Therapeutic Conferences

Respiratory Failure

FROM THE DEPARTMENTS OF THERAPEUTICS AND CLINICAL PHARMACOLOGY AND MEDICINE, UNIVERSITY OF ABERDEEN

British Medical Journal, 1972, 1, 170-172

DR. K. N. V. PALMER: Patients with a history of chronic lung disease who develop respiratory failure require immediate and precise management, as the patient to be discussed this morning illustrates.

Chronic Obstructive Bronchitis

HOUSE PHYSICIAN: This 56-year-old man, who was until recently a heavy cigarette smoker, has a long history of chronic airways obstruction. He had to stop work as a labourer five years ago because he was dyspnoeic on minimal exercise. He was admitted one hour ago because of increasing breathlessness and confusion during a "'flu-like" illness. On admission he was deeply cyanosed and his cough was ineffective: the sputum was tenacious and purulent; he had a regular pulse of 100 per minute, and obvious right heart failure—peripheral oedema and enlargement of the liver.

DR. PALMER: In *respiratory* failure hypoxaemia with or without hypercapnia is present when breathing air. Hypoxaemia without hypercapnia—hypoxaemic respiratory failure—is commonly seen in asthma, pneumonia, and cardiac failure and is due mostly to disordered ventilation/perfusion balance in the lung. Even so, the degree of ventilation of the alveoli is normal or even increased.

In hypoxaemia with hypercapnia—that is, *ventilatory* failure—the level of alveolar ventilation is diminished and there is usually ventilation/perfusion imbalance as well. This is seen most commonly in patients with obstructive bronchitis. Hypercapnia may occur with normal or raised arterial oxygen levels (Pa_{O_2}) if the patient is receiving oxygen when the arterial blood is taken, but these patients still have ventilatory failure.

Clinically it is not always possible to differentiate between hypoxaemic and ventilatory respiratory failure, and the arterial blood gas tensions have to be measured.

HOUSE PHYSICIAN: I have just got the blood gas measurements from the pulmonary function laboratory. The Pa_{O_2} is 30 mm Hg and the Pa_{CO_2} 70 mm Hg, with an arterial pH of 7·35.

DR. PALMER: He is clearly in severe ventilatory failure and has rather severe hypercapnia. In addition to his basic lung disease this may have resulted from either incorrect use of oxygen therapy or inappropriate sedation.

Appointments of Speakers
K. N. V. PALMER, M.D., F.R.C.P., Reader in Medicine
J. C. PETRIE, M.B., M.R.C.P., Senior Lecturer in Therapeutics and Clinical Pharmacology
R. A. WOOD, B.SC., M.R.C.P.ED., Lecturer in Therapeutics and Clinical Pharmacology

HOUSE PHYSICIAN: He did not have oxygen in the ambulance.

DR. R. A. WOOD: Just as well—in cases such as this no oxygen in the ambulance is safer than excessive oxygen.

HOUSE PHYSICIAN: Also, his general practitioner specifically stated that he had prescribed no hypnotic for him.

DR. J. C. PETRIE: I doubt if there is such a thing as a "safe" sedative drug for patients like this.

OTHER PRECIPITATING FACTORS

STUDENT: We have been taught to identify and treat other precipitating factors. This man had an upper respiratory infection, and so the first possibility is that he may have developed bronchopneumonia. Secondly, is there any evidence of pneumothorax or pulmonary embolism?

DR. PALMER: Infection is the commonest trigger to an acute exacerbation of ventilatory failure in obstructive bronchitis. In my experience pneumothorax and pulmonary embolism are unusual. Even so, you are right to make the point and the initial chest *x*-ray film will be helpful.

DR. WOOD: We have seen three patients recently who presented with an acute exacerbation of ventilatory failure precipitated by a pneumothorax.

DR. PETRIE: In this patient we must deal with the infection, the heart failure, the airways obstruction and sputum retention, and, of course, the blood gas disturbances.

We have previously discussed the treatment of infection in a similar patient (*B.M.J.*, 2 October 1971, p. 42), and we will give this man ampicillin, 500 mg four times daily. We have also discussed the treatment of heart failure (*B.M.J.*, 27 March 1971, p. 716), and he is on frusemide, 160 mg daily, and potassium chloride supplements.

