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Maximum rate of change in oesophageal pressure assessed from unoccluded breaths: an option where mouth occlusion pressure is impractical

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Maximum rate of change in oesophageal pressure assessed from unoccluded breaths: an option where mouth occlusion pressure is impractical. C-H. Hamnegård, M.I. Polkey, D. Kyroussis, G.H. Mills, M. Green, B. Bake, J. Moxham. ©ERS Journals Ltd 1998.

ABSTRACT: The mouth occlusion pressure 100 ms after onset of inspiration ($P_{0.1}$) is considered a clinically useful measure of the combined output of the respiratory centre and muscle pump. However, theoretical and practical difficulties can arise when using $P_{0.1}$ in the assessment of patients with severe chronic obstructive pulmonary disease (COPD). It was hypothesized that the maximum rate of change in oesophageal pressure ($dP_{oes,max}/dt$) may be an alternative to $P_{0.1}$.

To test this hypothesis $P_{0.1}$ was compared with mean $dP_{oes,max}/dt$ measured from neighbouring unoccluded breaths in five normal subjects during CO_2 rebreathing.

In all subjects a close correlation was found between both $dP_{oes,max}/dt$ and $P_{0.1}$ and carbon dioxide tension (P_{CO_2}). In six patients with severe COPD performing exhaustive treadmill walks, $dP_{oes,max}/dt$ was found to increase progressively with walking time. Mean $dP_{oes,max}/dt$ at the start was 6.2 $cmH_2O \cdot 100\ ms^{-1}$ and at the finish was 18.7 $cmH_2O \cdot 100\ ms^{-1}$ ($p<0.03$).

In conclusion, the maximum rate of change in oesophageal pressure measured from unoccluded breaths could be an alternative in circumstances where it is not feasible to use measurements of the mouth occlusion pressure 100 ms after onset of inspiration.

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In animals phrenic nerve activity is related to pressure in the trachea 100 ms after the onset of inspiration [1] and thus in humans the measurement of mouth occlusion pressure 100 ms after onset of inspiration ($P_{0.1}$) against a closed shutter has been suggested as a measure of central drive [2, 3]. $P_{0.1}$ is widely used in clinical studies and considered to be of practical value [4–6]. However, various technical issues raise concerns about the validity and suitability of $P_{0.1}$ in patients with chronic obstructive pulmonary disease (COPD). In conscious COPD patients, for example those undertaking heavy treadmill exercise, the sensation of airway occlusion may be uncomfortable and it can be technically difficult to mount an occlusion valve close to the mouth. Incomplete transmission of pressure between pleura and mouth diminishes the accuracy of $P_{0.1}$ in COPD, particularly if the mechanical properties of the lung change as, for example, during exercise [7]. Finally, even if $P_{0.1}$ is measured from oesophageal pressure (P_{oes}) difficulties may still occur because of uncertainty in deciding at exactly which point the inspiratory downturn in P_{oes} occurs [8]. Moreover, if, as is usual, there is positive end-expiratory pressure (PEEP), the first 100 ms of inspiration as judged by the P_{oes} does not correspond to the first 100 ms as judged by mouth pressure (P_{mo}).

The maximum rate of pressure change measured at the mouth (dP_{mo}/dt) is a possible alternative to $P_{0.1}$ in both normal subjects and patients with COPD [9]. However, varying values for dP_{mo}/dt can be obtained if different parts of the first 200 ms of the inspiratory cycle are examined separately [10]. In severe COPD, because of intrinsic PEEP, the first portion of inspiration is not transmitted to the mouth. Consequently, the measured dP_{mo}/dt does not necessarily correspond to the maximal rate of change in oesophageal pressure ($dP_{oes,max}/dt$). Moreover, to measure dP_{mo}/dt a brief upper airway occlusion is still required. It was hypothesized that in normal subjects there might be a close relationship between $dP_{oes,max}/dt$ obtained from unoccluded breaths and $P_{0.1}$. Thus, in this study $P_{0.1}$ and $dP_{oes,max}/dt$ were compared in normal subjects over a range of values induced by CO_2 rebreathing. In the second part of the study $dP_{oes,max}/dt$ was measured in a group of subjects with COPD undergoing exhaustive treadmill exercise. This model was chosen since it was considered to represent an environment where measurement of $P_{0.1}$ presents substantial technical difficulties and also because in a previous study the instantaneous rate of change of transpulmonary pressure was shown to increase with exercise [11].

