

## MEAN AND BREATH-BY-BREATH PATTERN OF BREATHING IN MAN DURING STEADY-STATE EXERCISE

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### SUMMARY

1. The breathing pattern, that is the relation between tidal volume ( $V_T$ ) and the inspiratory ( $T_I$ ) and expiratory ( $T_E$ ) durations, has been studied for individual breaths (forty in each steady state).

2. Five healthy subjects were studied in steady-state exercise on a bicycle ergometer breathing air; three of them were also studied in hypercapnia, at rest and during exercise, and two of them also during exercise on a treadmill.

3. Tidal volume and respiratory frequency both increased with work load. The increase in frequency was largely due to a progressive decrease in  $T_E$ ;  $T_I$  also decreased.

4. At any constant level of respiratory drive (constant work load or chemical load)  $V_T$  was positively correlated with both  $T_I$  and  $T_E$  in more than 95 % of cases.

5. A simple model of the respiratory cycle which fits both the observed mean and breath-by-breath patterns and which involves no new assumptions is presented.

### INTRODUCTION

The study of the regulation of breathing pattern has been intensified during the last decade in an attempt to clarify the mechanisms involved. In the earlier studies the classic variables were studied: ventilation ( $\dot{V}_E$ ), tidal volume ( $V_T$ ) and respiratory frequency ( $f$ ) or its reciprocal, total breath duration ( $T_T$ ) (e.g. Hey, Lloyd, Cunningham, Jukes & Bolton, 1966; Euler, Herrero & Wexler, 1970). More recently the subdivisions of total breath duration, inspiratory ( $T_I$ ) and expiratory ( $T_E$ ) duration have also been studied (e.g. Clark & Euler, 1972).

The mean pattern of breathing in man at different steady states obtained

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by chemical stimulation has recently been described as a virtually constant  $T_I$  and a decrease in  $T_E$  with increasing  $V_T$  (Cunningham & Gardner, 1972). A similar mean pattern in early exercise whilst ventilation was still increasing has been reported by Jennett, Russell & Warnock (1974). The pattern in steady-state exercise has not previously been described in this way (but see Kelman & Watson, 1973). In conscious man, however, breathing is not completely regular, and breath-by-breath studies may lead to further knowledge of the factors affecting the pattern. In the steady state at rest and during  $\text{CO}_2$ -breathing it has been shown that  $V_T$  and  $T_T$  are positively correlated breath by breath (Priban, 1963; Dejours, Puccinelli, Armand & Dicharry, 1966; Cunningham, Pearson & Gardner, 1973) as are  $V_T$  and  $T_I$  (Newsom Davis & Stagg, 1973). Information about these relationships over a wider range of ventilations is, however, scanty. They have not been studied in exercise breathing air, and the possible contribution of changes in  $T_E$  to the breath-by-breath changes in  $T_T$ , finally, has not previously been examined.

The present study consequently describes both the mean and the breath-by-breath pattern of breathing air in steady-state exercise, and also the effect of adding  $\text{CO}_2$  to the inspired air during exercise. A short communication of part of this work has been presented (Kay, Petersen & Vejby-Christensen, 1975*a*).

#### METHODS

The experiments underlying these results were described in a previous paper (Kay, Petersen & Vejby-Christensen, 1975*b*) where the full method is given.

Five healthy subjects (18–22 years old) were studied during steady-state exercise of different intensities (50–200 W) on a bicycle ergometer (Ergotest, Jaeger, Würzburg). The pedalling rate was either 50 or 70 rev/min. Breathing was recorded in open circuit spirometry; the wedge spirometer (Oxford Instruments, Oxford) was emptied during the inspirations (cf. Cunningham, Lloyd, Miller, Spurr & Young, 1965). For each breath the inspiratory duration ( $T_I$ ), the expiratory duration ( $T_E$ ) and the expired tidal volume ( $V_T$ ) were recorded with a multi-channel hot-stylus recorder (M8 Devices Ltd, Welwyn Garden City) ( $V_T$ : 1 l. = 20 mm,  $T_I$ ,  $T_E$  and  $T_T$ : 1 sec = 10 mm).

