electrolytes in hypoxic respiratory alkalosis have been little studied and the results of data are confusing.

We have maintained rats in an environmental chamber either hypoxic (inspired O₂ 12%, balance N₂) producing a respiratory alkalosis or hypercapnic (inspired O₂ 20%, CO₂ 6%, balance N₂) producing a respiratory acidosis for 1, 7 or 28 days. The extracellular and intracellular water content and the plasma and tissue potassium content was measured.

The results are shown in Table 1. No change in plasma potassium was seen in hypoxia but there was a significant rise in the hypercapnic group. Left ventricular intracellular potassium (K⁺) expressed as a concentration (mmol/kg of cell water) did not change in any group. If the K⁺ is expressed as a content in mmol/kg of fat-free dry solid there is a significant rise after 7 days hypoxia and hypercapnia. In quadriceps both potassium content and intracellular concentration rose in hypoxia and fell in hypercapnia.

These results stress again the constancy of LV K⁺ concentration compared to that in quadriceps. In both tissues changes in K⁺ content occur in hypoxia and hypercapnia but in cardiac muscle these are compensated by appropriate shifts of water.

53. THE RESPONSE TO OXYGEN THERAPY IN ACUTE EXACERBATIONS OF CHRONIC RESPIRATORY FAILURE

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Increase in CO₂ retention during controlled oxygen therapy in patients in acute exacerbation of chronic bronchitis is conventionally attributed to the removal of a peripheral hypoxic drive to breathing, in patients in whom the central sensitivity to CO₂ is already reduced. This theory has recently been challenged by Rudolf et al. (1977, Lancet, ii, 483) who propose that oxygen depresses the central drive arising from cerebral anaerobiosis, with production of lactate. We have examined data in such patients (Alroy & Flenley, 1967, Clinical Science, 33, 335; Flenley & Warren, 1977, Clinical Science and Molecular Medicine, 33, 15) in light of these two theories.

In 18 admissions in 16 patients (group A) in an acute exacerbation of type II respiratory failure (mean Pa, O₂ 4-1 kPa, Pa, CO₂ 8-9 kPa, pH 7-25) when breathing air on admission, controlled oxygen therapy increased CO₂ retention, with a fall in Pa, O₂ in the first 8 h (mean Pa, O₂ 7-2 kPa, Pa, CO₂ 10-4 kPa and pH 7-25). However, in another 21 admissions in 19 patients (group B) mean Pa, O₂ 4-9 kPa, Pa, CO₂ 8-3 kPa, pH 7-33, when breathing air on admission, the rise in Pa, CO₂ within 8 h was accompanied by either a fall or no change in Pa, O₂ (mean Pa, O₂ 6-8 kPa, Pa, CO₂ 7-7 kPa, pH 7-35). These former patients (group A) were significantly more hypoxic on admission than those in whom Pa, CO₂ fell, but there was no significant difference in the initial Pa, CO₂ or pH between the two groups. We can confirm that some patients with a marked increase in Pa, CO₂ in an acute exacerbation had a minimal rise in Pa, CO₂ with oxygen when studied in remission, supporting the idea that a central drive is operating at these very low levels of Pa, O₂ in the acute exacerbations (Rudolf et al., 1977).

However, the initial fall in Pa, CO₂ was not maintained in all patients in group B, for in eight after 18-30 h of controlled oxygen, Pa, CO₂ rose on average to 10-0 kPa, when Pa, O₂ was raised on average to 7-9 kPa. Lactate levels in lumbar CSF were inversely related to Pa, O₂ in six patients, and in one increasing Pa, O₂ over 48 h led to a fall in CSF lactate. However, we feel that another mechanism than removal of the central hypoxic drive is necessary to explain the response to controlled oxygen therapy in some patients, which may be of importance for seven of the 21 patients showing an initial fall in Pa, CO₂ with oxygen subsequently died in that admission. Furthermore, acute hypoxia in normal subjects depresses central ventilatory drive (Weiskopf & Gabel, 1975, Journal of Applied Physiology, 39, 911).

54. THE EFFECT OF INHOMOGENEITY OF LUNG EXPANSION ON RESPIRATORY DRIVE IN THE DOG

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Tachypnoea is frequently present in the breathless patient with obstructive airway disease, particularly asthma; its mechanism is not clear, but it does depend on intact vago. The airway obstruction is patchy, causing different rates of inflation and deflation throughout the lungs and different relative volumes (due to alveolar collapse and air trapping). We, and others, have wondered whether inhomogeneity of lung volume information going to the respiratory centre might be a stimulus to breathing; this study is an analysis of the effect on breathing of the interaction of differences in expiratory volume between the two lungs.

Mongrel dogs were anaesthetized with chloralose, paralysed, intubated with a specially designed endotracheal tube, and their chests were opened. Each lung was ventilated by its own respirator which delivered volume determined by the 'integrated' phrenic neurogram recorded from the left C5-7 root. The integrated phrenic amplitude (equivalent to the size of the breath), inspiratory and expiratory times were measured from the same signal.

The resting volume of each lung was set independently by using expiratory threshold loads, the control levels being set to correspond to the transpulmonary pressure measured at functional residual capacity (FRC) prior to opening the chest. Alteration of the expiratory load caused a change in expiratory lung volume which resulted in a marked change in respiratory rate, due almost entirely to changes in expiratory time (the Hering–Breuer deflation reflex). There was little effect on tidal volume. By applying unilateral or bilateral changes of expiratory load, we have shown that the response to any alteration of expiratory lung volume is the arithmetic sum of the effect of the volume present in each lung at that time. That is, quantitatively predictable summation applies for any combination of changes in volume above and below FRC. These results suggest that, at least in the dog, an area of relatively reduced lung expansion may not stimulate breathing, if there are other areas of lung which are relatively overexpanded.

55. DOES HYPOXIC DRIVE INCREASE IN EXERCISE?

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The role of the peripheral chemoreceptors in the hyperpnoea of exercise seems uncertain. Lugliani, Whipp, Seard & Wasserman (1971, New England Journal of Medicine, 285, 1105-1111) demonstrated that the ventilatory response to increasing exercise was normal in a group of patients who had undergone bilateral carotid body resection. They concluded that these peripheral chemoreceptors provided little ventilatory drive in exercise breathing air.

Well et al. (1972, Journal of Applied Physiology, 33, 813–819) studied the hypoxic sensitivity of the peripheral chemoreceptors in normal subjects at rest and during three levels of exercise. By extrapolating the experimental data they estimated that the hypoxic drive accounted for 37% of the ventilation at rest and up to 59% in exercise. It was concluded that a normal Pa, O₂ provided a significantly greater stimulus to ventilation during moderate exercise, than at rest.