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Hypoxaemia in chronic obstructive bronchitis

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ABSTRACT Arterial blood gas tensions were studied for six years in 85 patients (59 men, 26 women, mean age 58·8 years) with hypoxaemia associated with chronic bronchitis.

All patients who died had a precipitous fall of arterial oxygen tension (Pao_2) breathing air. In patients dying within two years of the first appearance of ankle oedema the mean rate of fall of Pao_2 was 0·11 kPa/month. Patients who survived two years appeared to deteriorate more slowly (0·017 kPa/month) until some months before death, when they too deteriorated rapidly.

Hypoxaemic patients with obstructive airways disease suffer a terminal rapid decline in arterial oxygen tension, which probably indicates real pathological change in the lungs and has important implications for long-term domiciliary oxygen treatment.

Hypoxaemia is a well-recognised feature of many patients with chronic obstructive bronchitis. When severe it is associated with recurrent attacks of ankle oedema and a poor prognosis; two-thirds of the patients dying within five years (Renzetti *et al*, 1966; Ude and Howard, 1971). The natural history of hypoxaemia in obstructive airways disease has not been fully reported. In this study arterial blood gases and other parameters were measured at regular intervals in a group of patients attending a bronchitis clinic. The development of these physiological features has been related to the progress of the disease.

Patients and methods

Since 1972 all patients attending the bronchitis clinic who were judged to be centrally cyanosed by the colour of the tongue and who admitted to ankle oedema on at least one occasion were admitted to the study. Patients with good evidence of ischaemic heart disease clinically or electrocardiographically or with other identifiable causes of oedema were excluded, as were those who developed carcinoma of lung or died from causes other than respiratory failure. All patients had airways obstruction by spirometric tests. Most admitted to the production of sputum on most days, and all had breathlessness at least limiting their walking pace on the level.

Arterial blood samples were taken from the subjects while breathing air at outpatient examination at least once a year, and blood gas tensions were measured polarographically. Haematocrit, spirometry (Monaghan-Sandoz Ltd), and pulmonary artery pressure were measured while the subject was clinically stable at the beginning of the study. Pulmonary artery pressure, using thin polyethylene floating catheters inserted via a brachial vein were measured manometrically from a point level with the sternomanubrial junction and recorded by a Cambridge recorder (Pye Instruments). Haematocrit and spirometry were repeated whenever blood gas measurements were made.

Linear regressions of the change of arterial oxygen (Pao_2) and carbon dioxide ($Paco_2$), haematocrit, forced expiratory volume (FEV_1), and forced vital capacity (FVC) were made with time. Mortality was calculated by life table analysis, and is presented as a continuous function with time; survival probabilities at four-monthly intervals were calculated.

Patients took small daily doses of diuretics (frusemide 40–80 mg or cyclopenthiazide 0·25–0·5 mg daily), antibiotics for chest infections, and oral salbutamol. Some patients were given oxygen at home at flow rates of 2 l/min through nasal catheters for between 12 and 15 hours a day. The remainder did not have oxygen.

Results

Eighty-five patients were studied, 59 men and 26 women. Men had a mean age of 59·8±7·2 years and women 57·8±8·2 years at entry. Mean dur-

ation of follow-up was 49±26 months. During the course of the study 35 patients died. They had a mean survival of 32·1±27·8 months.

At entry, the mean Pao_2 after incidence of oedema was 5·5±1·10 kPa and mean $Paco_2$ 7·36±1·45 kPa. Mean FEV_1 was 0·74±0·32 and mean FVC 1·70±0·68 l. Transfer factor for carbon monoxide (single breath) was measured for 45 patients: mean 40·6±12·7% of predicted values. Of 85 patients, 54 (63·5%) had electrocardiographic evidence of right ventricular hypertrophy (R dominant in a VR; predominant S in V5, dominant R and an inverted T wave in chest leads V1–3). Mean haematocrit was 51·7±5·9%.