Subjects and methods

The study comprised two protocols; in the first the relationship between $dP_{oes,max}/dt$ and $P_{0.1}$ was examined in five healthy male subjects who were members of the laboratory staff. In the second $dP_{oes,max}/dt$ observed during exhaustive treadmill walks performed by six males with severe COPD (mean forced expiratory volume in one second (FEV1) 0.61 L) was examined as part of a series of studies investigating respiratory muscle work, aspects of which have been presented elsewhere [12–15]. The protocols were approved by the Ethics Committee and all subjects gave their written informed consent.

Data acquisition and analysis

*P*oes was recorded using a conventionally placed balloon catheter (PK Morgan, Rainham, UK). The catheter position was checked using the technique of BAYDUR *et al.* [16]. For study 1, mouth pressure was sampled from a side port using a narrow lumen catheter. The catheters were connected to differential pressure transducers (Validyne MP45, Northridge, CA, USA), carrier amplifiers (PK Morgan), a 12-bit NBMIO-16 analogue-digital board (National Instruments, Austin, TX, USA) and a Macintosh Quadra Centris 650 personal computer (Apple Computer, Cupertino, CA, USA) running Labview™ software (National Instruments). The sampling rate was 100 Hz and the frequency response of the balloon catheter system was 20 Hz [17].

For data analysis *P*0.1 was defined as the pressure measured at the mouth after 100 ms of occluded inspiration. d*P*oes,max/d*t* was determined from the two breaths before and after an occluded inspiration. The mean of these values was used for analysis. The value of d*P*oes,max/d*t* was computed using a semiautomated modification of Labview software developed by the authors, in which the 50 ms epoch exhibiting the greatest rate of change in *P*oes was identified. To facilitate comparison d*P*oes,max/d*t* was arbitrarily assigned units of $cmH_2O \cdot 100\ ms^{-1}$.

Protocol study 1

To obtain values for *P*0.1 and d*P*oes,max/d*t* over a range of values subjects performed CO_2 rebreathing using a modification of the circuit described by READ [18]. In the present study circuit occlusion was achieved by rapid and inaudible inflation of a balloon invisible to the subject in the inspiratory limb of the circuit. The balloon was inflated in expiration and automatically deflated 130 ms after the start of negative mouth pressure. The timing of the occlusions was determined randomly using a custom-designed modification of Labview software. End-tidal CO_2 was sampled from a port in the expiratory limb and analysed (Beckmann Medical Gas analyser LB-2, Stockholm, Sweden) and these data were digitized and stored on to a personal computer (see above). Two runs were performed by each subject.

Protocol study 2

The exhaustive runs were performed by subjects with severe COPD who were experienced in exhaustive treadmill walking. Treadmill walks were performed at a fixed speed determined before the study day to be the subject's habitual brisk walk. Subjects were given strong verbal encouragement to continue until severe dyspnoea forced them to stop.

Statistics

For study 1, correlations between both *P*0.1 and carbon dioxide tension (P_{CO_2}) and d*P*oes,max/d*t* and P_{CO_2} were sought using simple regression analysis. Data for *P*0.1 and d*P*oes,max/d*t* were compared using simple regression. The regression coefficients were tested by the use of t-distributed test statistics. For study 2, the relationship between d*P*oes,max/d*t* and walking time was sought using simple regression analysis and differences between the start and finish of walking were tested using Wilcoxon's Signed Rank test. All statistics were computed using Statview 4.0 (Abacus Concepts, Berkeley, CA, USA).

Results

Study 1

Typical pressure tracings are shown in figure 1. In each subject a highly significant correlation was found ($p< 0.0001$) between both d*P*oes,max/d*t* and *P*0.1 and P_{CO_2}. The

