

# Effective time of the forced expiratory spirogram in health and airways obstruction

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**ABSTRACT** We have calculated the effective time ( $t_{\text{eff}}$ ) of the forced expiratory spirogram in healthy non-smokers, in patients with simple chronic bronchitis, and in patients with chronic obstructive lung disease. Effective time was obtained by dividing the area underneath the forced expiratory spirogram by the forced vital capacity (FVC) and is equal to the time constant of lung emptying if the FVC-time curve is a single exponential. In 75 healthy non-smoking adults,  $t_{\text{eff}}$  showed a linear increase with age but no difference between the sexes. In 37 patients with low forced expiratory volume in one second ( $FEV_1$ )/FVC ratios,  $t_{\text{eff}}$ , as expected, was increased. In 19 subjects with simple chronic bronchitis and normal  $FEV_1$ /FVC ratios,  $t_{\text{eff}}$  was longer than or at the upper limit of 2 SE above the mean for healthy subjects of the same age. A comparison of  $t_{\text{eff}}$  with  $FEV_1$ /FVC suggested that in most normal subjects and patients the forced expiratory spirogram was a multiple exponential and that  $t_{\text{eff}}$  was a more sensitive index for the evaluation of airway obstruction than the  $FEV_1$ /FVC ratio.

The forced expiratory spirogram has been widely used for the assessment of lung function but most of the parameters derived from this curve are dependent on the age, sex, and lung size of the subject. For these reasons several attempts have been made to measure a time factor characteristic of the curve and independent of lung volume. The only commonly used measurement is the ratio of forced expiratory volume in one second ( $FEV_1$ ) to forced vital capacity (FVC). More elaborate measurements have been made by Dayman (1961), who described the ratio of change of flow ( $dV$ ) to change of volume ( $dV$ ) derived from the maximal flow-volume curve. Fish *et al* (1974) provided preliminary results on the mean transit time of the forced expiratory spirogram, and this was measured in healthy young subjects aged 9-22 years and in patients with cystic fibrosis by Neuburger *et al* (1976a and b). These authors claimed that the mean transit time may serve as a single overall measurement of airway function because of its sensitivity to both large and small airways obstruction.

In this paper we describe measurements of the effective time of the forced expiratory spirogram in healthy adults, in patients suffering from simple chronic bronchitis with normal  $FEV_1$ /FVC ratios, and in patients with chronic obstructive lung disease with low  $FEV_1$ /FVC ratios. The results suggest that

effective time, which can be derived by a simple mathematical procedure, is a more sensitive detector of airway disease than the  $FEV_1$ /FVC ratio.

## Methods

The area under any forced expiratory spirogram (FVC-time curve) may be considered as equal to that of a rectangle, the sides of which are the FVC and a segment on the time axis, which we call effective time ( $t_{\text{eff}}$ ) (fig 1), that is,

$$\int V dt = \text{FVC} \cdot t_{\text{eff}} \quad (1)$$

and

$$t_{\text{eff}} = \int V dt / \text{FVC} \quad (2)$$

Where  $V$  is the volume change at any time  $t$  and  $\int V dt$  is the area underneath the FVC- $t$  curve. It can be shown mathematically that  $t_{\text{eff}}$  is equal to the time-constant ( $T$ ) in single exponential curves (see appendix). Effective time is equivalent to mean transit time.

Forced expiratory spirometry was obtained from three groups of healthy non-smoking subjects:

- (a) 75 subjects (46 men and 29 women) aged 20-69 years,
- (b) 73 subjects (44 men and 29 women) aged 23-72 years, and

