Artificial Ventilation in Obstructive Lung Disease

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Intermittent positive pressure respiration (IPPR) has been used at Oxford in the treatment of a variety of forms of respiratory failure since 1953, and from 1964 it has been used increasingly in the treatment of patients with obstructive lung disease, largely due to the special interest shown in these patients by Dr John Lloyd of the Department of Anaesthetics.

It should be emphasised that IPPR can only gain time for the patient with obstructive lung disease and that it is only successful medical treatment that will restore the patient's *status quo*. It should also be emphasised that if IPPR can be discontinued after twenty-four hours and replaced by more conventional forms of medical treatment, the prognosis is materially altered for the better. Medical treatment includes physiotherapy, which is most important, the use of the appropriate antibiotic, the treatment of heart failure, the management of fluid and electrolyte balance, and large doses of steroids. In status asthmaticus, and more and more in bronchitis with an element of spasm, doses of betamethazone (Betnesol) equivalent to 600 mg of hydrocortisone are given intravenously every four hours, and these large doses have occasionally been stopped at the end of forty-eight hours without any 'tailing off'.

The treatment of respiratory failure falls easily into three phases. Initially, small carefully controlled amounts of oxygen are added to the patient's inspired air. If this causes a serious increase in the arterial pCO_2, or if increasing drowsiness occurs, IPPR is given through an oral endotracheal tube for twenty-four hours. It is often possible to dispense with artificial ventilation at the end of this period, but it is sometimes necessary to continue to give IPPR for a longer period through a tracheotomy tube.

The use of controlled supplements of oxygen in inspired air (Campbell, 1965) is a most significant advance in the treatment of patients in respiratory failure from obstructive lung disease. Campbell (1960) considered four patients with an average arterial pO_2 of 23 mm Hg, saturation 40 per cent and pCO_2 of 80 mm Hg. These figures are about as bad as they could be but are similar to

figures encountered in Oxford patients who are subsequently discharged from hospital. Increasing the inspired pO_2 by 28 mm Hg (from air to 25 per cent oxygen at sea level) raised the arterial pO_2 in Campbell's patients by 17 mm Hg. The saturation of the haemoglobin with oxygen, however, rose to 70 per cent and, of course, this remarkable increase in saturation for a small increase in oxygen in inspired air is due to the shape of the oxygen dissociation curve at these very low levels of oxygen. Campbell further argued that if ventilation should be completely insensitive to CO_2 and the patient now under-ventilates until the original hypoxic stimulus is restored at an arterial pO_2 of 23 mm Hg, the rise in arterial pCO_2 will be only about 13 mm Hg, and such an increase is unlikely to be narcotic.

Experience has shown that many patients need no other form of ventilatory therapy. Twenty-five or 28 per cent oxygen in the inspired air combined with general medical measures will return the patient to the state in which he was before the episode that led to his admission to hospital. If, on the other hand, even small increases in the patient's inspired oxygen concentration lead to a persistent and narcotising rise in the arterial pCO_2, this form of therapy has failed and there is a clear indication for the use of IPPR even though the arterial pCO_2 has not risen to lethal levels.

RESULTS OF TREATMENT

For some two years we have applied IPPR to patients in respiratory failure from obstructive lung disease; an oral endotracheal tube was used for the first twenty-four hours. In all patients in status asthmaticus, and in a considerable proportion of patients with acute on chronic bronchitis, it has been possible to remove the endotracheal tube at the end of this period and substitute conservative treatment. In some cases, it has been necessary to proceed to tracheotomy and give IPPR for long periods.

In principle, the management of 'a twenty-four hour pump' is no different from the use of IPPR in other circumstances. Ventilation must be adequate, inspired air must be humidified, physiotherapy must be given, the patient must be turned, and so on. Some patients, however, in spite of the fact that their arterial pCO_2 has been reduced, are very restless and give the impression of being made uncomfortable by the oral tube. Many forms of sedation have been tried and a really satisfactory combination has not yet been found. A combination of pethidine with nitrous oxide and oxygen has been promising but is technically a little difficult to apply with absolute safety, and other anaesthetic agents are at present under consideration. It is probable that the patients are not as distressed as they appear because, although many give the impression of discomfort, they have no recollection of their treatment.

