J. Physiol. (1959), **149**, *pp.* 494–499
With 2 text-figures
Printed in Great Britain

CONSCIOUS APPRECIATION OF THE EFFECTS PRODUCED BY INDEPENDENT CHANGES OF VENTILATION VOLUME AND OF END-TIDAL pCO_2 IN PARALYSED PATIENTS

BY L. H. OPIE,* A. C. SMITH AND J. M. K. SPALDING

From the Nuffield Department of Anaesthetics, and the Respiration Unit, Department of Neurology, United Oxford Hospitals

(*Received* 17 *June* 1959)

In the normal subject changes in end-tidal carbon dioxide tension (pCO_2) are accompanied by changes in ventilation, and it is difficult to assess the conscious appreciation of either independently. It is, however, practicable to do this in patients whose respiratory muscles have been paralysed by disease, and this communication reports the results of such an assessment.

METHODS

The patients were severely paralysed by poliomyelitis. Each received artificial ventilation from a Radcliffe respiration pump (Russell, Schuster, Smith & Spalding, 1956) through a cuffed tracheotomy tube (Spalding & Smith, 1956) which provided an air-tight seal in the trachea. The expired tidal volume was measured over 10 breaths at room temperature with a Parkinson & Cowan type CD gas-meter. The respiratory frequency was 16 per minute.

End-tidal samples were obtained by a mechanical sampler (Smith, Schuster & Spalding, 1959) and pCO_2 was determined by a continuous flow-bridge analyser (Cunningham, Cormack, O'Riordan, Jukes & Lloyd, 1957). The end-tidal pCO_2 was raised by adding CO_2 to the inspired air, and the tidal volume was altered by varying the inspiratory pressure. The controls for making these changes were hidden from the patient.

Throughout the examination the patient was asked to report any unusual sensations. Shortness of breath was the sensation in which we were particularly interested, but questions about this were specifically avoided.

RESULTS

Six patients with vital capacities varying from nil to 450 ml. were examined on ten occasions. The patients had a low initial end-tidal pCO_2, average 20 mm Hg (Table 1), as is often found in patients receiving continuous artificial respiration. When carbon dioxide was added to the inspired air, the patient did not notice any shortness of breath until the end-tidal pCO_2 had risen an average of 18 mm Hg, to 38 mm Hg, a level which was reached after 5–50 min. The patient then very rapidly felt short of breath, and this feeling was so intense that he demanded immediate relief.

* Rhodes Scholar, Lincoln College, Oxford.

On four occasions the patient was ventilated with air and the tidal volume (V_T) was reduced by adjusting the respiration pump. The end-tidal pCO_2 rose and the patient felt short of breath after an average rise of only 6 mm Hg. The discomfort was often less extreme than when CO_2 was added to the inspired air and the patients were able to tolerate it for a period of minutes. Each patient was then ventilated with oxygen in place of air, and their sensation of shortness of breath remained unaltered.

TABLE 1. Respiratory frequency 16/min throughout

					Levels at which patient felt short of breath							
					Original		CO_2 added to inspired air			V_T reduced		
Subject	Sex	Age	Date (1958)	Vital capacity (ml.)	V_T (ml.)	pCO_2 (mm Hg)	V_T (ml.)	pCO_2 (mm Hg)	Rise in pCO_2 (mm Hg)	V_T (ml.)	pCO_2 (mm Hg)	Rise in pCO_2 (mm Hg)
J.O.	F	27	Apr. 11	0	410	22	375	41	19	—	—	—
			Apr. 16	0	460	19	440	40	21	—	—	—
			Apr. 25	200	525	17	525	32+	15+	312	25	8
			Apr. 28	200	370	19	360	35	16	—	—	—
P.B.	M	45	Aug. 21	450	650	22	735	33	11	590	24	2
				450	650	22	800	37	15	—	—	—
S.M.	F	34	Oct. 27	0	585	21	590	38	17	400	26	5
C.H.	M	30	Nov. 24	0	625	20	640	42	22	300	30	10
J.G.	M	24	Apr. 11	0	550	21	550	38	17	—	—	—
			Apr. 18	0	610	20	590	38	18	—	—	—
R.R.	F	46	June 7	0	525	15	630	34	19	—	—	—
				Average	541	20	567	38	18	400	26	6

