A clinicopathological study of fatal chronic airways obstruction

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Scott, K. W. M. (1976). *Thorax*, 31, 693–701. **A clinicopathological study of fatal chronic airways obstruction.** A clinicopathological study of 21 patients who died as a result of chronic airways obstruction was carried out. Thirteen patients had been in right ventricular failure for at least one year before death and the other eight patients did not have right ventricular failure. The patients with long-standing right ventricular failure died at a younger age, on average, than those without failure. There were no significant quantitative differences between the two groups in the length of history of chest disease, blood gas estimations, respiratory function tests or degree of polycythaemia. The group with right ventricular failure had significantly larger mean right and left ventricular weights than the group without failure, but there were no significant differences in amounts of emphysema, size of bronchial mucous glands, proportion of small airways lumen in the lung or number of thick-walled peripheral lung vessels between the two groups.

The findings did not support the division of this series of patients, with fatal chronic airways obstruction, into two distinct groups broadly defined as 'emphysematous' and 'bronchitic', either clinically or pathologically. A history of right ventricular failure correlated well with the finding of right ventricular hypertrophy at necropsy. Electrocardiographic evidence of right ventricular hypertrophy was found to correspond with the size of the right ventricle at necropsy in 66% of cases. The radiographic diagnosis of emphysema proved an accurate assessment when compared to the necropsy findings, and radiographic estimations of right ventricular enlargement were accurate in 65% of cases.

Histological evidence of acute bronchitis was present in 20 of the 21 patients (95%), and five patients showed histological evidence of minor pulmonary thromboembolism. Ten patients in the series showed an increase in the weight of the left ventricle as well as the right ventricle.

The fact that chronic pulmonary disease may result in heart failure was recognized by Laënnec in 1819. Several authors have attempted to divide patients with obstructive airways disease into two broad groups, one known as 'bronchitic' who usually have heart failure, and the other known as 'emphysematous' who do not have such a high incidence of heart failure (Ogilvie, 1959; Richards, 1960; Fletcher *et al.*, 1963; Burrows *et al.*, 1964; Briscoe and Nash, 1965). Burrows *et al.* (1966) found that chronic or recurrent heart failure occurred in what they termed type B disease where there was absent or mild emphysema. They

also included a type X disease for patients who did not fulfil the criteria for type A (severe emphysema) or type B disease. Heath, Brewer, and Hicken (1968) suggested that right ventricular hypertrophy was more common in centrilobular than in panlobular emphysema. The aim of the present study was to determine from clinical and pathological data whether there are two distinct groups of patients who die from obstructive airways disease and also to establish whether quantitative differences existed in the airways or alveoli. The study also yielded information on the accuracy of clinical examination and tests in predicting the presence of right ventricular hypertrophy and on the nature of the process in the lungs which precipitated death in these patients.

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MATERIAL AND METHODS

Twenty-one known cases of chronic airways obstruction which had been investigated in the Department of Medicine at Sheffield Royal Hospital and subsequently came to necropsy were studied.

All the patients had a history of cough and daily sputum production for at least three months in the year, for two or more successive years (Ciba Guest Symposium Report, 1959). They all had dyspnoea which was sufficiently severe to make them stop while walking on the level and they all had a normal systemic blood pressure.

The case records were examined to determine the total length of history of chest disease and also the length of time the patients had been in cardiac failure. This was defined as the presence of ankle oedema and raised jugular venous pressure (greater than 2 cm of water above the manubriosternal junction at an angle of 45°) (Anderson *et al.*, 1973). Electrocardiograms were performed during the terminal illness. These were examined for evidence of right ventricular hypertrophy judged by a dominant R or an inverted T wave in V1-3 or a dominant R in aVR and dominant S in V5. The presence of P pulmonale was also ascertained and was considered to be present if the P wave was greater than 2 mm in S2 (Anderson *et al.*, 1973). Chest radiographs were examined during the terminal illness for signs of emphysema (judged by the degree of peripheral pruning of vessels and the presence of visible bullae) and cardiac enlargement. Before the terminal admission, in a quiescent phase of the disease, forced expiratory volume at one second (FEV₁) and forced vital capacity had been determined with a Poulton spirometer. Also at this time total lung volume and residual volume were determined by a closed-circuit helium dilution technique. During the terminal illness arterial blood gas estimations were performed using EIL electrodes, and the haemoglobin and packed cell volume were determined on venous blood.