The results of treatment can be seen in Table 1. Fifty-two patients were ventilated. Eight patients in status asthmaticus were ventilated for twenty-four hours, all were successfully weaned at this time, and all subsequently did well on conservative treatment. This group has been especially gratifying, and now our physicians probably tend to recommend IPPR earlier in status asthmaticus because they know that a tracheotomy will almost certainly not be performed. Of 30 patients with acute on chronic bronchitis who were ventilated for twenty-four hours, 24 were weaned at the end of this period and 6 died. Of 9 patients with bronchitis who had been ventilated for twenty-four

TABLE 1. Results

	Alive	Dead	Total
Patients ventilated for 24 hours in status asthmaticus	8	0	8
Patients ventilated for 24 hours with acute on chronic bronchitis	24	6	30
Patients ventilated for 24 hours proceeding to tracheotomy and IPPR	4	5	9
Patients with initial tracheotomy	4	1	5

hours and who proceeded to tracheotomy and IPPR, 5 died. Five patients with bronchitis had a tracheotomy performed at the beginning of their treatment, and of these 1 died. These 5 patients occurred early in the series and the low mortality suggests that some could have been ventilated for twenty-four hours only. So in 52 patients with obstructive lung disease treated with IPPR, 12 died, a mortality of 23 per cent. Eight patients in status asthmaticus were treated with IPPR; there were no deaths, and none proceeded to tracheotomy.

The causes of the deaths in this series are interesting. Two patients died from 'other causes' although their respiratory failure had been successfully treated. One died from a massive haemoptysis from a carcinoma of the lung, and one from haematemesis and renal failure.

It is regrettable that two deaths must be ascribed to technical failures. In one patient, a tension pneumothorax went unrecognised. The other patient was a man who had been ventilated twice during one admission, on the second occasion for seven days, and in this period he made steady improvement. After weaning, while breathing air through a metal tracheotomy tube, his $PaCO_2$ was 60 mm Hg and his PaO_2 70 mm Hg. Four days later, apparently in the same clinical condition, he was seen to be cyanosed. One hundred per cent oxygen was given through the tracheotomy tube and the patient soon became dangerously narcotised with CO_2. Nikethamide produced only temporary improvement and the patient ceased to breathe. The dangers of 100

per cent oxygen for these patients cannot be over-emphasised. It will never be known whether there had been a change in this patient's condition before oxygen was given, or whether his usual plethoric and rather dusky facies was misinterpreted.

Three patients died from overwhelming infection. One had inhaled gastric contents before IPPR was given, one had moniliasis and one developed pneumonic consolidation which could not be controlled. Patients with chronic bronchitis are often properly treated at home with a variety of antibiotics, but this may mean that the organism causing a life-threatening exacerbation is resistant. The examination of a Gram-stained specimen of sputum often helps to narrow the choice of antibiotics even though sensitivities are not available.

One patient developed a bronchial fistula from a ruptured emphysematous bulla. Conservative measures were tried for a long period to encourage the air leak to close, but finally a thoracotomy was performed. The patient survived the operation, but the fistula recurred, and finally, infection caused his death. Rupture of a bulla is a most serious complication. In the acute situation it may make adequate artificial ventilation impossible, and, in the long term, if the fistula cannot be closed, the patient may die from infection or from inadequate spontaneous ventilation.

Two patients probably died from over-ventilation. One of these became extremely hypotensive shortly after artificial ventilation was begun and died in spite of efforts to raise his blood pressure. A fall in blood pressure is not uncommon in these circumstances, and is thought to be due to the failure of the return of blood to the right heart against a raised mean intrathoracic pressure. Riding and Ambiavagar (1967), describing the treatment of the moribund asthmatic, believed that the rapid infusion of two or three litres of fluid will prevent hypotension, but this might be less appropriate in the patient with chronic bronchitis and heart failure. Observations by Prys-Roberts and Kelman (1966) suggest that cardiac output is adversely affected by a low arterial CO_2 pressure in the anaesthetised normal subject. The hypotension seen in patients with obstructive lung disease shortly after artificial ventilation has begun could be of similar origin. In the later cases in this series life-threatening hypotension has been avoided by spending some time gently assisting the patient's respiration with an anaesthetic machine, until the arterial pCO_2 has been reduced just enough to make the patient apnoeic before he is connected to a respirator.

The other over-ventilated patient had a very long history of obstructive lung disease and had obviously been chronically acidotic for many months. Controlled oxygen therapy failed in her case and after three days she was

intubated and ventilated. Six hours after ventilation was begun the patient had a generalised convulsion, and twelve hours after ventilation was begun, was thought to have had a pontine thrombosis. She was unconscious with generalised spasticity, fixed divergent pupils, and hyperpyrexia. The histology of the pons is not yet known, but at the time when this diagnosis was made the patient's arterial pO_2 was 300 mm Hg, her pCO_2 32 mm Hg, and her pH 7.71. The dangers of too rapid changes in arterial pCO_2 are now recognised and the pH as well as the pCO_2 is used as a guide to the appropriate level of ventilation.

Only two patients had insufficient useful lung to sustain life. One patient was ventilated twice during one admission without real improvement, refused further treatment, and soon died. The other patient survived on a ventilator for six weeks but could not be weaned. She died of recurrent chest infections.