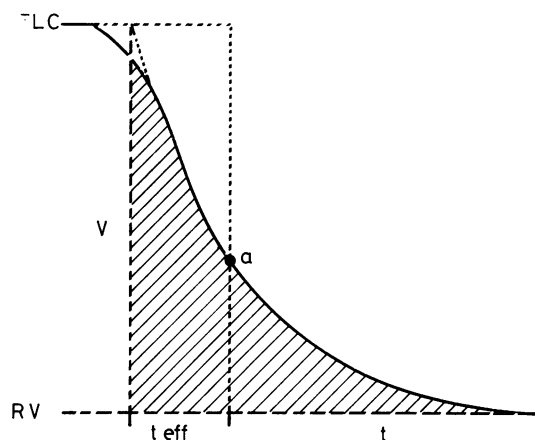


Fig 1 Diagram showing a forced expiratory spirogram. Change in volume ( $V$ ) between total lung capacity (TLC) and residual volume (RV) is plotted against time to give forced vital capacity-time (FVC-t) curve. Origin of curve is found by extrapolation of fast phase of curve towards horizontal TLC level. Striped area underneath spirogram represents integral  $\int V dt$ . This area is equal to area of a rectangle, the sides of which are FVC and effective time ( $t_{eff}$ ). If FVC-t curve is a single exponential  $t_{eff}$  corresponds to  $0.63 \times FVC$  (point  $a$ ).

(c) 17 men aged 24 years with a height range 1.61–1.85 m.

In none of these subjects was there a history of lung, thoracic wall, or heart disease; examination showed no abnormalities and the chest radiographs were normal. The values for  $FEV_1$ , FVC, and  $FEV_1/FVC$  were within normal limits ( $\pm 1$  SD predicted by the nomograms of Cotes (1968)). We also studied 56 male patients, who were divided into two groups:

(d) 37 patients aged 20–75 years suffering from chronic obstructive lung disease with an  $FEV_1/FVC$  ratio more than 7% below the predicted value, and

(e) 19 patients aged 25–75 years who were heavy cigarette smokers (20–25 cigarettes daily for more than five years) and who suffered from simple chronic bronchitis, that is, chronic cough and expectoration with a normal  $FEV_1/FVC$  ratio for their age. In this group of patients the  $FEV_1/FVC$  ratio differed from the predicted normal ratio by +2% to –7%.

Measurements were made with the subject in the sitting position and breathing through a mouthpiece (id 2.55 cm) that was connected with the cone of a heated Fleisch pneumotachograph screen type 4. After a deep breath up to the total lung capacity (TLC), the subject performed a forced expiratory manoeuvre to residual volume (RV). The subject's maximum effort was maintained until no further gas could be expired. The screen was connected with a

Statham PM 15 transducer, the signal from which was amplified by a Hewlett-Packard 1100C pre-amplifier. FVC-t curves were obtained by integration of flow by a Hewlett-Packard 3700 A integrating preamplifier and were recorded on a 7700 pen-recorder. The speed of the paper was 25 mm/s. The system (screen-transducer-amplifiers) was calibrated by the use of a rotameter at a constant flow of 200 l/min. In four normal subjects in whom the peak expiratory flow was between 600 and 700 l/min a calibration curve for volume was constructed. The origin of the FVC-t curve, when necessary, was determined by extrapolation of the fast phase of the curve (Smith and Gaensler, 1975) (fig 1). The area of the FVC-t curve was computed by the use of a program written on a magnetic card and inserted in the 65 Hewlett-Packard electronic calculator. The time axis ( $t$ ) was divided into a number ( $n$ ) of equal divisions ( $n$  was usually 10–12, but was as many as 35 in subjects with pronounced curvilinear FVC-t curves). Volume above RV ( $V'$ ) was sampled at these times and a rectangular approximation made by assuming  $V'$  was unchanged during the time interval ( $t/n$ ). The area  $\int V dt$  was then calculated from the equation

$$\int V dt = (t/n) [(FVC/2) + (\sum_{i=1}^{n-1} V'_i)] \quad (3)$$

which gave values practically equal to those measured by planimetry (difference less than 2%). The sensitivity of the preamplifiers (1100 C and 3700 A) was such that for every subject the deviation of the pen for the FVC was not less than 25 mm. On the FVC-t curve the  $FEV_1$  was also measured. Three or four FVC-t curves were obtained successively in each subject with a time interval between the FVC manoeuvres of 2–3 minutes and the curve with the maximum value for FVC was used for analysis. If two or more curves with the same FVC values showed different values of  $t_{eff}$ , the curve with the minimum  $t_{eff}$  was selected.