STUDENT: Is there a place for digoxin in these patients with cor pumonale?

DR. PALMER: The effect of digoxin in right ventricular failure secondary to chronic obstructive bronchitis is uncertain because right ventricular failure in this condition is also related to raised pulmonary arterial pressure secondary to hypoxaemia. But recently it has been shown that left ventricular function is depressed when there is hypoxaemia and hypercapnia, but particularly hypercapnia, and some of these patients benefit from digoxin probably because of its effect in improving left ventricular function.

DR. WOOD: The sputum retention is striking and this

patient will need hourly physiotherapy, with coughing exercises and postural drainage. Nasotracheal suction was carried out on admission and he is to have frequent steam inhalations.

DR. PALMER: Have you given a bronchodilator?

DR. WOOD: He was given aminophylline (0·25 g in 10 ml) by intravenous injection over five minutes just before he had the initial physiotherapy. I would emphasize that this injection must be given slowly because this drug is a potent stimulus to cardiac arrhythmia. Aminophylline acts on the bronchi (*B.M.J.*, 23 January 1971, p. 220) but also has a direct stimulant effect on the respiratory centre and a slight diuretic action, which may be useful in this man.

DR. PALMER: The selective beta-adrenergic-receptor stimulant bronchodilator drugs, such as salbutamol or orciprenaline (*B.M.J.*, 23 January 1971, p. 220), may be given in severe cases of respiratory failure by inhalation using intermittent positive pressure ventilation. Terbutaline, another selective beta-adrenergic stimulant drug, may be given by subcutaneous injection, and this may be a useful route.

DR. PETRIE: This man is now on salbutamol, 4 mg three times a day by mouth. These drugs have a place if there is appreciable airways obstruction, but in patients such as this much of the obstruction is irreversible. These drugs stimulate the heart much less than isoprenaline, but they must still be used with caution especially in hypoxaemic patients.

We now ought to discuss oxygen therapy.

OXYGEN THERAPY

DR. PALMER: The important point to emphasize is that oxygen therapy must be very carefully controlled if there is initial hypercapnia, as the $Paco_2$ may rise fairly acutely—particularly if there is severe hypoxaemia. The lower the initial Pao_2 the more likely is a steep rise in $Paco_2$, but even so individual hypercapnic patients respond differently to oxygen therapy. Patients who have hypoxaemia with low or normal $Paco_2$ levels may be allowed unrestricted oxygen, as there is no problem with a rising $Paco_2$.

DR. WOOD: Nevertheless, we give low concentrations of oxygen to all patients who have a history of pre-existing lung disease or are known to have carbon-dioxide retention. The normal concentration of oxygen in air is 20·94%. Masks which operate on the principle of high air flow with oxygen enrichment—the Ventimask or Edinburgh mask—deliver oxygen concentrations at 24-28%. We always start with the Ventimask using 24% or the Edinburgh mask with a flow rate of 1 l. per minute of oxygen, which gives roughly the same oxygen concentration. If the $Paco_2$ does not increase or if it increases by only a small amount (say, 5 mm Hg) and the patient's level of consciousness is not depressed, the concentration can be increased to 28%.

HOUSE PHYSICIAN: In patients with hypoxaemia and hypercapnia the response of the respiratory centre to carbon dioxide is depressed and hypoxaemia becomes important as a drive to respiration.

DR. PALMER: You are quite right. Carbon dioxide is normally the most powerful stimulus to respiration. When hypercapnia develops the response to CO_2 diminishes and oxygen lack becomes an important factor in respiratory drive. The mechanisms are complex and not fully understood. The point to emphasize from a clinical point of view is that high oxygen concentrations must not be administered to hypoxaemic hypercapnic patients.