Runs of 40 breaths from each steady state were analysed. Irregular breaths were excluded in collecting the forty, if: (1)  $V_T > 1.5$  times the mean  $V_T$  value or, (2)  $T_I > \text{twice}$  the mean  $T_I$  value, or (3) mis-recording occurred. The two breaths following such irregularities were also discarded.

In all the experiments mentioned above the subjects inspired air. In three of the subjects exercise was also performed in hypercapnia. Such sessions consisted of (1) 6 min work (80 W at 70 rev/min) on the bicycle ergometer breathing air, (2) 10 min at rest breathing air with 15 torr  $\text{CO}_2$  added followed by 6 min work breathing 15 torr  $\text{CO}_2$ , and (3) a period as (2) with 25 torr  $\text{CO}_2$  in the inspired air. The subjects rested for half-an-hour between periods. Recordings were made as in the first series from each of the five conditions.

Data from the treadmill experiments described in the previous paper (Kay *et al.* 1975*b*) have also been analysed breath by breath.

RESULTS

*Mean pattern of breathing*

Data presented in the previous paper (Kay *et al.* 1975*b*) have been replotted in Fig. 1. The figure shows for one subject the  $V_T:T_I:T_E$  relations from the steady state of bicycle ergometer work at different intensities. Presenting  $T_I$  to the right, and  $T_E$  to the left of the same origin and on the same axis separates the points representing the variables; furthermore  $T_T$  may be obtained as the horizontal distance between the points. It is seen that both  $T_I$  and more markedly  $T_E$  decreases with increasing  $V_T$ ; no difference is seen between the patterns obtained at the two pedalling speeds (cf. Kay *et al.* 1975*b*).

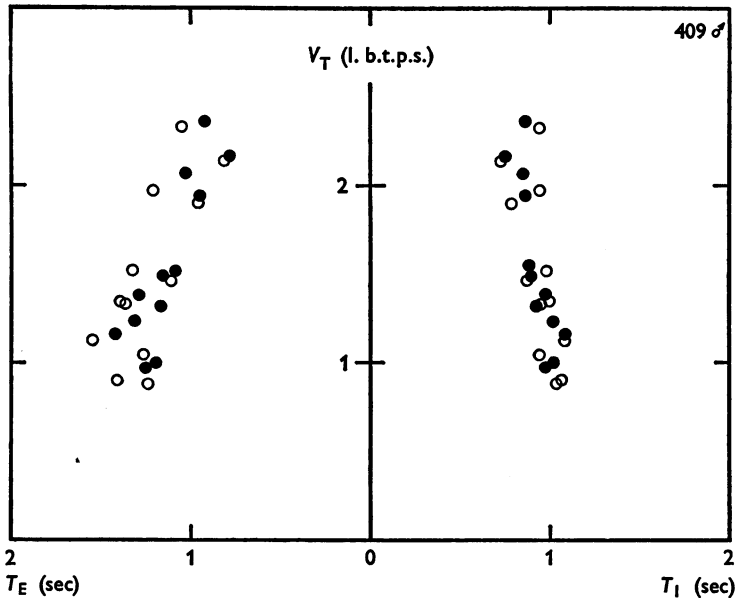


Fig. 1. Tidal volume ( $V_T$ ) plotted against inspiratory duration ( $T_I$ ) to the right and against expiratory duration ( $T_E$ ) to the left for subject 409 during bicycle ergometer exercise.  $\circ$ , runs performed at 50 rev/min;  $\bullet$ , runs performed at 70 rev/min. Each point represents the mean values of forty breaths in a steady state. Note common origin of  $T_I$  and  $T_E$  on the  $x$ -axis.

The  $V_T:T_I$  and the  $V_T:T_E$  relations for each subject were calculated by regressing each variable on  $\dot{V}_{CO_2}$  (see Table 1 in Kay *et al.* 1975*b*) and solving the linear equations. The form of the solution is:  $T_x = aV_T + b$ ; the values of  $a$  and  $b$  and the correlations of  $V_T$  with  $T_E$  and  $T_I$  are given in Table 1. Table 1 and Fig. 1 show that absolute changes in  $T_I$  are smaller than those in  $T_E$  and contribute less to the decrease in  $T_T$  (or increase in

respiratory frequency) as respiratory drive and  $V_T$  increase. In the range studied the relations between  $V_T$  and  $T_I$  and between  $V_T$  and  $T_E$  are described as linear, and there is no sign of any break-point. The values of  $a$  (changes in phase duration expressed as msec/l. increase in  $V_T$ ) in Table 1 indicate the relative shortening of inspiration and of expiration for each subject. On average the change in  $T_I$  contributed less than one-third to the total change in  $T_T$  (calculated as  $a_I/(a_I + a_E)$ ).