## Results

Effective time ( $t_{eff}$ ) increased with age in 75 healthy subjects (group A) between 20 and 69 years (fig 2). Age and  $t_{eff}$  were related to each other by the linear regression equation

$$t_{eff} \text{ (secs)} = 0.1573 + 0.0141 \times \text{age (years)} \quad (4)$$

For comparison the results for the mean transit time in normal children obtained by Neuburger *et al* (1976a) are also plotted in fig 2. There was a weak inverse relation between  $t_{eff}$  and FVC in 73 normal subjects (44 men, 29 women) aged 23–72 years (group B) and at a given FVC,  $t_{eff}$  tended to be shorter in women than in men (fig 3). In 17 normal men of the same age (24 years), but with different

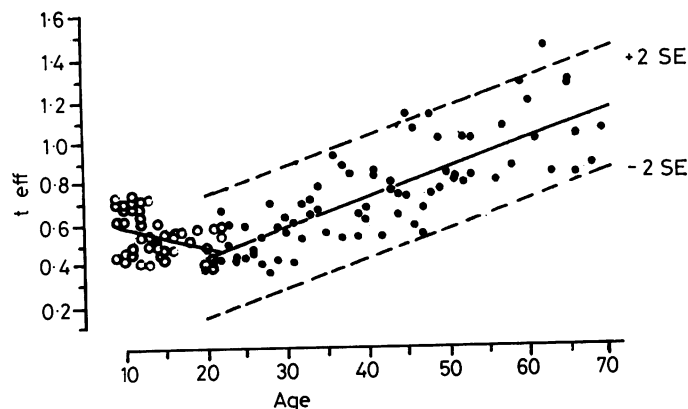


Fig 2 ● = Relationship between effective time ( $t_{eff}$ ) (in seconds) and age (in years) in 75 normal subjects. — represents mean value for  $t_{eff}$  at considered age while ---- correspond to  $\pm 2$  SE. Age and  $t_{eff}$  were related to each other by linear regression equation:  $t_{eff}(s) = 0.1573 + 0.0141 \times \text{age (years)}$  ( $r^2 = 0.6255$ ; paired  $t$  test,  $0.0005 < P < 0.0025$ ). ○ represent data of Neuburger et al (1976a) for mean transit time in children and young adults.

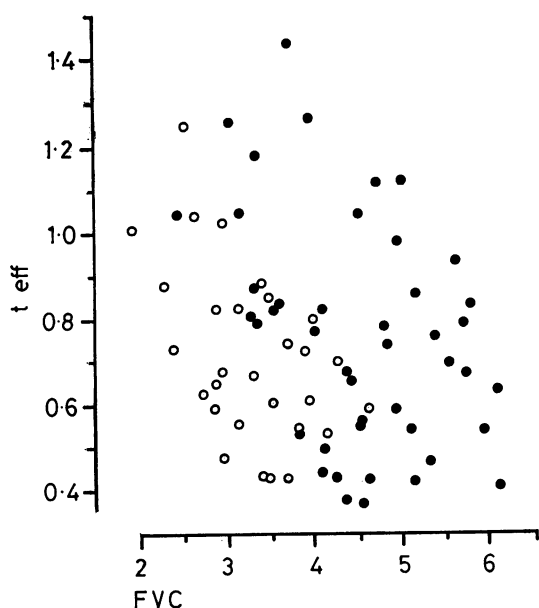


Fig 3 Relation of effective time ( $t_{eff}$ ) (in seconds) to forced vital capacity (FVC) (in litres) in 73 normal subjects of various ages. ● represent men and ○ women. Statistical analysis of results shows that  $t_{eff}$  is related to FVC according to linear regression equations  
 $t_{eff}(\text{sec}) = 1.2921 - 0.1173 \times \text{FVC (l) (men)}$   
 $t_{eff}(\text{sec}) = 1.1443 - 0.1332 \times \text{FVC (l) (women)}$   
 In these equations:  $r^2 = 0.1572$  (men) and  $r^2 = 0.1812$  (women); paired  $t$  test,  $0.01 > P > 0.005$ .