Figure 1 shows an example in which the patient was rendered short of breath by both methods. Figure 2, derived from Table 1, shows the relationship between tidal volume and end-tidal pCO_2 when the patients felt short of breath. All tolerated a higher pCO_2 when the tidal volume was higher.

DISCUSSION

These observations indicate that the sensation of shortness of breath in well oxygenated patients is affected by two factors, the end-tidal pCO_2 on the one hand and the ventilation (tidal volume) on the other. The addition of carbon dioxide to the inspired gases produces a severe sensation of shortness of breath after an average rise of end-tidal pCO_2 of 18 mm Hg, to 38 mm Hg. A similar phenomenon is found in normal subjects who have become acclimatized to the overventilation that occurs

at high altitudes. Provided that such subjects are adequately oxygenated they can hold their breath until the end-tidal pCO_2 has risen an average of 16 mm Hg (Rahn, Bahnson, Muxworthy & Hagen, 1953). The end-tidal pCO_2 is then little above that which normally obtains at sea level.

The alveolar gas composition, however, is not the only factor determining the length of breath-holding, as Fowler (1954) has demonstrated.

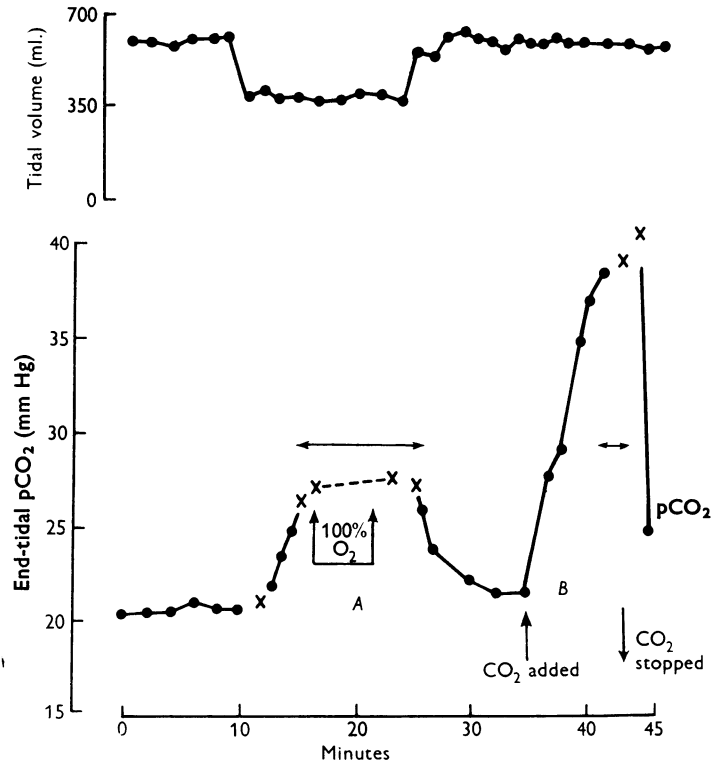

Fig. 1. End-tidal pCO_2 and tidal volume in patient S.M. (F, 34, poliomyelitis; vital capacity nil). Shortness of breath was induced by reducing tidal volume (*A*) and by adding CO_2 to inspired air (*B*). ⟷ = 'short of breath'.

Untrained subjects held their breath as long as possible, and were then allowed to breathe a gas mixture whose pO_2 and pCO_2 approximated respectively to the subjects' arterial pO_2 estimated by ear oximeter, and to the end-tidal pCO_2. The subjects experienced sufficient relief to resume breath-holding for a further period. This experiment suggests that a factor related to respiratory movements modifies the subjects' sensations in these circumstances.