Mortality was high for four years but then subsided, leaving about 45% of the group reasonably stable and declining at a lesser rate with a much lower mortality (fig 1).

The rate of decline of Pao_2 for the whole group derived from a linear regression was 0·0184 kPa/year. The changes in $Paco_2$, FEV_1, FVC, and haematocrit with time were not significant. As the mortality curve showed rapid mortality within the first two years and a plateau after four years we compared the data from the 19 patients who died within two years and the 27 who survived at least four years. Pao_2, $Paco_2$, haematocrit, FEV_1, and FVC were analysed. The regression line for Pao_2 was the only line with a slope significantly different from 0 (fig 2). For the 19 patients who died within two years the slope was −0·11 kPa/month and the intercept 6·8 kPa (r=0·502; P<0·0005). For 27 patients who survived four years, slope for Pao_2 was −0·017 kPa/month and the intercept 7·32 kPa (r=0·32; P<0·0005). Thus patients who die soon after their first visit have a rate of decline of Pao_2 some six times greater than those who live four years or more, and this difference is statistically significant. Among other features (see table) there was a considerable difference between the mean convalescent Pao_2 of each group but not between convalescent $Paco_2$ or Pao_2 at the first attack of oedema. There were differences between the groups with respect to haematocrit and pulmonary artery pressure but these were not as pronounced as Pao_2 (see table).

Inspection of the individual Pao_2 lines of those who died shows many to have deteriorated uninterruptedly from the time of first presentation but a number to have followed the mean path of lesser decline for several years before declining more rapidly (fig 3). All who died from respiratory failure at whatever time showed a final accelerated decline in Pao_2. The decline in Pao_2 in the final two years of life of the 16 patients who died more than two years after their entry into the study had a slope of 0·068 kPa (r=0·389; P≤0·0005), signifi-

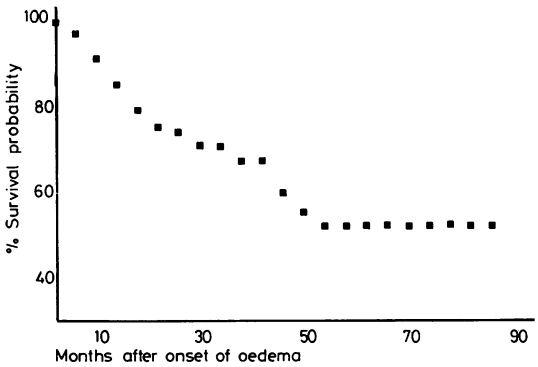

Fig 1 *Survival probability after onset of peripheral oedema.*

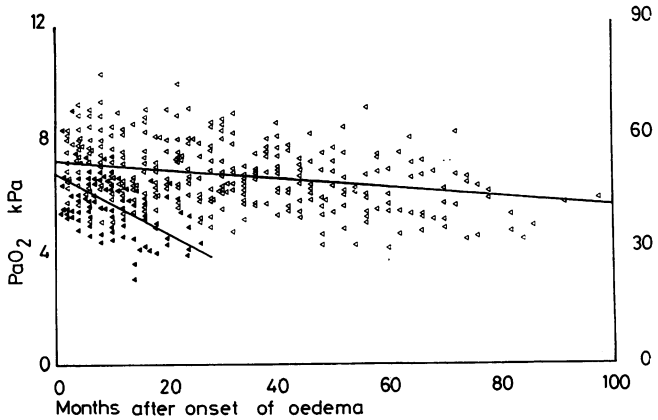

Fig 2 *Arterial oxygen tension (breathing air) for 19 patients who died within two years of onset of oedema, ▲, and for 27 patients who survived at least four years from first episode of oedema, △.*

Comparison of two and four year groups. Mean blood gas tensions during convalescence were calculated for each patient. Tabled values are means of these individual patient means