The results from the  $\text{CO}_2$  stimulation experiments and the treadmill experiments in subject 409 (cf. Fig. 1) are shown in Fig. 2 together with the lines for the mean pattern of breathing in bicycle exercise. Apart from the points showing the effect of  $\text{CO}_2$  breathing at rest all points lie near the  $V_T:T_I$  and the  $V_T:T_E$  lines from the original bicycle experiments. The different stimuli thus seemed to produce a similar pattern of breathing in the range of overlap.

TABLE 1

Subject	n	Inspiration $T_I = aV_T + b$			Expiration $T_E = aV_T + b$		
		a	b	r	a	b	r
		(msec l. <sup>-1</sup> b.t.p.s.)	(msec)		(msec l. <sup>-1</sup> b.t.p.s.)	(msec)	
454	24	-255	1371	-0.556**	-603	2104	-0.735**
409	24	-165	1186	-0.742**	-363	1732	-0.780**
438	24	-200	1316	-0.254	-556	2150	-0.653**
445	22	-92	1113	-0.347	-294	1706	-0.436*
439	12	-374	1815	+0.022	-1283	3782	-0.529

Solution to the equation  $T_x = aV_T + b$ , where  $x$  is I or E. Each of the variables was regressed on  $\dot{V}_{\text{CO}_2}$ , and  $\dot{V}_{\text{CO}_2}$  was subsequently eliminated. In each correlation ( $T_x$  and  $V_T$ ) degrees of freedom =  $n - 2$ . Only points obtained in bicycle exercise breathing air have been included. (\* =  $P < 0.05$ ; \*\* =  $P < 0.01$ .)

### Breath-by-breath pattern of breathing

In the previous description of the results only the mean values of the variables in the forty breaths analysed from each steady state have been used. The individual breaths and the breath-by-breath variation at each of these steady states has also been analysed.

In Fig. 3 each of the forty breaths from one steady state of work is shown in the  $V_T:T_I:T_E$  diagram. A positive correlation between  $V_T$  and  $T_I$  and between  $V_T$  and  $T_E$  is seen. In this example both the correlations are highly significant ( $p < 0.01$ ). In Fig. 4 the mean values for steady-state bicycle ergometer work are shown together with the regression lines of  $T_I$  or  $T_E$  on  $V_T$  for each point for subject 409. The lines have been drawn of equal length and do not indicate the actual scatter of the forty breaths. In