In those of our patients whose tidal volume was reduced, shortness of breath was experienced at an average end-tidal pCO_2 of 26 mm Hg,

12 mm Hg below the level that causes shortness of breath when the tidal volume is unaltered. This sensation, moreover, persists even when the patient inspires pure oxygen. This eliminates hypoxia as the cause of the shortness of breath, for the alveolar-arterial oxygen gradient is little disturbed during mechanical artificial ventilation (Campbell, Nunn & Peckett, 1958). The sensation of shortness of breath is not therefore attributable either to oxygen lack or to the CO_2 tension by itself. The

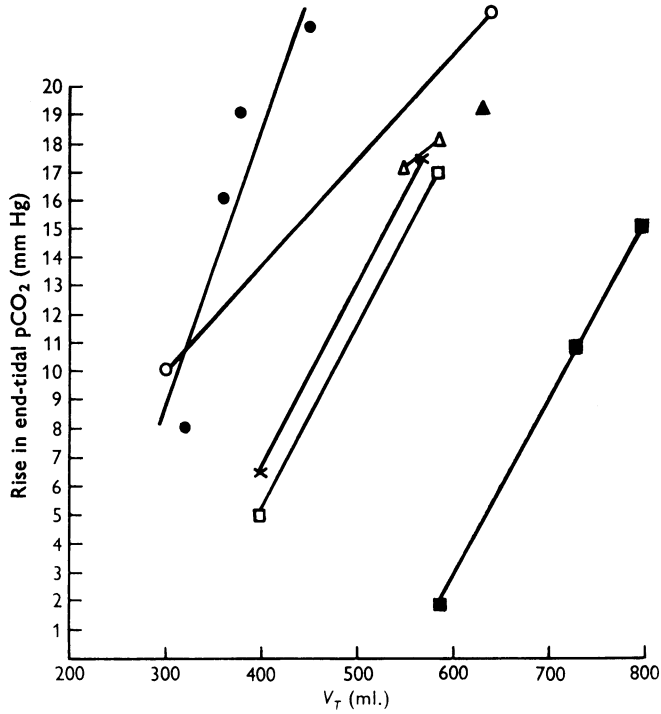

Fig. 2. Relationship between tidal volume and rise in end-tidal pCO_2, when patients felt short of breath. ●, J.O., ○, C.H., △, J.G., ▲, R.R., □, S.M., ■, P.B., ×, average.

remaining variable is the ventilation, changed in these experiments by alterations in the tidal volume, and in any one patient the greater the tidal volume the greater the rise in end-tidal pCO_2 which is required to produce shortness of breath (Fig. 2).

Parallel observations have been made by other workers observing paretic patients and normal subjects over a wide range of end-tidal pCO_2. Mithoefer, Stevens, Ryder & McGuire (1953) examined subjects who rebreathed at a specified frequency from a bag containing various proportions of O_2, CO_2 and N_2. When hypoxia was absent, the larger the bag the higher the CO_2 tension that the subjects could tolerate without departing

from the specified frequency. Affeldt, Collier, Crane & Farr (1955) showed that paretic patients receiving artificial respiration in a tank respirator became short of breath at lower end-tidal pCO_2 than that which they maintained for themselves when breathing spontaneously.

