Physiological Flow Studies Unit,
Imperial College, London, England

A QUANTITATIVE DESCRIPTION OF THE PRESSURE-VOLUME CURVE IN HEALTH AND IN ASTHMA

R. C. Schroter,

Introduction

In asthma, the considerable changes in airway calibre are associated with a somewhat abnormal pressure-volume curve. As the result of this, it is difficult to assess the intrinsic change of airway properties because of the interdependence between bronchial tone and parenchymal recoil. In order to obtain a clearer picture of the behaviour of the airways, it is therefore necessary to gain a better understanding of the changes in parenchymal properties. Furthermore, the increases in total lung capacity and functional residual capacity that occur in this disease must also be the result of changes in the pressure-volume curve.

The measurement of compliance, obtained at functional residual capacity, which is so often used, is of little value when one wishes to obtain an objective description of the shape of the pressure volume curve. The curve is distinctly non-linear and the changes in functional residual capacity which occur in disease diminish its usefulness as a reference volume for compliance. In an attempt to overcome these limitations a number of attempts have been made to describe an extended portion of the pressure-volume curve by a mathematical function. Salazar and Knowles [1] were the first to suggest that, in man, the upper part of the deflation pressure-volume curve could be fitted by a mono-exponential function.

In a previous study [2] we developed this approach to provide an objetive description of the pressure-volume curve in dog and monkey lungs. We used a mono-exponential function to fit the upper portion (above the inflection point) of both the inflation and deflation curves. The form of the equation used can be wirtten as

$$V = V_{max} - (V_{max} - V_o)\ e^{-kp}$$

where V_{max} is the volume the lung, or lobe, would achieve at infinite distending pressure P, V_o is the lung volume at zero distending pressure and k is an index of the stiffness of the lung parenchyma. At any lung volume V, the incremental compliance $\frac{dv}{dp}$ is given by:

$$\frac{dv}{dp} = k\ (V_{max} - V)$$

and thus is directly related to k but can be seen to diminish as lung volume is increased towards total lung capacity.

The slope of the alveolar plateau or phase III of a single breath gas bolus washout curve was shown to depend upon the regional variations of k within the lungs (Glaister et al. [3]). It was also demonstrated that the inflection point was coincident with the onset of airway closure on deflation and the completion of opening of units on inflation.

Glaister [4] extended this approach to study the mechanics of intact man; it was found that the elastic constants (V_{max}, V_o and k) in normal man were similar to those found by us earlier and that again the inflection point of the deflation limb was coincident with the onset of airway closure.

Gibson and Pride [5] have used our exponential curve analysis to study the changes in elastic properties of the parenchyma that occur in fibrosing alveolitis and Colebatch et al. [6] reported a critical appraisal of the method as used in normal man. We have recently published an extended study of the changes in the elastic properties that occur in a number of diseases [7], and recent observations of Colebatch [8] show similar trends. Studies have been concentrated on deflation rather than inflation properties mainly because of the relative difficulty of obtaining good inspiratory data.

When fitting the exponential curve to the deflation pressure volume curve in man, the range of volumes used is ussually from TLC to FRC. It is important, however, that the lower volume limit chosen should be above the inflection in the curve because below this point the observed curve results from both progressive closure of units and the deflation of the remaining patent units. Furthermore, at very low volumes, oesophageal pressure measurements may contain artefacts.