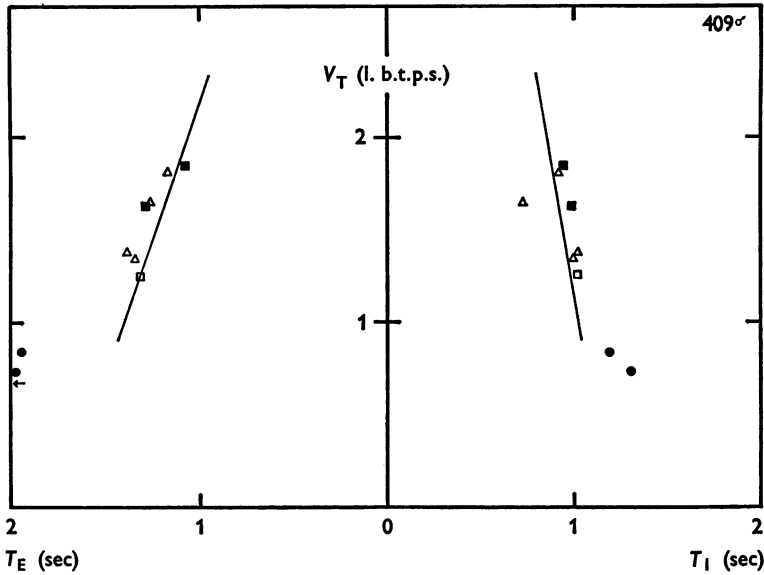


Fig. 2. The lines fitted to the points of Fig. 1 are shown. Points obtained under different forms of stimulation have been added:  $\Delta$ , treadmill exercise;  $\bullet$ , hypercapnia at rest;  $\square$ , normocapnic bicycle exercise;  $\blacksquare$ , hypercapnic bicycle exercise. The lowest level of drive produced a  $T_E$  of 2.8 sec (this point is marked with an arrow as it lies beyond the scale; the corresponding  $T_I$  is well within the scale). Each point represents the mean value of forty breaths in a steady state.

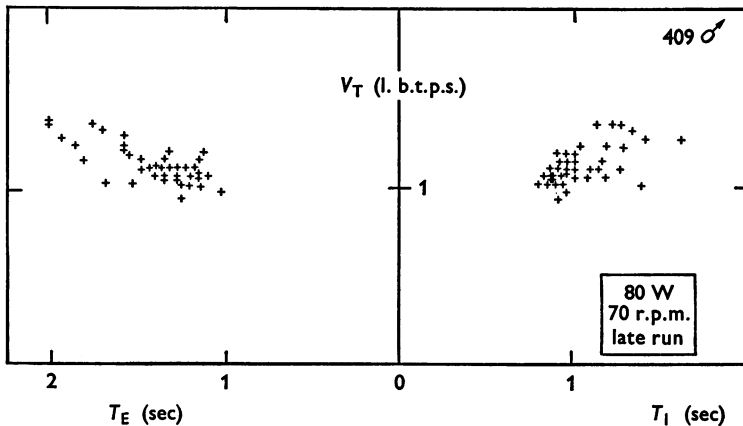


Fig. 3. The forty breaths from a single steady state (subject 409, 80 W, 70 rev/min, late run) are shown.

this subject nearly all correlations were positive and significant ( $p < 0.05$ ). A similar diagram for subject 438 may be found in our earlier communication (Kay *et al.* 1975*a*).

In a total of 106 steady-state determinations each of forty breaths in bicycle ergometer work breathing air in five subjects,  $V_T$  and  $T_I$  were positively correlated in 103 runs and  $V_T$  and  $T_E$  in 102 runs. A similar breath-by-breath analysis of the determinations made in hypercapnia at rest and during work, and during treadmill exercise, also revealed positive correlations between  $V_T$  and  $T_I$  and between  $V_T$  and  $T_E$ .

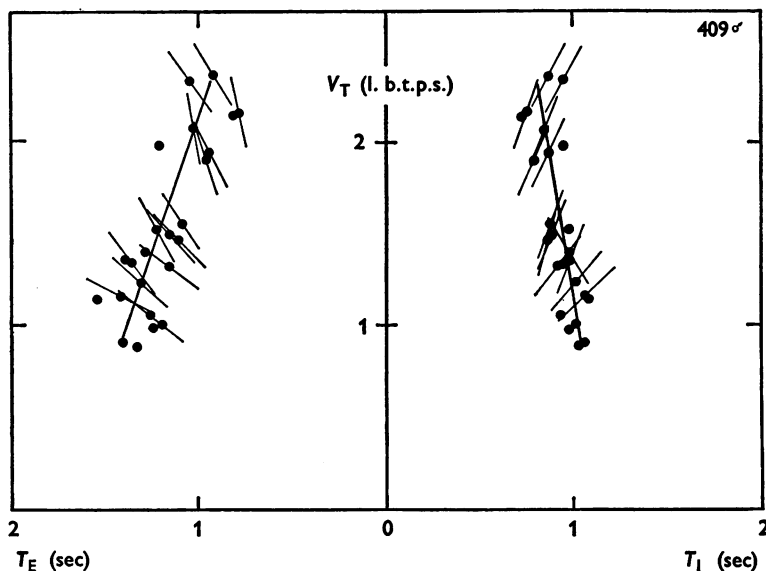


Fig. 4. The two long continuous lines from Fig. 2 are shown. Through the points from Fig. 1 regression lines of  $T_I$  and  $T_E$  against  $V_E$  have been drawn where their correlation was significantly different from zero. These short lines are of equal length and do not reflect the scatter around the mean. Each of the short lines is derived from a distribution analogous to that shown in Fig. 3.

