compressed segment (Rds-Ruaw) with that of the same segment in the uncompressed state shows that its resistance increases about six times by the time maximum flow is reached. (Compare Rds-Ruaw at $\dot{V}_{max}$ in Fig. 12*A* and *B*). This would require a reduction in cross section of slightly more than 50% in a cylinder in which flow is turbulent.

APPENDIX II

Experiments testing range over which maximum flow is independent of effort. We examined the extent of the effort-independent range with a second method suggested by the work of Hyatt et al. (15). They pointed out that in some circumstances maximum flow would be uninfluenced by additional resistances at the mouth: the effect of additional resistance would be to reduce transpulmonary pressure but as long as this pressure remained equal to or above that necessary to achieve maximum flow, flow would not be changed. Figure 13 represents average data for five subjects who, after maximum inspiration, expired maximally through known resistances. The flow-volume curves are shown on the left. Resistance as great as 5 cm H_2O/LPS had no discernible influence on maximal flow at volumes below 50% of vital capacity.

These same data, together with mouth pressures, can be used to greater advantage to define the maximal volume at which added resistances fail to influence flow. On the right in Fig. 13, flows are plotted against mouth pressure with mouth pressure increasing to the left of the ordinate. We will now show that these curves are essentially segments of IVPF curves.

Since all efforts were maximal, the forces developed by the respiratory muscles at a given volume must have differed only to the extent that the velocity of shortening of the muscles differed at the same volume. We are most interested in the flatter portions of the pressure-flow curves. In these regions the rates of flows differ between resistors by comparatively small amounts. It follows that the velocity of shortening of the muscles must, in this case, be nearly independent of the external resistance. Accordingly, the total driving pressure supplied by the respiratory muscles must, in the flatter portions of the curves, be nearly constant. This total driving pressure is dissipated in the flow resistance of the chest wall, the lungs and airways, and the external resistance. Since flow-resistive losses within the chest wall must be extremely small as compared to those in the airways and external resistances, the pressure developed by the muscles must be very nearly divided between the airways and external resistance. At a given lung volume, then, any increases, as resistance is added, in pressure measured at the mouth must be matched by corresponding decreases in transpulmonary pressure. Accordingly, pressure-flow curves plotted with mouth pressure increasing to the left are comparable to isovolume pressure-flow curves based on transpulmonary pressure.

To recapitulate these ideas; at a fixed lung volume the total driving pressure during maximal expiratory effort should be nearly independent of the amount of external resistance in the range of greatest interest, namely, where maximal flow changes little with external resistance. This driving pressure is, to a close approximation, the sum of transpulmonary pressure and mouth pressure. It follows that, driving pressure being nearly constant, any changes in mouth pressure must be very nearly equal and opposite to changes in transpulmonary pressure and that the curves in Fig. 13*B* are essentially IVPF curves. These are seen to be nearly flat up to volumes of 70% VC. We conclude that the effort-independent range of maximum flow extends to at least 70% of VC, or over most of the declining phase of flow.

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