34. THE EFFECT OF RESISTIVE LOADING UPON THE VENTILATORY TIDAL VOLUME AND FREQUENCY RESPONSE TO INHALED CO₂

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It is recognized that there is a wide variation in the respiratory response to inhaled CO₂ between normal individuals. We have shown that in 'low responders' to CO₂, the increase in ventilation during CO₂ rebreathing is achieved largely by increase in VT, whereas in 'high responders' increase in ventilation is achieved largely by increase in respiratory rate (Lyall and Cameron, 1976, Clinical Science and Molecular Medicine). It is recognized that there is a wide variation in the pattern of changes in tidal volume and respiratory rate in response to inhaled CO₂, assessed by a rebreathing method. Ten normal subjects embracing a wide range of CO₂ response (range 1.1–8.48 VC min⁻¹ kPa⁻¹, mean 4.16 VC min⁻¹ kPa⁻¹) were studied. The breath-by-breath responses during a standard CO₂ rebreathing response were recorded both unloaded and loaded, and processed by computer. Standard plots of minute ventilation against PCO₂, respiratory minute volume against VT, and VT against inspiratory and expiratory time were obtained. The relative contributions of VT and respiratory rate to the increment in ventilation during rebreathing were also calculated. Resistive loading significantly reduced the ventilatory response to inhaled CO₂. (Unloaded response 4.6 ± 0.79 VC min⁻¹ kPa⁻¹, loaded response 2.3 ± 0.64 VC min⁻¹ kPa⁻¹; mean ± SEM, P < 0.01). For the unloaded CO₂ response 69.0 ± 9.9% (mean ± SEM) of the increase in ventilation was attributable to increase in VT, and for the loaded CO₂ response 69.2 ± 11.1% (mean ± SEM) was attributable to increase in VT. The difference is not significant. The ventilatory response of these subjects to inhaled CO₂ was reduced by resistive loading, but this was brought about by a decrease both in the tidal volume and frequency so that the proportion contributed by each to the total increase in ventilation remained the same.

35. DRIVE AND TIMING COMPONENTS OF VENTILATION IN ISOCAPNIC STEADY STATE CO₂ RESPONSES, EXERCISE AND PROGRESSIVE HYPOXIA IN NORMAL MAN

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Milic-Emili & Grunstein (1976, Chest, 70, 1318–1338) point out that any minute ventilation (FE) results from a combination of an inspiratory drive (as the mean inspiratory flow rate, VT/Ti), and the inspiratory timing (expressed as the proportion of the breath duration, Ti/Ttot), so that

\[ \dot{V}_E = \frac{V_T}{T_i} \times \frac{T_i}{T_{tot}} \]

where \( V_T \) is tidal volume, \( T_i \) is inspiratory time, and \( T_{tot} \) breath duration.

We have analysed this relationship in over 300 breaths in each of four subjects, using an on-line PDP-11/40 computer and mass spectrometer, under the following conditions:

1. Four normal men during measurement of the steady state isocapnic ventilatory response to CO₂ at two constant levels of increased minute ventilation (isosines), achieved by alterations of both end tidal PO₂ (PET,CO₂) and PCO₂ (PET,CO₂), so as to maintain this minute ventilation constant.

2. The same four subjects, during steady state level treadmill walking when breathing 14% oxygen, at three grades of exercise, as assessed by carbon dioxide output.

3. In four other normal men, during steady state level treadmill walking when breathing air, at three grades of exercise, as above.

4. During progressive isocapnic hypoxia when at rest, in the same four subjects as studied under (3).

Inspiratory drive (VT/Ti) increases as minute ventilation rises, whereas the inspiratory proportion of breath duration (Ti/Ttot) appears to change little even at high ventilation values. Preliminary results suggest that VT/Ti and Ti/Ttot remain relatively constant during any given level of ventilation in (1), irrespective of variation in PO₂ and PCO₂, suggesting that these chemical stimuli combine to set a demand for ventilation, which is met by a mechanism which is itself uninfluenced by the arterial blood gas tensions. This is in contrast to the traditional view (Haldane, Meakins & Priestley, 1918, Journal of Physiology, 52, 420–432) that during progressive hypercapnia and hypoxia tidal volume and frequency are affected differently. If this difference between progressive steady state responses is sustained by the analysis of our results in progressive isocapnic hypoxia (4) (currently in preparation for this presentation), this will be further evidence that these two methods of studying the chemical control of ventilation in man are not necessarily measuring the same thing (Cameron, Davies, Linton & Poole-Wilson, 1972, Journal of Physiology, 226, 56–57).

As alveolar ventilation and arterial blood gas tensions at rest depend upon VTi, in addition to ventilation perfusion relationships, changes in VT/Ti and Ti/Ttot might be relevant to the development of CO₂ retention in human disease.

36. THE RESTING REFLEX HYPOXIC DRIVE TO RESPIRATION IN NORMAL MAN

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The reflex hypoxic drive to respiration contributes very little to the total ventilation of normal man at rest. Dejours, Labrousse Raynaud, Girard & Teillac (1958, Revue Francaise d'Études Cliniques et Biologiques, 3, 105–123) used the oxygen breath test to estimate the size of this drive. Following one or two breaths of oxygen, ventilation fell transiently, 10% below the control level, approximately 20 s after the start of the first breath of oxygen. However, no fall in ventilation was observed, following one breath of oxygen, if the subjects were already hypoxic. This led to the conclusion that the threshold of hypoxic activity of the peripheral chemoreceptors was about 22.7 kPa.

Preliminary experiments showed that when a normal subject inhaled one or two breaths of oxygen, the arterial PO₂ rose to a maximum of 24.0 and 29.0 kPa respectively, 20 s from the commencement of the first