The results in this series should be interpreted with care. The majority of patients admitted with acute or chronic bronchitis are treated with controlled supplements of oxygen and therefore do not appear in these results. It is also probable that there is a number of patients who were believed by the physician who admitted them to have a hopeless prognosis and were therefore not submitted to IPPR.

PHYSIOLOGICAL ASPECTS

Artificial respiration by intermittent positive pressure can have a number of effects as well as the direct improvement in oxygen and carbon dioxide exchange. The effects fall into two groups: those resulting from the rise in intrathoracic pressure, and those from consequences of the rapid change in ventilation.

Raised intrathoracic pressure produces effects both on the circulation and on renal function. In most subjects raised intrathoracic pressure causes a reflex increase in venous tone, or, more correctly, a decrease in capacity vessel distensibility (Watson, 1961, 1962). The vessels on the venous side of the circulation become less easy to distend and so help to maintain venous return to the right heart in the face of the raised intrathoracic pressure. In the subject with congestive heart failure, however, venous tone is already high, and right atrial pressure is too high for efficient working of the heart (Sharpey-Schafer, 1963). In such a subject raised intrathoracic pressure may reduce venous return to the right heart, reduce right atrial pressure, and so improve cardiac output.

Reflex circulatory changes in the capacity vessels serve to control venous return to the heart and, therefore, cardiac output in the face of rapid changes in circulatory stress. More gradual and prolonged changes are largely

compensated by adjusting the circulating blood volume (Gauer and Henry, 1963), and changes in intrathoracic pressure can also affect this. A continuous raised intrathoracic pressure produces a reduction in urinary flow in normal subjects. It cannot be accounted for solely on the basis of an alteration in renal haemodynamics (though this may occur), and is due primarily to a decrease in free water clearance, probably induced by increased ADH activity (Murdaugh *et al.*, 1959). It is likely that the stimulus for increased ADH secretion arises from a volume receptor region within the chest, perhaps the left atrium. This work has been done with normal subjects whose airway pressure was raised to a steady 25 mm Hg for periods of a half to one hour. In patients receiving artificial respiration by intermittent positive pressure the mean airway pressure is usually much less than this, because the airway pressure is raised during inspiration but returns to, or nearly to, atmospheric during expiration. It is, however, raised for very much longer. We have repeatedly seen, in patients requiring artificial respiration for any of a variety of causes, that the plasma sodium is liable to be low, sometimes below 120 mEq./l. This may be a dilution effect, due to increased ADH secretion.

Raised intrathoracic pressure also affects urinary electrolytes and, in particular, causes a decrease in the urinary Na/K ratio, no doubt due to the increase in aldosterone excretion which occurs at the same time (Cox *et al.*, 1963). The effect of this is to conserve body sodium. This work also has been done with normal subjects whose airway pressure was 25 mm Hg above atmospheric pressure for half an hour. We have not seen evidence of sodium retention in our patients receiving artificial respiration, but it would be most likely to occur in patients with severe pulmonary disease who require very high airway pressures to produce adequate artificial respiration.

The rapid increase in ventilation that artificial respiration can produce results in a variety of changes in a patient who has been chronically or subacutely under-ventilated. The changes may be important because proper treatment may depend on recognising them. The biochemical chart of a recent patient illustrates the problems that may arise (Fig. 1). When she was first seen she had already received substantial amounts of oxygen. Her arterial pCO_2 was 108 mm Hg (normal 40), and pH was 7·2 (normal 7·4). The respiratory acidosis had no doubt resulted in the kidney excreting acid urine containing chloride, and plasma chloride had fallen to 82 mEq./l (normal 100). Owing to the increase in arterial pCO_2 and excretion of hydrogen ion by the kidney the plasma bicarbonate was raised to 41 mEq./l (normal 24). In short, the kidney had produced, as usual in these circumstances, an alkalosis which partially compensated the respiratory acidosis. The importance of this lies in the fact that some patients, including this one, have difficulty in overcoming the renal