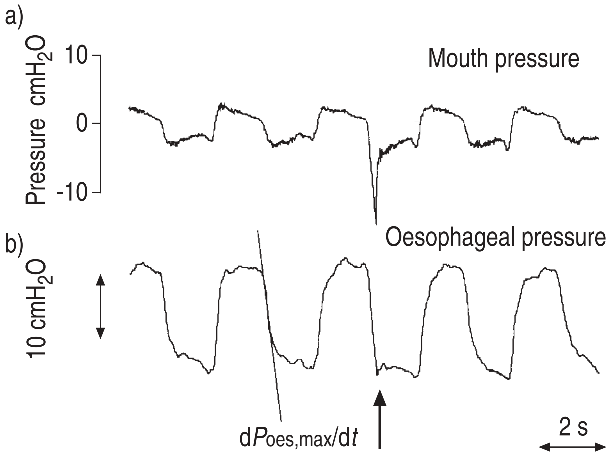

Fig. 1. – Example trace from a typical subject. a) Mouth pressure and b) oesophageal pressure have been vertically separated for clarity of presentation. ↑: occluded breath. The maximum rate of change in oesophageal pressure (d*P*oes,max/d*t*) was measured from the steepest portion of neighbouring unoccluded breaths.

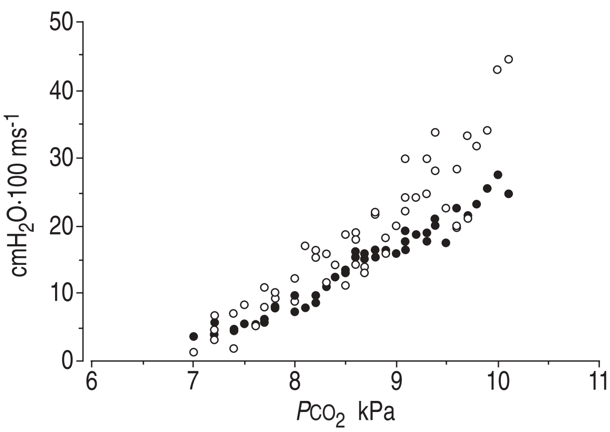

Fig. 2. – Representative data from one subject showing the relation between carbon dioxide tension (P_{CO_2}) and both the mouth occlusion pressure 100 ms after onset of inspiration (*P*0.1) (○) and the maximum rate of change in oesophageal pressure (d*P*oes,max/d*t*) (●).