At necropsy the hearts were fixed, after examination of the coronary arteries and valves, in 10% formol saline for 72-96 hours and were then dissected according to the method of Fulton, Hutchinson, and Jones (1952). None of the cases showed gross coronary artery atheroma, valvular disease, myocardial infarction or fibrosis. The right ventricle and the left ventricle plus the septum were weighed separately, and the ratio of the left to right ventricular weight was calculated. After removal from the thorax the lungs

were distended with 10% formol saline introduced by a catheter into the main bronchus at a pressure of 30 cm of water, using a modification of the apparatus designed by Heard (1969). In 12 cases both lungs were distended while in the other nine only the left lung was examined. After fixation in this state samples of the bronchial tree were taken from three sites in the left lung: (a) the left main bronchus just proximal to its bifurcation; (b) the bronchus to the basal segments (the bronchus immediately below the origin of the bronchus to the apical segment of the lower lobe), and (c) the bronchus to the inferior segment of the lingula, 5 mm beyond its origin (Restrepo and Heard, 1963). Transverse blocks were embedded in paraffin and 5 μ sections were stained by haematoxylin and eosin and periodic acid Schiff after which they were projected at a magnification of 20 diameters on to a point-counting grid (the points were at angles of equilateral triangles on side 0.6 cm) (Dunnill, Massarella, and Anderson, 1969). The number of points falling on bronchial mucous glands was expressed as a percentage of the total number of points falling on all tissues, and a mean was taken of the values for each of the three sites. The lungs were then sliced in the parasagittal plane at 1 cm intervals, and after barium sulphate impregnation (Heard, 1958) three or four slices were examined to determine the amount and type of emphysema present. This was done using a plastic grid and a point-counting technique (Dunnill, 1962). The type of tissue under each point in the grid was noted and a count was made of the following components in each slice: panlobular emphysema, centrilobular emphysema, normal lung, and non-parenchyma (blood vessels, bronchi, pleura, etc). The amount of each type of emphysema was expressed as a percentage of the total number of points counted, and a mean was taken of the three or four slices examined. Where both lungs were examined a mean was taken of the amount of emphysema in each lung. Using a stratified random technique (Dunnill, 1968), six blocks of lung were taken from each case. These were approximately 2.5 $\times$ 1.5 $\times$ 0.5 cm in size, and after paraffin embedding and sectioning they were stained with haematoxylin and eosin. The relative proportions of small airways lumen of diameter less than 2 mm were calculated in these sections using an eyepiece graticule with 25 equidistant points. Each point was scored as either small airways lumen or other lung tissue, and the proportion of small airways lumen (Q) in the lung was expressed as a percentage of the total number of points

counted (Matsuba and Thurlbeck, 1971). It was assumed that shrinkage due to fixation and processing was equal in small airways and in the remainder of the lung tissue, and Q was not corrected for the degree of inflation as this has been found not to be of major significance (Matsuba and Thurlbeck, 1972).

Sections from the same six random blocks of lung tissue were also stained by the Weigert-van-Gieson method. The whole section was examined with a $\times 25$ objective lens to determine the number of small vessels of less than 100μ in diameter which had a double elastic lamina with a layer of muscle between the laminae. This was done using a modification of the technique of Hunter *et al.* (1974). All small vessels with a definite elastic coat were counted, and the number of them which had a double elastic layer was expressed as a percentage of the total number of vessels counted. Small venules were included with the arterioles as it is very difficult to distinguish these without seeing them join an artery or vein (Brenner, 1935). Vessels of diameter less than 100μ were counted since this is the upper limit of size of pulmonary arterioles found by Brenner (1935). The criteria of Hunter *et al.* (1974) were used to distinguish thick-walled peripheral lung vessels from normal small vessels. A double elastic lamina was said to be present when two laminae, with a space between them, were visible for at least half the

diameter in cross section, or half the length of the wall in longitudinal section. Twenty random sections of lung were examined to establish the presence of acute suppurative bronchitis and bronchiolitis. This was defined as an exudate of acute inflammatory cells mixed with mucus which appeared to fill small airways. The sections were also examined for the presence of pneumonia and for evidence of thromboembolism in the small pulmonary arteries. None of the cases showed major thromboembolism in the large pulmonary arteries.