The effects of fitting the curve to an inappropriately large volume range can be seen in figures 1 and 2. In figure 1, the exponential curve is fitted to the

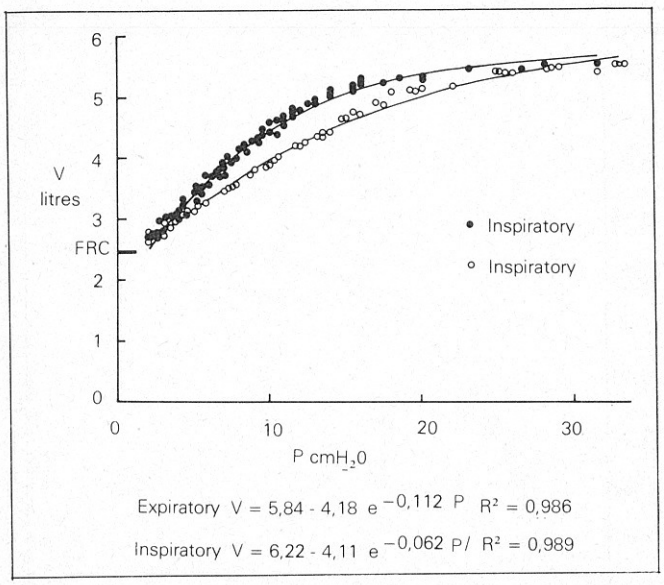

Fig. 1. Expiratory and inspiratory static pressure (P) volume (v) data obtained in one subject. An exponential equation was fitted over the whole range from total lung capacity to functional residual capacity.

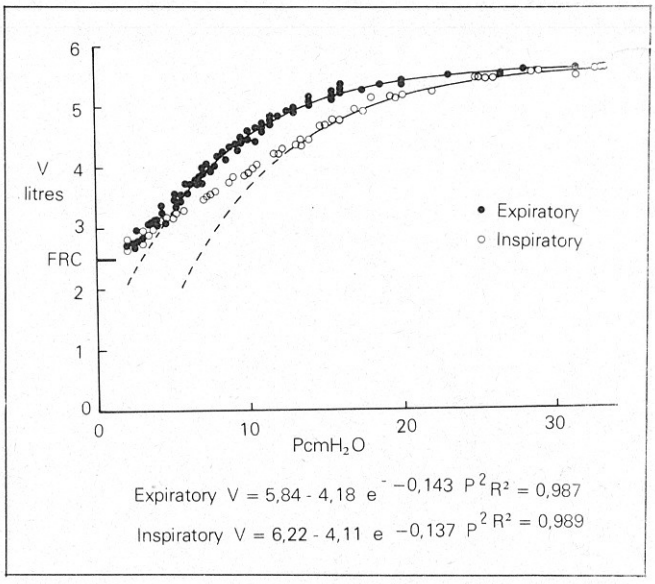

Fig. 2. Data from the same subject as in figure 1 with the exponential equation fitted after exclusion of data from lower lung volumes.

full vital capacity range for both the inflation and deflation limbs of the static pressure-volume curve of a normal subject. It can be seen that there are gross systematyc deviations of the mathematical curve from the experimental data. However, when only data above the deflation and inflation inflection points are used (fig. 2), then the curve fits the data much more satisfactorily and the systematic desviations are eliminated.

In normal subjects the values of the inspiratory and expiratory V_{max} are similar though the inspiratory value is usually slightly larger, being typically 107 % TLC compared with 102 % TLC on expiration. The values of expiratory k tend to be slightly higher than the inspiratory values (approx. 0.09 compared with 0.12 cm H_2O^{-1}). The differences may be real or an artefactual consequence of fitting the curve to a shorter range of data on inspiration.

In normal subjects the value of the deflation k increases very slightly with age though the change is very small:

$$k = 6.64 \times 10^{-4} \times \text{age} + 0.082 \text{ cm } H_2O^{-1}$$

There is a more significant increase in the value of V_o/V_{max} with age

$$\frac{V_o}{V_{max}} = 0.001 \times \text{age} - 8.49$$

Application in asthma

Asthma is associated with relatively small but definite changes in the pressure-volume curve and as can be seen from figure 3 the deflation limb of the curve is somewhat to the left of the normal range. There is a rise in residual volume and an increase in TLC. These changes in lung volumes are discussed by Dr. Pride later.