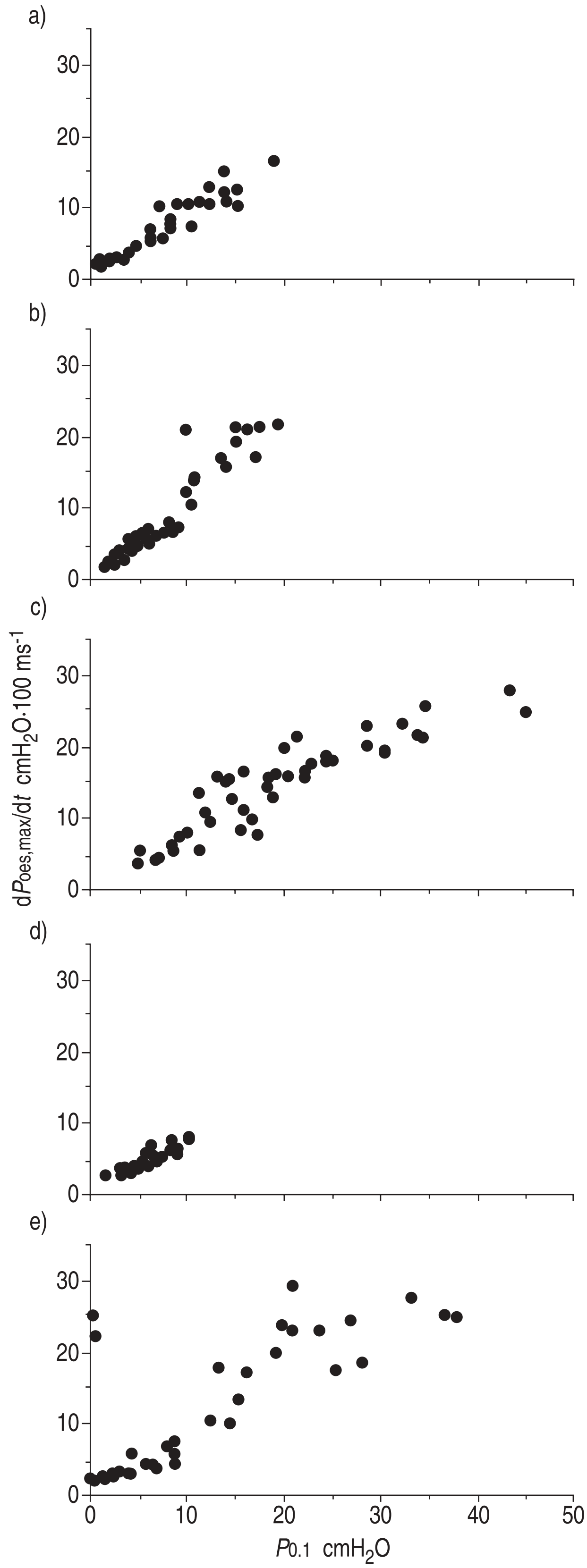

Fig. 3. – Relationship between the mouth occlusion pressure 100 ms after onset of inspiration ($P_{0.1}$) and the maximum rate of change in oesophageal pressure (d$P_{oes,max}$/dt) in normal subjects (n=5). a) Subject 1, r=0.95; b) subject 2, r=0.95; c) subject 3, r=0.91; d) subject 4, r=0.89; and e) subject 5, r=0.80.

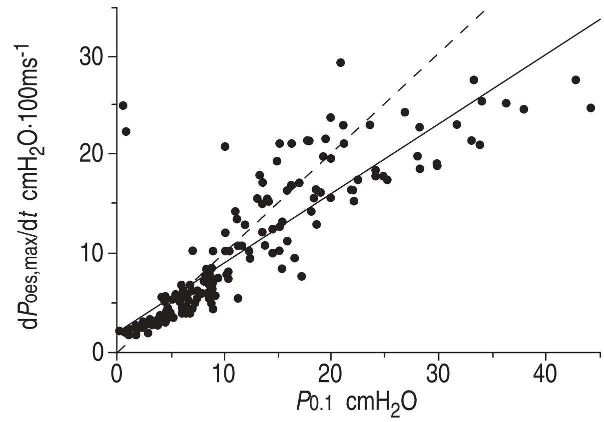

Fig. 4. – Group data regression plot for the mouth occlusion pressure 100 ms after onset of inspiration ($P_{0.1}$) against the maximum rate of change in oesophageal pressure (d$P_{oes,max}$/dt); ——: regression line; – – : line of identity. For a fuller explanation see the Results section.

strength of this correlation for d$P_{oes,max}$/dt was, in each case, equal or superior to that observed for $P_{0.1}$ and results from a representative subject are shown in figure 2. A linear relation was found between $P_{0.1}$ and d$P_{oes,max}$/dt in each subject (fig. 3). Regression analysis of the group data is shown in figure 4. The intercept of the slope was significantly larger than zero ($p<0.001$), indicating that low values of d$P_{oes,max}$/dt may sometimes be obtained without a measurable $P_{0.1}$ (fig. 3). Moreover, the slope of the regression was significantly less steep than that of the line of identity ($p<0.001$); specifically, there was a trend for d$P_{oes,max}$/dt to yield lower numerical values than $P_{0.1}$ at higher values. However, on two occasions no $P_{0.1}$ was measured despite substantial values for d$P_{oes,max}$/dt, suggesting glottic closure.

Study 2

In each subject a progressive increase in d$P_{oes,max}$/dt was observed as walking time increased ($p<0.0001$ for each subject, mean r-value 0.78); a representative example is shown in figure 5. Data for all six subjects are shown in table 1. Mean d$P_{oes,max}$/dt at the start was 6.2 $cmH_2O \cdot 100\ ms^{-1}$ and at the finish was 18.7 $cmH_2O \cdot 100\ ms^{-1}$ ($p<0.03$). The mean minute ventilation at the end of exercise was 25 $L \cdot min^{-1}$.

Discussion

In study 1 it was shown that $P_{0.1}$ is closely related to the d$P_{oes,max}$/dt observed in neighbouring unoccluded breaths. This indicates that d$P_{oes,max}$/dt could be used to assess respiratory drive in circumstances where it is difficult or inappropriate to use $P_{0.1}$. In study 2 this method was retrospectively applied to data obtained from patients with severe COPD performing exhaustive treadmill walks.

Does it matter that unoccluded breaths are not isometric?