RESULTS

The 21 patients were divided into two groups according to the presence or absence of the clinical signs of right ventricular failure. Thirteen patients had been in right ventricular failure for at least one year before death, and their clinical details are shown in Table I. The other eight patients had never shown signs of right ventricular failure during life or only developed them during the terminal episode of the disease. The clinical details of these patients are shown in Table II. By the criteria of Burrows *et al.* (1966) all the patients had airways obstruction. The FEV₁ was less than 1.25 l in all the patients where it was measured, and the FEV₁:FVC ratio was 50% or less in all patients except case 66 in whom it was 55.5%.

TABLE I
CLINICAL DETAILS OF 13 PATIENTS WITH RIGHT VENTRICULAR FAILURE

Case	Age at Death (yr)	Sex	History (yr)	Duration of RV Failure (yr)	ECG	CXR	FEV ₁ (l)	FVC (l)	RV/TLC (%)	Pao ₂ (mmHg)	Paco ₂ (mmHg)	pH	Haemoglobin (g/dl)	PCV (%)
16	62	F	10	4	PP RVH	EH	0.50	1.0	61	38	63	7.35	16.5	61
21	47	M	12	5	RVH	H	0.60	1.8	—	29	70	7.32	14.7	57
27	76	M	10	2	NAD	E	0.25	0.85	—	44	62	7.36	—	57
30	51	M	17	1.5	PP	H	0.50	2.1	53	26	68	7.44	14.8	—
34	60	M	30	1.5	RVH PP	E	0.30	1.4	—	38	78	7.30	16.7	56
45	61	M	13	1	RVH PP	EH	0.50	1.8	—	36	86	7.28	20.6	70
46	38	F	20	2.5	RVH PP	EH	0.40	1.75	65	27	72	7.32	16.7	—
49	66	M	20	11	NAD	EH	0.60	1.8	35	42	54	7.36	17.8	61
51	64	M	15	1	NAD	EH	0.45	2.3	65	45	59	7.39	11.3	—
66	70	M	20	6	PP	—	1.0	1.8	—	54	45	7.50	16.6	50
70	49	F	3	1	PP RVH	EH	0.30	1.5	—	41	53	7.50	12.9	45
73	61	M	10	1.5	PP	EH	0.53	1.46	59	37	63	7.31	22.2	69
80	63	M	10	1.5	PP RVH	EH	0.60	1.58	62	40	62	7.39	17.4	59
Mean	59		14.6	3			0.50	1.63	55.7	38.2	64.1	7.37	16.5	58.5
SD	10.2		6.8	2.8			0.17	0.38	10.0	7.7	10.8	0.20	2.9	7.6

ECG=electrocardiogram; PP=P pulmonale; RVH=right ventricular hypertrophy (see text); CXR=chest x-ray; E=emphysema (peripheral pruning of vessels and bullae); H=enlargement of right heart; FEV₁=forced expiratory volume at one second; FVC=forced vital capacity; RV=residual volume; TLC=total lung capacity; Pao₂=arterial oxygen tension; Paco₂=arterial carbon dioxide tension; PCV=packed cell volume (haematocrit); NAD=normal.