Application by Colebatch [8] of the exponential curve fitting procedure to the deflation pressure-volume curve, in a number of asthmatic patients, showed that the value of k is slightly higher than for normal subjects - though not very significatly so if the few very high values are excluded (fig. 4). We have carefully studied a limited number of asthmatic patients before and after the administration of a bronchodilator. It can be seen (fig. 5) that in all cases the values of k were in the high normal range and that in all but one instance the effect of the bronchodilator was to slightly reduce k.

The changes in the nature of the curve in one subject are shown in fi-

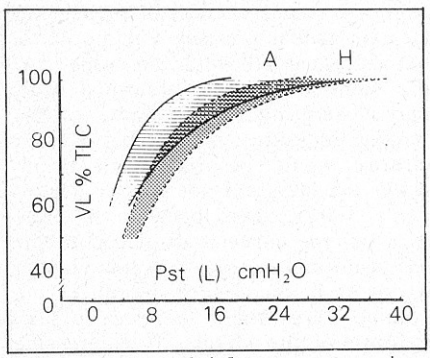

Fig. 3. The range of deflation pressure volume curves in normal (H) and asthmatic subjects (A) of similar age ranges. From Colebatch et al [8].

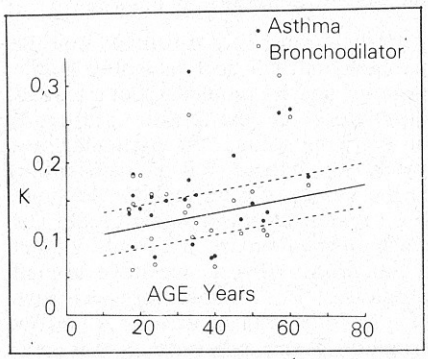

Fig. 4. Values of k (cm H_2O^{-1}) in asthmatic subjects. The solid and dotted lines are for normal subjects (mean ± 1SD). From Colebatch et al. [8].

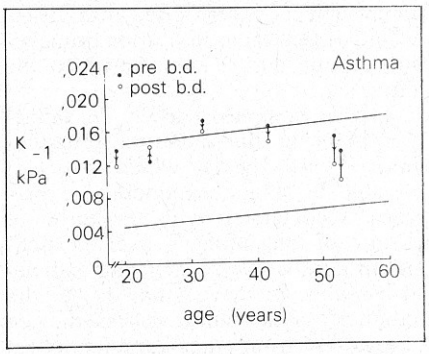

Fig. 5. The effect of bronchodilator action on k in a group of asthmatic subjects. Also shown is the value of k (and 95 % confidence limits) based on Gibson et al. [7].