I would also stress that the low flow rates of oxygen should be continuous, as severe degrees of hypoxaemia may develop if oxygen is given intermittently. This is because there is a rise in $Paco_2$ when alveolar ventilation is depressed during oxygen therapy. If the enriched oxygen is now stopped the alveolar Po_2 will fall because the alveolar Pco_2 has risen and the patient in ventilatory failure is unable to increase ventilation to overcome the effect. If hypoxaemia cannot be improved without an appreciable rise in $Paco_2$, endotracheal intubation and possibly tracheostomy and intermittent positive pressure ventilation have to be considered.

DR. PETRIE: The benefit of low oxygen concentrations is easy to understand if the shape of the oxygen dissociation curve is studied (Fig. 1). In severely hypoxaemic patients as

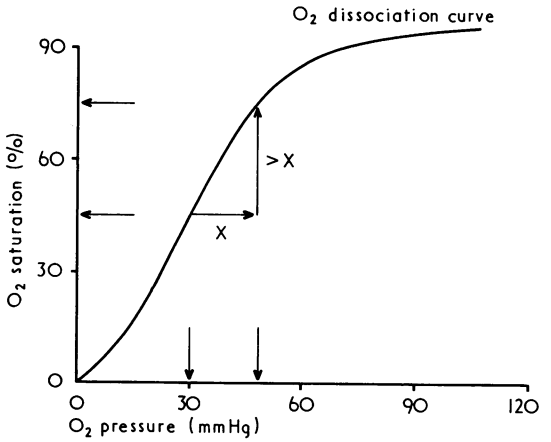

FIG. 1—An increase in oxygen pressure (x) results in a larger (> x) increase in the saturation of haemoglobin.

the oxygen pressure rises the percentage saturation of haemoglobin rises steeply because of the shape of this curve. So a small increase in oxygen tension results in a larger increase in the oxygen saturation.

DR. PALMER: We must continue treating him with oxygen until the factors precipitating the respiratory failure have been treated. Some doctors go on giving oxygen until the Pao_2 is at least 50 mm Hg. But it may not be possible to maintain the Pao_2 at that level without an unacceptable degree of hypercapnia, and a lower oxygen tension may be preferable. Of course, we're always worried about the effects of hypoxaemia on tissue but the $Paco_2$ may rise quite precipitously if oxygen is given too enthusiastically. A conscious cyanosed patient is safer than unconscious pink one.

MUCOLYTIC AGENTS

STUDENT: Is there a place for mucolytic agents? This man's sputum was very tenacious on admission.

DR. PALMER: It is difficult to assess the clinical value of some of these agents because, though one can show definite activity in a test-tube, it is not always easy to prove an equivalent beneficial action clinically. Other factors making this assessment difficult are that adequate hydration, physiotherapy, the treatment of infection, and inhalation of steam are usually being given at the same time. Most people have found that the results of inhaling aerosol preparations of enzymes and detergents are rather disappointing. Even so, there is evidence that a freshly prepared solution of ascorbic acid, sodium percarbonate, and copper sulphate (Ascoxal) or acetyl cysteine by aerosol have a definite mucolytic action and these drugs

have been shown by controlled clinical trial to have a beneficial effect.

Clinically the value of the traditionally prescribed expectorants by mouth has not been clearly established by controlled clinical trial. However, a derivative of vasicine, bromhexine (in a dose of 16 mg thrice daily by mouth), has been shown to increase sputum volume and reduce sputum viscosity in double-blind controlled trials in bronchitic patients.

HOUSE PHYSICIAN: This patient's doctor has prescribed bromhexine for him already.

DR. PETRIE: We must mention the "test tube" approach to the management of respiratory failure. For example, carbonic-anhydrase inhibitors such as dichlorphenamide may have a role in the most difficult cases.

DR. WOOD: These drugs cause a metabolic acidosis. They may exert a central effect, which results in a stimulus to ventilation and a reduction in $Paco_2$. This biochemical approach does not correct the basic dysfunction of inadequate ventilation and ventilation-perfusion imbalance and is condemned by some British workers. On the other hand, some American workers find the carbonic anhydrase inhibitors useful as an adjunct to therapy in very ill patients. We don't use these drugs ourselves.

ACID-BASE BALANCE

STUDENT: Dr. Palmer, I suppose another biochemical approach is the use of THAM (Tris-(hydroxymethyl) aminomethane), to try to return the blood pH towards a normal level.