TABLE II
CLINICAL DETAILS OF THE EIGHT PATIENTS WITHOUT RIGHT VENTRICULAR FAILURE

Case	Age at Death (yr)	Sex	History (yr)	ECG	CXR	FEV ₁ (l)	FVC (l)	RV/TLC %	Pao ₂ (mmHg)	Paco ₂ (mmHg)	pH	Haemoglobin (g/dl)	PCV %
9	69	M	25	PP	EH	0.35	1.0	64	38	97	7.24	16.0	50
15	70	F	20	RVH	—	—	—	—	32	110	7.20	16.5	—
19	74	M	16	NAD	—	—	—	—	45	53	7.42	17.9	62
20	60	M	9	PP	E	0.55	1.45	66	26	53	7.39	16.5	57
50	64	M	5	RVH	EH	0.30	1.6	—	36	45	7.35	14.4	—
68	68	M	3	RVH	—	—	—	—	21	85	7.23	—	59
72	68	M	10	RVH	E	0.77	2.28	64	66	52	7.39	15.0	—
74	70	M	50	PP	EH	0.44	1.14	66	55	40	7.44	15.2	47
Mean	67.8		17.2			0.48	1.49	65.0	39.8	66.8	7.33	15.9	55
SD	4.8		15.1			0.17	0.50	1.1	16.1	9.2	0.10	1.14	6.2

Of the 11 patients who had lung volume studies, 10 had RV/TLC ratios greater than 50%, and one (case 49) had a value of 35%. Analysis of the arterial blood gas tensions showed that all the patients had respiratory failure (Pao₂ < 75 mmHg and/or Paco₂ > 47 mmHg) (Ciba Guest Symposium Report, 1959). Thirteen patients had a haemoglobin or haematocrit which could be considered to be in the polycythaemic range (haemoglobin > 18.0 g/dl in male or > 16.4 g/dl in female; PCV > 54% in male or > 47% in female) (De Gruchy, 1964). Nine of these patients were in the group with right ventricular failure and four were not. There was no significant difference between the number of polycythaemic patients in failure and the number not in failure ($\chi^2=0.79$, $p>0.30$). The mean values for each of the two groups were compared for all the clinical parameters using Student's *t* test (Hill, 1971). The results of these comparisons are shown in Table III. It will be seen that the mean age at death was significantly lower in the group with right ventricular failure but that there were no other significant differences in respiratory function tests,

arterial blood gases or haematological parameters between the two groups.

The pathological details for the 13 patients with right ventricular failure are shown in Table IV. These include heart weights, amounts of emphysema, bronchial mucous gland sizes, proportion of small airways lumen in the lung, and proportion of thick-walled peripheral lung vessels. Similar details for the eight patients who did not have right ventricular failure are shown in Table V. The mean values for each of the two groups were compared using Student's *t* test, and the results of this are shown in Table VI. The group with right ventricular failure had a mean left ventricular weight of 195.3 g and this was significantly greater than the mean of the group who did not have failure (155.2 g). There was also a significantly greater mean right ventricular weight (132.9 g) in the group with right ventricular failure than in the non-failure group (70.8 g).

The ratio of the weight of the left to the right ventricle was significantly smaller in the right ventricular failure group. There were no significant differences between the two groups in the mean amount of emphysema (total or either type), the size of the bronchial mucous glands, the proportion of small airways lumen or the number of thick-walled peripheral lung vessels. Five patients had normal right ventricular weights (< 65 g) (Fulton *et al.*, 1952) and all of these were in the group who did not have right ventricular failure. All the patients who had clinical evidence of right ventricular failure had right ventricular hypertrophy (> 80 g). Left ventricular hypertrophy (> 225 g) was present in only one case (66), but there were a further nine cases in whom the left ventricular weight was greater than the accepted

TABLE III
COMPARISON OF MEAN VALUES OF CLINICAL PARAMETERS IN THE TWO GROUPS (*t* TEST)

Parameter	<i>t</i>	<i>P</i>	
Age at death	2.26	< 0.05	Significant
Length of history	0.55	> 0.50	
FEV ₁	0.22	> 0.80	
FVC	0.63	> 0.50	
RV:TLC (%)	1.81	> 0.10	
Pao ₂	0.33	> 0.70	
Paco ₂	0.58	> 0.50	
pH	0.57	> 0.50	
Haemoglobin	0.50	> 0.60	
Packed cell volume	0.89	> 0.30	