Mithoefer *et al.* (1953) attributed their findings to increased stimulation of stretch receptors in the chest with larger tidal volumes, and Affeldt *et al.* (1955) also believed that the stimulation of stretch receptors by the tank respirator was important in their observations, though they were unable to offer any precise explanation of them. There is, however, an alternative explanation of the sensation of shortness of breath. Stimuli acting on the respiratory centre normally cause it to discharge at a certain frequency and intensity. In many circumstances which are accompanied by shortness of breath the discharge of the respiratory centre is less than that dictated by the stimuli acting on it, and it is possible that it is this disparity that causes the sensation of shortness of breath. If this is so, discharge of the respiratory centre will in itself give relief from shortness of breath. In our patients, however, there was lower-motor-neurone paralysis of the respiratory muscles. The respiratory centre was therefore free to discharge at any frequency and intensity, and this freedom was unaffected by changes in ventilation (tidal volume). Increases in ventilation in our patients must therefore provide relief by affecting directly the afferent, not the central or efferent side of the respiratory reflex arc, in short, by stimulation of stretch receptors in the lungs or chest wall. The afferent impulses that result modify the effect of chemical stimuli on the conscious appreciation of the adequacy of ventilation.

SUMMARY

1. Six patients, paralysed by poliomyelitis and with vital capacities varying from nil to 450 ml., were examined on ten occasions. They were chronically over-ventilated with an average end-tidal pCO_2 of 20 mm Hg. When CO_2 was added to the inspired air at a constant tidal volume, the patients felt short of breath after an average rise in end-tidal pCO_2 of 18 mm Hg. When, however, the patients received room air or oxygen and the tidal volume was reduced they felt short of breath after an average rise in end-tidal pCO_2 of only 6 mm Hg.

2. It is concluded that a factor other than pO_2 and pCO_2 is implicated in producing the sensation of shortness of breath, and this factor is related to the ventilation (tidal volume). It is argued that the effect of chemical stimuli on the conscious appreciation of the adequacy of ventilation is modified by stretch receptors in the lungs and chest wall.

We wish to thank Dr D. J. C. Cunningham and Mr B. B. Lloyd of the University Laboratory of Physiology, Oxford, for much advice and helpful criticism. We also wish to thank

Professor Sir Robert Macintosh and Dr W. Ritchie Russell for their encouragement, and Dr Harold Rotman for assistance. One of us (J.M.K.S.) received grants from the Nuffield Committee for the Advancement of Medicine and the Medical Research Council during the period when this work was done.

REFERENCES

AFFELDT, J. E., COLLIER, C. R., CRANE, M. G. & FARR, A. F. (1955). Ventilatory aspects of poliomyelitis. *Curr. Res. Anes. Analg.* **34**, 41–53.

CAMPBELL, E. J., NUNN, J. F. & PECKETT, B. W. (1958). A comparison of artificial ventilation and spontaneous respiration with particular reference to ventilation–blood flow relationships. *Brit. J. Anaesth.* **30**, 166–175.

CUNNINGHAM, D. J. C., CORMACK, R. S., O'RIORDAN, J. L. H., JUKES, M. G. M. & LLOYD, B. B. (1957). An arrangement for studying the respiratory effect in man of various factors. *Quart. J. exp. Physiol.* **42**, 294–303.

FOWLER, W. S. (1954). Breaking point of breath-holding. *J. appl. Physiol.* **6**, 539–545.

MITHOEFER, J. C., STEVENS, C. D., RYDER, H. W. & MCGUIRE, J. (1953). Lung volume restriction, hypoxia and hypercapnia as interrelated respiratory stimuli in normal man. *J. appl. Physiol.* **5**, 797–802.

RAHN, H., BAHNSON, H. T., MUXWORTHY, J. F. & HAGEN, J. M. (1953). Adaptation to high altitude: changes in breath-holding time. *J. appl. Physiol.* **6**, 154–157.

RUSSELL, W. R., SCHUSTER, E., SMITH, A. C. & SPALDING, J. M. K. (1956). Radcliffe respiration pumps. *Lancet* **270**, 539–541.

SMITH, A. C., SCHUSTER, E. & SPALDING, J. M. K. (1959). An end-tidal air sampler for use during artificial respiration. *Lancet* **276**, 277–280.

SPALDING, J. M. K. & SMITH, A. C. (1956). A new tracheotomy tube. *Lancet* **271**, 1247–1248.