	Two year group	*Four year group*	*P value*
Mean convalescent Pa_{O_2}	5·7±0·6 kPa	6·7±0·7 kPa	≤0·0005
Mean convalescent Pa_{CO_2}	7·4±0·8 kPa	7·1±0·9 kPa	Not significant
Pa_{O_2} at time of first oedema	5·6±2·1 kPa	5·1±1·1 kPa	Not significant
Mean haematocrit	54·5±5·5%	49·5±4·7%	≤0·05
Mean pulmonary artery pressure	31·0±12 mmHg	22·0±13 mmHg	≤0·025

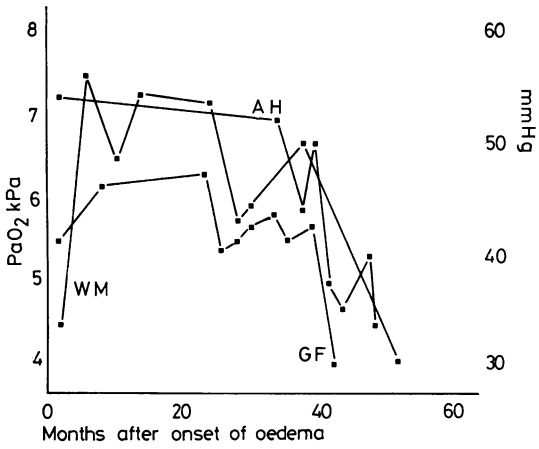

Fig 3 *Arterial oxygen tension (breathing air) for three patients showing initial plateau and subsequent precipitous decline.*

cantly steeper than the mean rate of decline of Pa_{O_2} in the same patients in the months before their final two years.

Seven of the 19 patient group and 12 of the 27 group had domiciliary oxygen. There was no significant difference when considered as a two by two contingency table.

Discussion

This is a prospective study of patients with hypoxaemia and chronic obstructive bronchitis who had suffered at least one attack of oedema. The mortality is similar to other published studies. Stuart-Harris and Hanley (1957) found 57% mortality at four years, Renzetti *et al* (1966) a 73% mortality at four years, Ude and Howard (1971) a 60% at four years, and Stevens *et al* (1963) a 50% at 3·8 years. Clinical features in terms of age, haematocrit, Pa_{O_2}, and FEV_1 were similar in all groups.

Pa_{O_2} is confirmed as the major measurement showing change in those who die. The decline of Pa_{O_2} has prompted therapeutic trials of domiciliary oxygen therapy, though this study was not designed to investigate this. The striking feature of our data is the apparently discontinuous decline of Pa_{O_2}. Hypoxaemia appears to be only slowly progressive and well tolerated in many patients even in the presence of clinical and electrocardiographic evidence of right ventricular hypertrophy. Our group includes 27 such patients who have survived at least four years. On the other hand, in other patients hypoxaemia is rapidly progressive, death occurring within two to three years. Clearly many of our patients were already at this stage when first studied but there were sufficient numbers who were relatively well in the early part of the study and who then declined rapidly to indicate that the phase of accelerated decline probably has a previously compensated phase in most patients. This is analogous to high altitude hypoxaemia (Rotta *et al*, 1956) when subjects may live and work quite happily with a Pa_{O_2} around 7 kPa, but a few decompensate to enter a state of extreme hypoxaemia, drowsiness, and oedema (Monge's disease).

The development of hypoxaemia in individual patients reported in our study suggests that the phase of accelerated decline appears quite abruptly, and denotes real pathological change. There was no indication as to why this should occur as all other physiological measurements were unchanged. This finding has important implications for long-term oxygen treatment and raises several questions. Should treatment be started in the compensated phase to prevent the onset of accelerated decline? In the decompensated phase are the changes so entrenched as to be beyond the reach of treatment? Patients who died while on oxygen treatment declined at a rate similar to those who died without treatment. There was no indication from this study as to whether treatment in the phase of accelerated decline could return patients to the compensated stage. The current trials may shed more information on this point.

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