heights (range 1.61–1.85 m) (group C), however,  $t_{eff}$  showed very little relation to the FVC (fig 4). The values of  $t_{eff}$  in relation to age were increased in patients suffering from chronic obstructive lung disease (group D) and also in patients with simple chronic bronchitis (group E) (fig 5). The relation of  $t_{eff}$

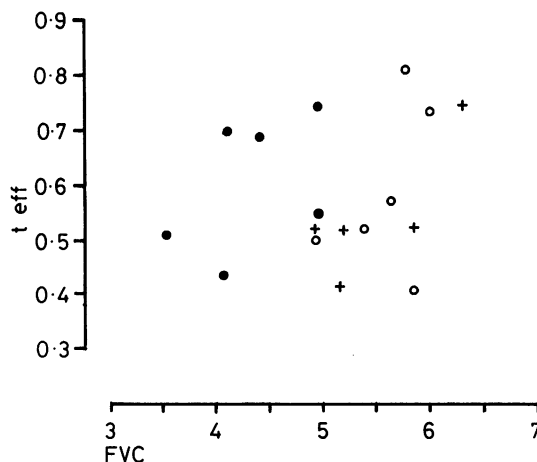


Fig 4 Relation of effective time ( $t_{eff}$ ) (in seconds) to forced vital capacity (FVC) (l) in 17 normal men (group C), all 24 years old but with a height range 1.61–1.85 m. ● correspond to six subjects with a height of 1.61–1.66 m, ○ to six subjects with a height of 1.80–1.85 m, and + to five subjects with a height of 1.67–1.79 m.

$t_{eff}$  to the  $\text{FEV}_1/\text{FVC}$  ratio in these 56 patients is shown in fig 6 together with results for 75 normal subjects (group A).

The ideal relationship between  $t_{eff}$  and  $\text{FEV}_1/\text{FVC}$  ratio in single exponential FVC- $t$  curves is given by the equation

$$\text{FEV}_1/\text{FVC} = 1 - e^{-1/t_{eff}} \quad (5)$$

It can be seen that in the great majority of subjects  $t_{eff}$  was longer than the ideal value at a given  $\text{FEV}_1/\text{FVC}$  ratio. The 131 subjects in fig 6 were divided into eight groups according to the value of  $\text{FEV}_1/\text{FVC}$ . In each group the coefficient of variation of  $t_{eff}$  was greater than for  $\text{FEV}_1/\text{FVC}$  (see table).

## Discussion

The mean transit time of the forced expiratory spirogram (FVC-t curve) has recently been introduced as a sensitive test suitable for the early detection of airway narrowing (Fish *et al*, 1974; Neuburger *et al*, 1976a,b). Mean transit time is a statistical parameter, the first moment of the curve, which is equal to the area under the FVC-t curve divided by the FVC (Neuburger *et al*, 1976a). The ratio  $\int Vdt/FVC$  is a time characteristic of the FVC-t curve that we have called effective time ( $t_{eff}$ ). Our results show that  $t_{eff}$  rises through adult life in normal subjects (fig 2). Combining our data for adults with the results of Neuburger *et al* (1976a) for mean transit time in normal children of nine years or older it appears that the minimum values of  $t_{eff}$  correspond to about the age of 22 years. Considering that  $t_{eff}$  of any volume-time curve is the product of the effective values of compliance and resistance (Jordanoglou *et al*, 1978), it seems that at this age the chest has its lowest value of effective resistance and compliance. This agrees with previous findings that at about this age the volume-pressure curve of the lung is supposed to go through its highest values of the lung recoil pressures and closing volume (as a percentage of vital capacity) goes through a minimum value (Mansell *et al*, 1972). The dispersion of the values for  $t_{eff}$  round the mean is greater beyond the age of 35 years than in the younger subjects, and this poses the question of how strict the criteria must be for the selection of normal subjects in the older age groups.