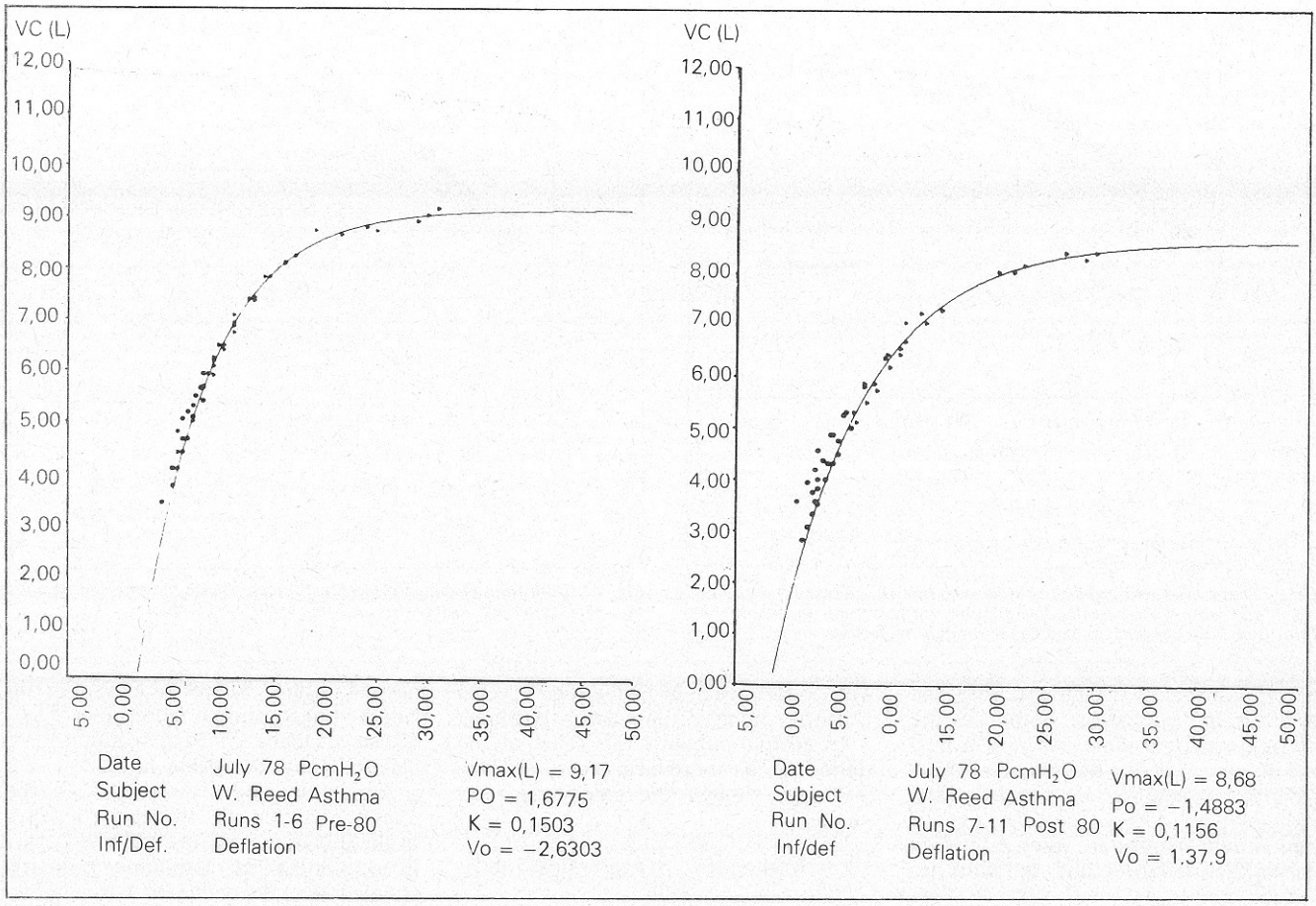

Fig. 6. The exponential fit to the pressure-volume data of a single asthmatic subject before and after bronchodilation.

gure 6. The values of both total lung capacity and V_{max} fell after bronchodilation as did residual volume. However, if the curves were to be superimposed, it would be seen that the curve is not displaced to the right after administration of the bronchodilator but rather rotated clockwise about the point at 55 % TLC. This is the point in both curves at which the cut off for curve fitting was made. This pattern of change was repeated in all the other subjects except one, in this case despite a reduction in k after bronchodilation the curve was shifted to the left.

As was explained earlier, the inflection point in the deflation pressure-volume curve below which it is not possible to fit the exponential expression is coincident with the onset of closure of lung units in excised lungs and in normal subjects. In the asthmatic patients we have studied, the deflation pressure-volume curves showed departures from the exponential at volumes higher above residual volume than is the case with normal subjects. At the same time, the phase III of the single breath nitrogen or bolus washout curve rises more steeply than in normal subjects. There is often no readily discernible phase IV, though in the mid-lung volume region the rising phas III may begin to rise even more steeply.

At present we have no explanation for the slightly elevated values of k in asthma nor can we explain the abnormal single breath washout pattern. It is, however, possible to hypothesise on the cause of this behaviour.