DR. PALMER: Yes, certainly. This agent combines with carbon dioxide to form bicarbonate and a buffer. Although the pH may be restored towards normal this may itself adversely influence ventilation and mechanical assistance should be available. These drugs have a small place in intensive respiratory care. The biochemical approach requires very careful handling and seems out of favour.

More often we use respiratory stimulants, particularly to tide patients over acute episodes of respiratory failure. These drugs stimulate respiration at doses which cause little central cerebral excitation. Nikethamide, 1-3 ml intravenously, is short-acting and may be repeated within 4-6 hours.

DR. PETRIE: Whether it increases the sensitivity of the respiratory centre to CO_2 levels, acts on the chemoreceptors of the carotid body, or simply wakens the patient to enable him to co-operate with coughing is not clear. Another indication for nikethamide is in respiratory depression after a drug overdose.

DR. WOOD: Unless, of course, the drug overdose is with morphine, when nalorphine is the specific antagonist.

HOUSE PHYSICIAN: We have used vanillic acid diethylamide (Ethamivan) to stimulate respiration in some patients.

DR. WOOD: This is similar structurally and pharmacologically to nikethamide. It acts for 10-30 minutes and is given as an infusion (3·24 g in 500 ml—0·05-0·15 mg/kg/minute). Drugs of this type also act as general stimulants. At higher doses they stimulate both respiratory and non-respiratory functions. This may use up oxygen and increase CO_2 production, to the detriment of the patient. Even so, on balance it seems that, in spite of this theoretical argument, there is a place for the short-term use of these drugs.

DR. PETRIE: In patients who require respiratory stimulants and are known to have hypoxaemia and hypercapnia a decision whether to ventilate them artificially or not must always be made, in consultation with anaesthetists, at an early stage in management (*B.M.J.*, 23 January 1971, p. 220). The decision is guided by the pre-existing lung function, the age of the patient, and particularly by the rate of rise of the carbon-dioxide tension.

DR. PALMER: The principles of management of respiratory failure in a patient such as this man are to establish a clear airway, to use oxygen rationally, and to identify and treat precipitating factors, principally infection. Respiratory stimulants may be used in the short term. Physiotherapy with mucolytic therapy to remove retained secretion is important, but the value of a biochemical approach to correcting acid-base imbalance remains to be established. If these measures fail, then assisted ventilation will be required. Finally, it is essential that all these patients stop smoking tobacco.

Any Questions?

We publish below a selection of questions and answers of general interest

Allergy to Nuts

What is the treatment for a man with a life-long allergy to nuts including food cooked in groundnut oil? Is desensitization feasible?

Allergic reactions to foods are commoner in childhood than in adult life and most affected children will grow out of their symptoms by the age of five to six years. Sensitivity to fish, eggs, or nuts commonly persists and should it do so after puberty is likely to be retained for life.[1 2]

Allergy to nuts is a relatively common condition and may cause violent symptoms. In actively sensitive patients a reaction may occur immediately the food is put into the mouth. Itching and burning of the lips and tongue lead the patient to spit out the offending food. If any is swallowed, flushing and itching of skin will develop in a few minutes, followed by generalized urticaria often with angio-oedema of the face and glottis accompanied by vomiting. Fully developed anaphylactic shock can occur, with asthma, hypotension, and syncope. In milder cases generalized urticaria may develop without any marked constitutional disturbance.

Emergency treatment for an allergic reaction causing severe symptoms is the immediate intramuscular injection of adrenaline (1 ml of 1:1000) followed by an antihistamine drug intravenously (promethazine hydrochloride 20-50 mg). In severe shock intravenous hydrocortisone (100 mg) may be necessary. The patient who may be accidentally exposed to the antigen should carry adrenaline with him. This is most conveniently administered by aerosol inhalation (10 puffs of "Medihaler Epi") but may not be so effective as injected adrenaline.

Desensitization can be attempted by injection of the causative antigen. This treatment is not without hazard even in mildly sensitive patients, as generalized anaphylactic reactions