The relation of  $t_{eff}$  to lung size is less clear. According to our data, FVC is inversely related to  $t_{eff}$ , and the relation is slightly different in the two sexes. There was no appreciable difference (less than 0.01 sec in any age group), however, in  $t_{eff}$  between men and women. The overlapping of long  $t_{eff}$  in men with short  $t_{eff}$  in women at any given FVC, below about 4.5 l, may be explained by the slope of the regression lines (see equations in the legend of

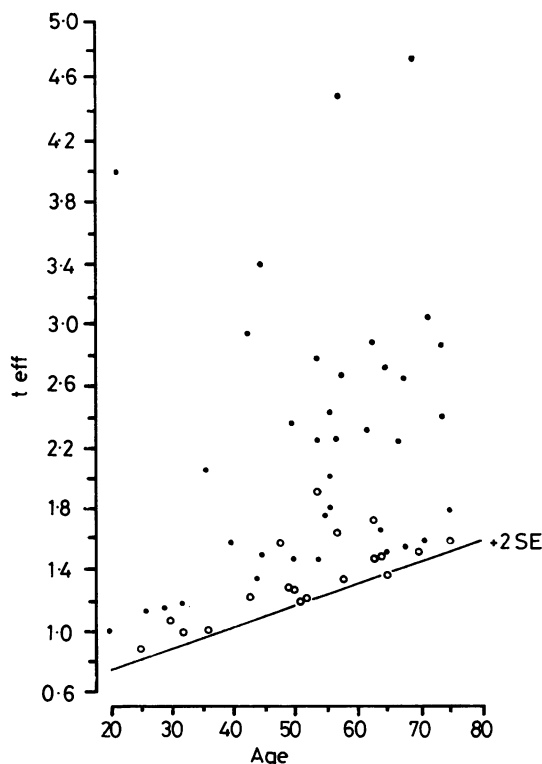


Fig 5 ● = Relation of effective time ( $t_{eff}$ ) (in seconds) to age (years) in 37 men suffering from chronic obstructive lung disease with reduced  $FEV_1/FVC$  ratio (group D). ○ show  $t_{eff}$  in relation to age obtained from 19 subjects suffering from chronic cough and expectoration with a normal  $FEV_1/FVC$  ratio (group E). — represents + two SE line for healthy subjects of fig 2.

fig 3). Furthermore, the points in fig 3 correspond to subjects of both sexes with different age and height. In order to study the effect of the height (and consequently lung volume) on  $t_{eff}$  we studied a group of 17 normal non-smoking men (group C), who were all

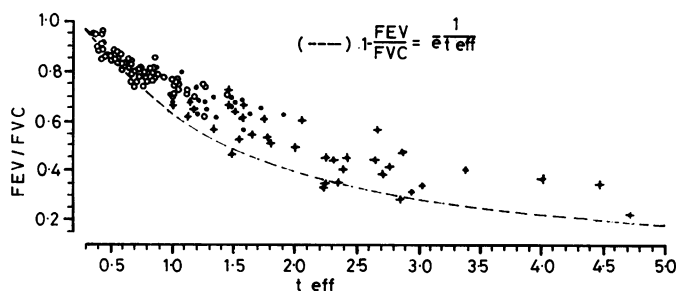


Fig 6 Relationship between  $FEV_1/FVC$  ratio (as a fraction of unity) and effective time ( $t_{eff}$ ) (in seconds) in all 131 subjects studied: ○ = normal subjects, + = patients with reduced  $FEV_1/FVC$  (group D), and ● = patients with normal  $FEV_1/FVC$  (group C). ---- represents ideal relationship between  $t_{eff}$  and  $FEV_1/FVC$  according to equation (5) (see text).