The scatter of  $T_I$  as measured by the coefficient of variation and its correlation with the level of respiratory drive ( $\dot{V}_{CO_2}$ ) are shown in Table 2. No consistent effect of drive appears. The mean coefficient of variation of  $T_E$  was of the same magnitude as that of  $T_I$ .

TABLE 2

Subject	<i>n</i>	CV of $T_I$ (%)	Rank correlation of CV( $T_I$ ) with $V_{CO_2}$
454	24	12	n.s.
409	24	8	+ 0.37 ( $P < 0.05$ )
438	24	16	n.s.
445	22	15	- 0.06 ( $P < 0.01$ )
439	12	16	n.s.

$$CV = \text{coefficient of variation} = \frac{SD}{\text{mean}}$$

The Spearman test of rank correlation has been used (Sokal & Rohlf, 1968)  
n.s. = not significant.

## DISCUSSION

The present study has revealed a consistent *mean pattern of breathing* in steady-state exercise in five healthy human subjects: progressive changes in tidal volume ( $V_T$ ) and total breath duration ( $T_T$ ) with increasing work load; the changes in  $T_T$  being due to changes in  $T_E$  and to a smaller extent also in  $T_I$ .

Neither Cunningham & Gardner (1972) in the steady states during chemical stimulation of breathing, nor Jennett *et al.* (1974) during re-breathing and in the early period of exercise observed any change in  $T_I$  when  $V_T$  increased. Clark & Euler (1972) also studying rebreathing in man agree with this description at low  $V_T$ . They did, however, in most cases observe a break-point at a  $V_T$  of 1.5–2 times its resting level above which  $T_I$  decreased hyperbolically. This finding has been confirmed by W. N. Gardner in an extension of his earlier studies (personal communication). No such break-point was observed in the present study. Our  $V_T:T_I$  findings might be interpreted as representing part of a hyperbola (or some other function). The absence of data at low and high ventilatory drives, and the relatively narrow range of observed  $T_I$  values would, however, make any attempt of a curvilinear description rather pointless. The same applies to expiration; the relationship between  $V_T$  and  $T_E$  seems to be curvilinear when a wider range of  $V_T$  is considered (Cunningham & Gardner, 1972). Our points at low drive produced by mild hypercapnia at rest (Fig. 2) also illustrate this phenomenon.

The finding of a nearly constant  $T_I$  with increasing drive suggests that the termination of inspiration is accomplished by a 'clock' (a pneumotaxic mechanism, see Euler *et al.* 1970), and that volume feed-back mediated via

pulmonary stretch-receptors and the vagi (e.g. Guz, Noble, Eisele & Trenchard, 1970) at least within these volume ranges is of little importance. Several factors may, however, complicate the interpretation of the  $V_T:T_I$  relations observed in different studies. Chemical stimulation may have an opposing effect to that of lung volume on the inspiratory off-switch mechanisms as suggested by Bradley, Euler, Marttila & Roos (1974). Cortical influences, neural stimuli related to exercise, and associated changes in central temperature might all influence the 'clock' mechanisms. Finally, of particular relevance in relation to the occurrence of break-point, absolute changes in end-inspiratory volume rather than changes in tidal volume should be considered. Measurements of the functional residual capacity (FRC), unfortunately, have not been carried out in any of the quoted studies including our own. If FRC had decreased more with increasing  $V_T$  in our study in exercise than it did in the study of Clark & Euler, a comparable degree of inflation of the lungs (and hence the break-point level) might not have been reached by us in spite of our larger  $V_T$  range. Significant decreases in FRC have been reported in exercise (Asmussen & Christensen, 1939; Linnarsson, 1974), whereas C. S. Garrard & D. J. Lane (personal communication) in rebreathing studies in man using a body-box found no changes in FRC.

Taking these various factors into consideration the different studies have revealed a remarkably uniform pattern. This suggests that the magnitude of the drive (as reflected by the total ventilation) rather than the nature of the drive determines the selection of breathing pattern.