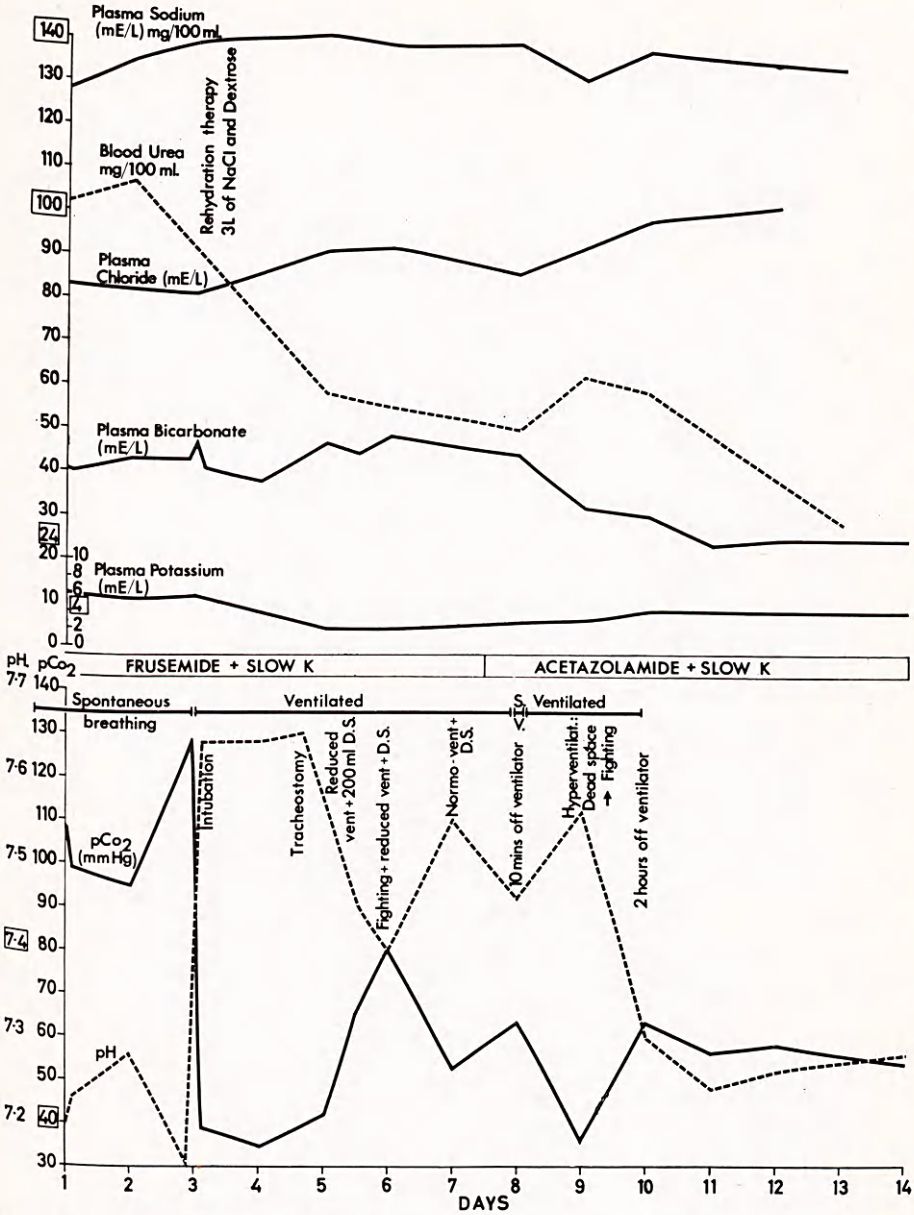

Fig. 1. Biochemical findings in Mrs D. E., aged 73, admitted to hospital with a respiratory insufficiency.

alkalosis when the respiratory acidosis is eliminated, for instance by artificial respiration. In this patient, artificial respiration was begun at the end of Day 2, the arterial pCO_2 was restored to normal but a severe alkalosis, pH 7·64, developed. The alkalosis was not corrected by the kidney during the next two days. Reducing the pulmonary ventilation either by reducing tidal volume or by introducing dead space between the patient and the respirator (Days 6 to 9) restored the pH more nearly to normal, but at the expense of a raised pCO_2 of 60–80 mm Hg. The kidney needed to secrete an alkaline urine containing bicarbonate, but it is unable to do this except in the presence of adequate chloride. Sodium chloride was therefore given (Day 3) to raise the plasma chloride level. On Day 7 acetazolamide (Diamox) was begun. It is a carbonic anhydrase inhibitor, and reduces the reabsorption of bicarbonate by the kidney tubules. From the time when it was first given the plasma bicarbonate fell steadily, the alkalosis was overcome, and the patient resumed spontaneous breathing.

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Book Reviews

The Myocardial Cell: Structure, Function and Modification by Cardiac Drugs. Edited by STANLEY A. BRILLER and HADLEY L. CONN, M D. University of Pennsylvania Press. Price 64*s*.

This book is based on a number of communications presented to an international symposium recently held in Pennsylvania on 'the structure and function of the myocardial cell and . . . the action of drugs at the cellular level'. It provides an excellent up-to-date survey of many aspects of the myocardial cell. Topics discussed include the fine structure and contractile mechanism of the heart, the function of the cell membrane, transmembrane potentials,