Relation between mean value of  $FEV_1/FVC$  and mean effective time ( $t_{eff}$ ) in groups divided according to value of  $FEV_1/FVC$

$FEV_1/FVC$ groups	$FEV_1/FVC$	$FEV_1/FVC$	$t_{eff}$	$t_{eff}$	$CV(t_{eff})$
	Mean	$\pm SD$	Mean (s)	$\pm SD$ (s)	$CV(FEV_1/FVC)$
0.90-0.962 (n=7)	0.9336	0.0238	0.4134	0.0273	2.59
0.80-0.899 (n=37)	0.8393	0.0295	0.6402	0.1444	6.43
0.70-0.799 (n=37)	0.7528	0.0310	0.9835	0.2251	5.56
0.60-0.699 (n=23)	0.6519	0.0258	1.4255	0.2765	4.90
0.50-0.599 (n=8)	0.5420	0.0267	1.7938	0.4017	4.54
0.40-0.499 (n=9)	0.4466	0.0261	2.5028	0.5178	3.54
0.30-0.399 (n=8)	0.3539	0.0220	2.9963	0.8317	4.46
0.23-0.299* (n=2)	—	—	—	—	—

SD=Standard deviation.

n=Number of subjects in each  $FEV_1/FVC$  group.

\*Only two subjects, so parameters not calculated.

CV=Coefficient of variation ( $=SD/mean$ ).

$FEV_1/FVC$  expressed as a fraction of unity.

aged 24 but with different heights (fig 4). There was no relation between  $t_{eff}$  and FVC; this finding is in contradiction to the data of Neuburger *et al* (1976a), in which mean transit time was directly related to the FVC.

The rate of change in lung volume during forced expiration has also been assessed from the slope of the maximum expiratory flow-volume curve ( $\Delta V/\Delta \dot{V}$ ), which is an index related to the product of compliance and resistance (Mead *et al*, 1967; Cotes, 1968; Jordanoglou and Pride, 1968a; Sykes *et al*, 1969; Agostoni, 1970; Dennis and Douglas, 1970; Yamabayashi *et al*, 1970; Bates *et al*, 1971; Gelb *et al*, 1973; Knudson *et al*, 1973). Dayman (1961) in maximal expiratory flow-volume curves reported a mean value of 0.37 seconds for  $dV/d\dot{V}$ . Takishima *et al* (1967) reported values between 0.3 and 0.7 s for the  $\Delta V/\Delta \dot{V}$  slope in normal maximal expiratory flow-volume curves, while Jordanoglou and Pride (1968b) found that the value of  $\Delta V/\Delta \dot{V}$  over the range between 40% and 60% of the FVC in normal subjects was about 0.42 s. The  $\Delta V/\Delta \dot{V}$  slope of the maximal expiratory flow-volume curve is a parameter with dimensions of time, but will vary over the course of a forced expiration unless the FVC-time curve follows a single exponential. When there is airways obstruction the values of  $\Delta V/\Delta \dot{V}$  characteristically increase as expiration continues (Takishima *et al*, 1967; Jordanoglou and Pride, 1968b) so that it is not possible to describe adequately such curves by a single value for the slope.

Lung emptying during forced expiration can also be assessed by the  $FEV_1/FVC$  ratio, which is considered by British authors to be the most satisfactory parameter for the detection of airways obstruction (Medical Research Council, 1965; Sartorelli, 1966; National Heart and Lung Institute, 1974). Normal values of  $FEV_1/FVC$  mainly depend on age, rather than on sex, lung volume, or height (Berglund *et al*,