In the normal lung it is likely that the parenchyma will be reasonably homogeneous and we would expect a narrow distribution of the elastic properties of the lung units. In particular, we would not expect a wide distribution in the values of k throughout the lung. As a result, during a single breath gas washout manoeuvre, we would expect a flat phase III - as we have argued previously [3]. Furthermore, closure of lung units will occur over a narrow range of closing pressures, and is consequently gravity dependent. The process commences at the base of the lung at low lung volume and progresses smoothly toward the apex as volume is further reduced. This is reflected in phase IV occurring at low lung volume and showing a rapid departure from the flat phase III.

In asthma, we could expect that there may be either a very wide single distribution of lung unit k values or even a bimodal distribution of high and normal k populations. These lung units would be spread randomly through the lung parenchyma. The wide dispersion of k values would still give rise to an exponential pressure-volume curve but the phase III would be rising. At the same time some abnormal units may close at high lung volume (or distending pressure); the pattern of their closure would be distributed throughout the lung and not gravity dependent. Furthermore, because the pressure volume curve is displaced to the left of normal we would expect closure to occur at an abnormally high lung volume We would therefore expect to observe the effects of progressive airway closure superimposed on the rising phase III with no clearly discernible phase IV.

Discusión

Dr. Palenciano: ¿Cómo medía usted el número de vías aéreas y el porcentaje de vías aéreas, que se han cerrado por la presión pulmonar progresiva?

Dr. Schroter: La inclinación de la curva real a cualquier presión dada, está dividida por la inclinación de la curva exponencial a la misma presión y la relación entre inclinación real y la inclinación teórica, es la fracción de unidades que quedan cerradas. Así, el traslado del cierre progresivo de unidades pulmonares, es sencillamente la porción o relación de estas dos inclinaciones, a presiones sucesivas. En el hombre, creo que es una cosa difícil de hacer y lo presento aquí, únicamente como una posibilidad.

Dr. Martín Escribano: ¿En qué volumen pueden encontrar juntos, a nivel experimental, para hacer una curva y para su determinación? ¿A qué volumen lo hace Ud.?

Dr. Schroter: Si una persona llega al laboratorio, se toman los datos de la relación volumen y presión, en una gama lo más amplia posible, ajustando la curva desde la capacidad residual funcional, hasta la capacidad pulmonar total. Mediante el ordenador, fijamos el punto de inflexión y entonces decimos que vamos a explorar los datos, por encima o por debajo, de este punto. Nosotros habíamos trabajado con los datos por encima del punto de inflexión. Bajo el punto de vista experimental, tengo libertad para poder hacerlo en los modelos.

Dr. Montemayor: ¿Ha estudiado las variaciones del tono bronquial y su influencia sobre las curvas que ha presentado, mediante estímulos químicos o experimentales?

Dr. Schroter: Esto es una respuesta muy sencilla: no lo sé. No hemos hecho estudios sobre este punto y es algo que estamos iniciando. No hemos hecho estudios sobre los cambios químicos; esto es bastante difícil. En resumen, estamos todavía en una etapa precoz.

Dr. Palenciano: Hace unos años, se realizaron unos estudios en Boston, que se hicieron muy populares. Se medía el volumen de cierre después de una inspiración profunda y, basándose en esta medida, pensaban que la respiración a volumen circulante, se hacía aproximadamente a la mitad, con las vías aéreas cerradas. Pienso que esto es erróneo. ¿Tiene Ud. algún comentario?

Dr. Schroter: Sí, creo que usted tiene razón. Lo que hablábamos antes tiene relación con esto y es importante. Creo que este tipo de problemas ocurre muchas veces en fisiología. Hacer una relación uno a uno y, por tanto, pensar en la parte del volumen circulante que se realiza con vías aéreas cerradas o con vías aéreas abiertas, plantea una problemática muy difícil de resolver. Creo que prácticamente imposible.