Tidal volume and total breath duration are positively correlated from breath to breath in man (Prihan, 1963; Dejours *et al.* 1966; Cunningham *et al.* 1973) and in the cat (Euler *et al.* 1970). This results in ventilation being more constant than either of its components. Our results in exercise confirm this finding (cf. Fig. 3 and 4). The breath-by-breath changes in  $V_T$  and  $T_T$  cross rather than follow the pattern described between steady states.

If the drive to respiration determines the rate of inflation of the lungs, as suggested by Euler *et al.* (1970) and Clark & Euler (1972), small variations in the 'clock' will result in a positive correlation between  $V_T$  and  $T_I$  in any steady state. Our results agree with this hypothesis. Volume information from the lungs does not seem essential for the termination of inspiration in the range presently studied (cf. Clark & Euler, 1972; Widdicombe, 1974).

Clark & Euler (1972) suggested that there was a linear relation between  $T_I$  and  $T_E$  over both of their ranges, in cats and in humans. It is important to ascertain whether both durations are selected by distinct mechanisms, or whether their relationship appears through their mutual linkage with end-inspiratory volume. The effects of changes in lung volume in the dog



(Bartoli, Bystrzycka, Guz, Jain, Noble & Trenchard, 1973) and airflow studies in the cat (Gautier, Remmers & Bartlett, 1973) provide evidence for separate mechanisms.

We found a highly significant shortening of  $T_E$  with increasing  $V_T$  on comparing mean values obtained in the steady states of exercise of increasing intensity (e.g. a negative correlation between  $V_T$  and  $T_E$ ). In any

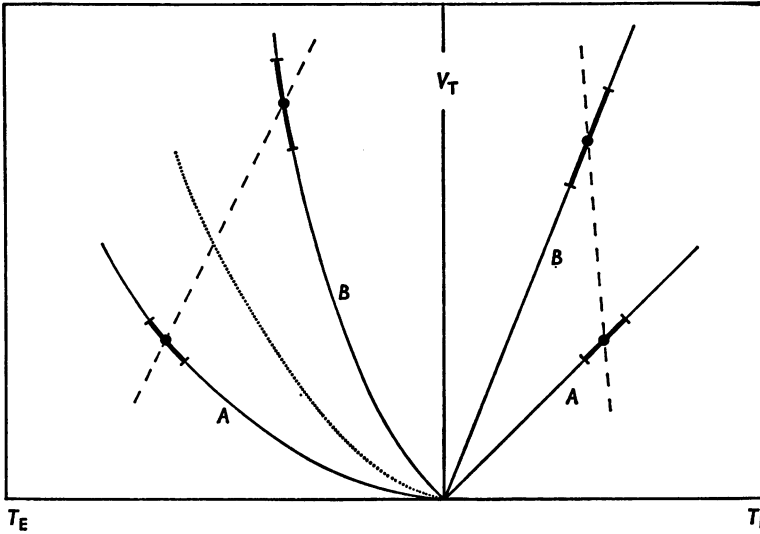


Fig. 5. A theoretical diagram showing the pattern obtained at two arbitrary levels of drive (A and B). The continuous lines represent the volume changes through a complete respiratory cycle. The dashed lines indicate idealized the pattern of change of  $T_I$  and  $T_E$  with change in respiratory drive (cf. Fig. 2), and the heavily drawn part of the continuous lines crossing these, the breath-by-breath pattern (cf. Fig. 4). The dotted line represents a passive expiration. See Text for further explanation.

given steady state a positive correlation between  $V_T$  and  $T_E$  from breath to breath was found in 96 % of runs.

If  $T_E$  was solely determined by *end-inspiratory volume* the same relation of  $V_T$  and  $T_E$  would maintain whether breaths from the same level of drive, or from different levels were compared. If, on the other hand, the duration of expiration was solely determined by *drive* no positive correlation between  $V_T$  and  $T_E$  would be expected to occur from breath to breath, and at a constant drive  $T_E$  would not be affected by variations in end-inspiratory volume. A certain variation in  $T_E$  (cf. discussion of inspiration) might still occur. As, however, at least at lower levels of ventilation, flow in the latter part of expiration is very low, and almost exponentially approaches 0, such small variations would not be expected to have any large effect on

the expired volume. At large  $V_T$  such variations might contribute to the observed positive correlation between  $V_T$  and  $T_E$ .