1963) and so it was thought that it would be useful to study the relation of  $t_{eff}$  to the  $FEV_1/FVC$  ratio. The effective time in all the patients with chronic obstructive lung disease with low  $FEV_1/FVC$  ratios was considerably longer than in normal subjects of the same age, and was at or above the upper limit of normal in patients with chronic cough and expectoration in whom the  $FEV_1/FVC$  ratio was normal or only slightly below the mean predicted value (fig 5). It is possible to construct an ideal relationship between effective time and the  $FEV_1/FVC$  ratio, because the  $FEV_1/FVC$  ratio is equal to  $(1 - e^{-1/t_{eff}})$  in single exponential FVC-t curves. In this case the time-constant (T) of the curve and the effective time ( $t_{eff}$ ) have the same value (see appendix). The minimum value of  $t_{eff}$  at any  $FEV_1/FVC$  level cannot be shorter than that determined by the ideal curve, corresponding to a single exponential FVC-t curve. In multiple exponential FVC-t curves, however, the  $FEV_1/FVC$  ratios are expected to have higher values at any given  $t_{eff}$  than that determined by the ideal curve. This is because the major part of the expired air in the first second is expelled from the fast emptying region of the lungs, resulting in high  $FEV_1/FVC$  ratios, whereas  $t_{eff}$  reflects the rate of emptying throughout expiration. In most of the subjects studied the points deviate from the ideal curve (fig 6) especially with  $FEV_1/FVC$  ratios below 0.85. This was found in both normal subjects and patients and suggests that in these cases the FVC-t curve is a multiple exponential. This finding agrees with the studies of Takishima *et al* (1967), who claimed that there are time-constant discrepancies within the lungs of normal subjects and patients. Consequently, the term "time-constant" of the respiratory system cannot be generally used unless the FVC-t curve is a single exponential. Lowell and Schiller (1953) showed that in a limited number of subjects the FVC-t curve was represented by a nearly straight line



on a semi-log paper, indicating that these curves were a single exponential but this was true only of a minority of our subjects.

The theoretical considerations above suggest that  $t_{\text{eff}}$  may be expected to be a more sensitive means for detecting airway obstruction than the  $\text{FEV}_1/\text{FVC}$  ratio, as it is accepted that the earliest changes in maximum expiratory flow are towards the end of expiration. This conclusion is supported by the present results which show that the scatter of the points on the  $t_{\text{eff}}$  axis was wider than those on the  $\text{FEV}_1/\text{FVC}$  axis (fig 6 and table).

Because  $t_{\text{eff}}$  reflects events throughout expiration it is also likely to be a more reliable parameter than the forced expired time (time to complete a full forced expiration) which depends heavily on the extent to which an individual sustains the final stages of his expiratory effort. As  $t_{\text{eff}}$  can be derived rather simply from a forced expiratory spiogram we believe it deserves further study as a sensitive measurement of airflow obstruction.

## Appendix

In a single exponential forced vital capacity versus time curve (FVC- $t$  curve), the time-constant ( $T$ ), the forced vital capacity (FVC), and the expired volume  $V$  at any time  $t$  are related to each other by the equation:

$$V = \text{FVC} \cdot e^{-\frac{t}{T}} \quad (6)$$

where:  $e = 2.71828 \dots \approx 2.72$  base of the natural logarithms. Integrating both sides of equation (6) with respect to time the following equations are obtained:

$$\int V dt = \text{FVC} \int e^{-\frac{t}{T}} dt \quad (7)$$

$$\int V dt = \text{FVC} \left( e^{-\frac{t}{T}} / -\frac{1}{T} \right)_0^\infty \quad (8)$$

$$\int V dt = -\text{FVC} \cdot T \cdot \left( e^{-\frac{t}{T}} \right)_0^\infty \quad (9)$$

$$\int V dt = -\text{FVC} \cdot T (e^{-\infty} - e^0) \quad (10)$$

$$\int V dt = \text{FVC} \cdot T \quad (11)$$

$$T = \frac{\int V dt}{\text{FVC}} \quad (12)$$

It is obvious that according to the equations (2) and (12)  $T$  is equal to  $t_{\text{eff}}$  in single exponential FVC- $t$  curves.

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