It is perhaps surprising that such a good relationship was found between d$P_{oes,max}$/dt and $P_{0.1}$ in normal subjects, given that unoccluded breaths are not isometric, although it should be noted that occluded inspiratory efforts are also not truly isometric. However, during occluded inspiration the highest values for dP_{mo}/dt are observed in the

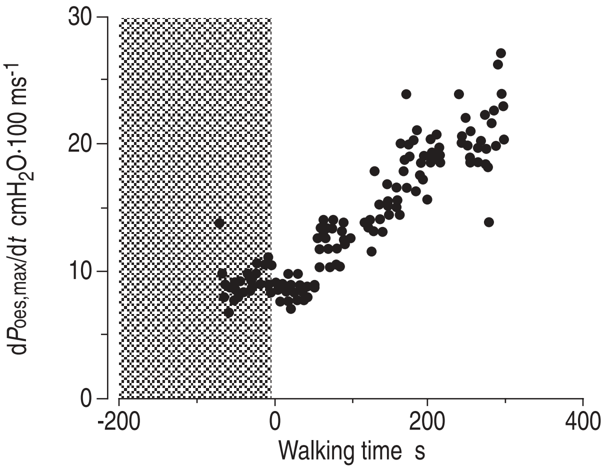

Fig. 5. – Plot of maximum rate of change in oesophageal pressure ($dP_{oes,max}/dt$) against walking time for a representative subject with chronic obstructive pulmonary disease. ▩ : pre-exercise.

first 75 ms [10]. At this point during quiet breathing inspiratory flow might typically be 500 mL·s^{-1} [10]; if so, the total volume change at the time of measurement of $dP_{oes,max}/dt$ would also be minimal. Conversely, during increased minute ventilation the volume change would be greater and this might account for the tendency for $dP_{oes,max}/dt$ to yield lower numerical values than $P_{0.1}$, particularly during hypercapnia (fig. 2).

For the measurements made in study 2 the steepest epoch of the P_{oes} trace was typically during the supra-atmospheric portion. At this point there was no airflow and the measurement may therefore be considered truly isometric, or at least isovolumic.

Validity of comparing $dP_{oes,max}/dt$ with $P_{0.1}$

Since $P_{0.1}$ is an established test it seemed logical to use it for comparison with $dP_{oes,max}/dt$. The use of $P_{0.1}$ is supported by the observation in animals that phrenic nerve activity is closely related to airway occlusion pressure [1]. Similarly, studies in anaesthetized humans suggest that occlusion pressure is a useful index of inspiratory activity [19]. Although it is necessary to consider possible confounding factors when using $P_{0.1}$ in clinical studies, the validity of $P_{0.1}$ in normal subjects undergoing CO_2 rebreathing has not been seriously questioned [3]. However, it is clear from the present data that, as noted above, $dP_{oes,max}/dt$ underestimates $P_{0.1}$ in normals at higher values of $dP_{oes,max}/dt$; this would be expected from the theoretical work of YOUNES and coworkers [19–21]. Nevertheless, although for normals $P_{0.1}$ seems superior to $dP_{oes,max}/dt$ (being longer established and noninvasive), the present data confirm a close relationship between $P_{0.1}$ and $dP_{oes,max}/dt$, suggesting a role for the latter where $P_{0.1}$ is impractical.

In figure 3 it is evident that, for two of the subjects, measurable (although small) values of $dP_{oes,max}/dt$ were obtained when the measured $P_{0.1}$ was zero. The authors believe that this is because when $dP_{oes,max}/dt$ is small the loss of pressure between the thorax and upper airway can lead to obliteration of the signal; this mechanism has previously been proposed by other investigators [22].

An additional advantage of the $dP_{oes,max}/dt$ technique is that data from the entire respiratory cycle may be obtained and stored for subsequent, more detailed analysis, for example of the pressure time product [15, 23]. However, because such analyses require manual checking they cannot accurately be performed in real time. By contrast, $dP_{oes,max}/dt$ may be obtained immediately by electrical differentiation of the P_{oes} signal [11, 24].