Dr. Capote: Los doctores West y Wagner, en estudios que han hecho con diferentes gases, han encontrado que en el asma hay dos poblaciones de alvéolos y piensan que muchos de los alvéolos permanecen cerrados, sin comunicación con la boca, incluso con volúmenes pulmonares muy altos. En estos casos, ¿cómo es posible tener una idea correcta de la curva volumen-presión? Creo que, posiblemente, es difícil decir si esta presión es correcta ahora.

Dr. Schroter: Efectivamente, creo que West y Wagner están de acuerdo que sus métodos tienen sus propios problemas de interpretación, desde el punto de vista físico. Esta es la limitación del trabajo del Dr. West, aunque es un trabajo precioso. Si es cierto que las poblaciones lineales pulmonares quedan cerradas, mientras se hace la curva presión-volumen, a mi me interesa y no me interesa. No dice nada en cuanto a la curva volumen-presión, porque no son parte de la misma. Lo que yo puedo hablar aquí es de las propiedades de las unidades que se abren, por lo menos parte del tiempo, pero no puedo decir nada sobre las que están cerradas siempre. Si hay algunos canales bilaterales de ventilación, esto se reflejaría en la curva volumen-presión, porque señala espacios comunicantes y, por tanto, espacios reales desde nuestro punto de vista. Depende a qué presión se cierren los canales colaterales.

Dr. Palenciano: En las diapositivas, el valor varía después de administrar broncodilatadores. Supongo que ha administrado un beta-estimulante. De 15 a 50' se puede determinar el valor K. Si cambia en espacios más cortos, las modificaciones en la elasticidad, cambian también muy rápido. ¿Cuál es el mecanismo de esto?

Dr. Schroter: No lo sé. Cuando examinamos la curva volumen-presión, estamos tratando no solamente de las estructuras alveolares, sino también de las vías aéreas pequeñas. Así que la interdependencia entre estas dos, me parece un problema extraordinariamente complicado. Si se puede alterar el tono de los músculos de las vías aéreas pequeñas, se afectará la curva total volumen-presión y es un buen modo de considerar este problema. Pero si Ud. piensa más en la propiedad de los alvéolos al determinar la curva volumen-presión, sería muy difícil encontrar una respuesta.

REFERENCES

1. SALAZAR, G. and KNOWLES, J. H.: An Analysis of pressure volume characteristics of the lungs. *J. Appl. Physiol.*, 19: 97, 1964.
2. GLAISTER, D. H., SCHROTER, R. C., SUDLOW, M. F. and MILIC-EMILI, J.: Bulk elastic properties of excised lungs and the effect of a transpulmonary pressure gradient. *Respir. Physiol.*, 17: 347, 1973.
3. GLAISTER, D. H., SCHROTER, R. C., SUDLOW, M. F. and MILIC-EMILI, J.: Transpulmonary pressure gradient and ventilation distribution in excised lungs. *Respir. Physiol.*, 17: 365, 1973.
4. GLAISTER, D. H.: The relationship between closing volume of the lung and transpulmonary pressure. Inst. Aviation Med. RAF Report No. 538, 1974.
5. GIBSON, G. J. and PRIDE, N. B.: Pulmonary mechanics in fibrosing alveolitis. *Am. Rev. Respir. Dis.*, 116: 637, 1977.
6. COLEBATCH, H. J. H., NG, C. K. Y. and NIKOV, N.: Use of an exponential function for elastic recoil. *J. Appl. Physiol.*, 46: 387, 1979.
7. GIBSON, K. J., PRIDE, N. B., DAVIS, J. and SCHROTER, R. C.: Exponential description of the static pressure volume curve of normal and diseased lungs. *Am. Rev. Respir. Dis.*, 120: 799, 1979.
8. COLEBATCH, H. J. H., GREAVES, I. A. and NG, C. K. Y.: Pulmonary mechanics in diagnosis in: Proceeding of International Symposium on the Mechanics of Airways Obstruction in Human Respiratory Disease, ed. by M. A. de Kock, J. A. Nadel and C. M. Lewis, South African Medical Research Council, Cape Town, 1978.