We conclude that  $T_E$  seems to be determined by both the drive and the end-inspiratory volume.

The operation of inflation and deflation reflexes during the expiratory phase has been studied in the anaesthetized cat by Knox (1973).

A model of the respiratory cycle which fits both the mean and the breath-by-breath pattern found and which involves no new assumptions is illustrated in Fig. 5. To the right are shown two inspiratory lines as might be produced by different levels of respiratory drive (cf. Clark & Euler, 1972) and a dashed line representing the termination of inspiration by the 'clock'. At an increased drive (line *B* compared to line *A*) tidal volume increases and the inspiratory duration decreases slightly producing the observed mean pattern (compare the two points shown in Fig. 5 with those in Fig. 1). Variations in the 'clock' result in termination of inspiration at slightly different times and volumes. The positive breath-by-breath correlation between  $V_T$  and  $T_I$  is thus produced (compare the short thick lines of Fig. 5 with those of Fig. 4). At higher levels of drive (larger end-inspiratory volumes) than those studied, a more marked shortening of inspiration may be caused by the Hering-Breuer inflation reflex producing a break-point as described by Clark & Euler (1972) (see also Widdicombe, 1974; Cunningham, 1974).

To the left in Fig. 5 the relation between  $V_T$  and  $T_E$  is shown at the two levels of drive. The continuous lines ending at the origin describe the decrease of lung volume during expiration. The slope of these lines at any point represents the instantaneous expiratory flow rate. The dotted line between these two represents passive recoil, in other words this line shows the rate of lung emptying during a passive expiration. Different 'recoil' lines may be followed if the compliance and resistance of the respiratory system or the driving (alveolar) pressure change. The effect of the variable laryngeal resistance in this respect has recently been quantified (Bartlett, Remmers & Gautier, 1973). An increase in the slope of the 'recoil' line (movements from the passive line towards line *B* in Fig. 5) could result from activation of expiratory muscles causing an increased driving pressure (cf. Gautier *et al.* 1973). A decrease in the slope (movement towards line *A*) could result from an increase in airway resistance (cf. Bartlett *et al.* 1973; Gautier *et al.* 1973), or from braking by continued contraction of inspiratory muscles into expiration which decreases the driving pressure (cf. Brody, 1954; Green & Howell, 1959; Petit, Milic-Emili & Delhez, 1960). The ranges in which these three mechanisms operate may well overlap. Small changes in end-inspiratory volume at any level of drive (and thus on the same recoil line) produce positively correlated changes in the

duration of expiration (compare the short thick lines of Fig. 5 with those of Fig. 4). The dashed line crossing the recoil lines represents the mean pattern at different levels of drive (compare the two points shown in Fig. 5 with those in Fig. 1). Increased drive affects the mechanisms described above which determine the mechanical properties and the driving pressure and results in a shift towards steeper 'recoil' lines (line *B* compared to line *A*). The decrease in mean  $T_E$  now occurs because the increased slope of the 'recoil' line overrides the increased end-inspiratory volume with increasing drive.

Expired tidal volume was measured in this study and it was assumed that the preceding inspired tidal volume did not differ systematically.

Breath-by-breath changes in the functional residual capacity have been described by Hlastala, Wranne & Lenfant (1973) in resting humans, and although an occasional large shift (rarely above 300 ml., once in every 200–400 breaths) in functional FRC was observed, the largest systematic change, the major oscillation, gives a value of less than 3 ml. per breath which is much less than the sensitivity of the present study.

The results of Asmussen & Christensen (1939) and Linnarsson (1974) indicate that the increased  $V_T$  during exercise encroaches on both the inspiratory and the expiratory reserve volumes to almost the same extent causing a decrease in FRC. If in Fig. 5 the  $V_T$  axis represents total lung volume, the implication of this would be that the lines labelled *B* should start at a point below the *x*-axis, and end at a correspondingly lower point causing an increased slope of the lines connecting mean  $T_I$  and  $T_E$  values. The basic argument as presented above, however, would not be affected.

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