Effect of airway occlusion

Intuitively, one might anticipate that the airway occlusion itself may increase dP_{oes}/dt in the following breath; however, no significant difference was found between dP_{oes}/dt in the breath before and after airway occlusion. Nevertheless, to avoid this as a potential source of error the average of four breaths was used to obtain a value for $dP_{oes,max}/dt$; such an approach is legitimate since, with an oesophageal catheter *in situ*, modern computer software permits analysis of every breath, as for example in figure 5. In figure 4 it should be noted that there are occasional outliers where a substantial $dP_{oes,max}/dt$ was obtained despite a negligible $P_{0.1}$. This was probably due to glottic narrowing or closure and suggests another, albeit minor, potential disadvantage of the $P_{0.1}$ measurement.

Could an even simpler measure be used instead of $P_{0.1}$ or $dP_{oes,max}/dt$?

As the combined respiratory centre/pump output increases (for whatever reason) other parameters, for example respiratory frequency or tidal volume, which are easier to measure than either $dP_{oes,max}/dt$ or $P_{0.1}$, also increase. It could be argued that these could also be alternative measurements to $P_{0.1}$. However, such variables can be altered by many factors, for example lung mechanics [25].

Table 1. – Maximum rate of change in oesophageal pressure ($dP_{oes,max}/dt$) during exercise for patients with chronic obstructive pulmonary disease

Patient No.	Age	Height	Weight	FEV_1	$dP_{oes,max}/dt$		Minute ventilation L·min^{-1}	
					Start exercise	End exercise	Start exercise	End exercise
	yrs	m	kg	L	$cmH_2O·100\ ms^{-1}$	$cmH_2O·100\ ms^{-1}$		
1	71	1.69	90.8	0.5	10.3	28.9	18.5	29.0
2	53	1.66	51.8	0.6	4.4	27.6	13.2	37.9
3	73	1.68	76.0	0.8	6.5	11.7	9.1	15.3
4	53	1.68	49.4	0.5	3.5	8.7	18.0	35.1
5	67	1.70	73.0	0.7	4.0	13.7	15.0	23.2
6	66	1.73	92.0	0.6	8.4	21.6	7.5	9.2
Mean	64	1.69	72.2	0.6	6.2	18.7	13.6	25.0
SD	9	0.02	18.4	0.1	2.7	8.5	4.5	11.2

Patient 6 had had a lung resection in their youth. FEV_1: forced expiratory volume in one second.

Significance of the findings

As noted above, in many circumstances $P_{0.1}$ has clear practical and theoretical advantages over d$P_{oes,max}$/dt. However, $P_{0.1}$ is not a reliable measure of respiratory drive in COPD and conflicting results have been obtained [5, 7, 8]. When such patients face increased respiratory muscle load, as for example during exercise, $P_{0.1}$ becomes especially difficult because the patients are obliged to use a mouthpiece. The method described here is simple and does not require airway occlusion (and hence the use of a mouthpiece or face mask). Furthermore, by selecting the maximal rate of change it does not require a judgement to be made on where inspiration starts. By measuring P_{oes} it minimizes concerns relating to incomplete pressure transmission. It is acknowledged that there may be differing airway time constants in different areas within an emphysematous lung; however, compared with a test based on P_{mo} this would still leave d$P_{oes,max}$/dt at a relative advantage.

d$P_{oes,max}$/dt was found to increase in a progressive and linear fashion when patients with COPD exercised. This observation is consistent with data reported by SUERO and WOOLF [11]; however, the contrast with respect to the quantity of data obtainable using a modern system is striking. Whereas all of the subjects in the present study could be analysed completely, SUERO and WOOLF [11] were only able to obtain complete data on two of their five subjects. In this study, d$P_{oes,max}$/dt did not fall at the time of exercise cessation; this seems to make a reduction in central drive unlikely as a cause of exercise termination. This is also consistent with other data obtained from patients with COPD during respiratory loading [5]. The possibility cannot be excluded that there was a gradual partial failure of central drive without which d$P_{oes,max}$/dt would have risen even more steeply. However, the rise observed (approximately threefold) was substantial and, as noted above, probably an underestimate.

In conclusion, the maximal rate of change of oesophageal pressure was shown to be closely related to the mouth occlusion pressure 100 ms after onset of inspiration in normal subjects. In the model of exhaustive treadmill walking in patients with severe chronic obstructive pulmonary disease, the maximal rate of change of oesophageal pressure was shown to increase progressively until the point of exercise cessation. This could, therefore, be a clinically useful technique in situations where measurement of the mouth occlusion pressure 100 ms after onset of inspiration is technically difficult.

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