TABLE IV
PATHOLOGICAL DETAILS OF 13 PATIENTS WITH RIGHT VENTRICULAR FAILURE

Case	Ventricular Weight (g)		LV/RV	Total Amount of Emphysema (%)	Centri-lobular Emphysema (%)	Panlobular Emphysema (%)	Bronchial Mucous Gland Size (%)	Small Airways Lumen (%)	Thick-walled Peripheral Lung Vessels (%)	Acute Bronchitis	Pulmonary Thrombo-embolism
	Left	Right									
16	180	140	1.3	31	30	1	19.7	1.57	10.6	+	—
21	209	115	1.8	21*	20	1	18.6	1.15	16.9	+	+
27	196	88	2.2	44	14	30	12.8	0.13	19.3	—	—
30	213	152	1.4	55*	8	47	14.1	0.86	19.6	+	—
34	160	95	1.7	21	10	11	26.0	0.61	13.6	+	—
45	200	160	1.2	45	16	29	19.7	0.74	22.5	+	—
46	203	199	1.0	62*	3	59	20.5	0.68	17.5	+	—
49	205	140	1.5	28	28	0	15.6	0.49	18.6	+	—
51	175	110	1.6	44*	3	41	14.0	1.01	13.5	+	—
66	250	110	2.3	7*	7	0	11.5	1.55	20.7	+	+
70	110	120	0.9	88	0	88	11.2	0.31	17.3	+	—
73	213	150	1.4	95*	0	95	21.5	0.22	15.7	+	—
80	225	150	1.5	37*	9	28	11.5	0.65	15.9	+	—
Mean	195.3	132.9	1.52	44.4	11.4	33.0	16.6	0.77	17.0		
SD	34.2	30.5	0.41	25.6	9.8	31.1	4.6	0.45	3.3		

*Mean of right and left lungs.

TABLE V
PATHOLOGICAL DETAILS OF THE EIGHT PATIENTS WITHOUT RIGHT VENTRICULAR FAILURE

Case	Ventricular Weight (g)		LV/RV	Total Amount of Emphysema (%)	Centri-lobular Emphysema (%)	Panlobular Emphysema (%)	Bronchial Mucous Gland Size (%)	Small Airways Lumen (%)	Thick-walled Peripheral Lung Vessels (%)	Acute Bronchitis	Pulmonary Thrombo-embolism
	Left	Right									
9	156	60	2.6	40*	38	2	21.8	1.40	19.2	+	—
15	186	43	4.3	18*	18	0	23.0	0.57	6.5	+	—
19	172	105	1.6	70	4	66	16.0	1.59	34.8	+	—
20	212	114	1.9	47	8	39	23.0	0.76	19.9	+	—
50	104	55	1.9	64	26	38	20.1	1.01	28.8	+	—
68	167	80	2.1	40*	8	32	14.0	1.28	10.6	+	—
72	125	60	2.1	66*	0	66	28.4	0.96	17.2	+	—
74	120	50	2.4	28*	6	22	14.3	0.72	15.4	+	—
Mean	155.2	70.8	2.28	46.6	13.5	33.1	20.0	1.04	19.0		
SD	34.2	26.2	0.79	18.8	12.9	25.0	5.0	0.35	8.0		

*Mean of right and left lungs.

TABLE VI
COMPARISON OF MEAN VALUES OF PATHOLOGICAL PARAMETERS IN THE TWO GROUPS (*t* TEST)

Parameter	<i>t</i>	<i>P</i>	
Left ventricular weight	2.54	< 0.02	Significant
Right ventricular weight	4.78	< 0.001	Significant
LV:RV ratio	2.70	< 0.02	Significant
Total amount of emphysema	0.21	> 0.80	
Centrilobular emphysema	0.43	> 0.60	
Panlobular emphysema	0.01	> 0.90	
Bronchial mucous gland size	1.58	> 0.10	
Small airways lumen	1.46	> 0.10	
Thick-walled peripheral lung vessels	0.70	> 0.40	

upper limit of normal (190 g) while being less than 225 g. Of the 10 cases, nine were in the group which had clinical evidence of right ventricular failure.

Electrocardiographic changes were compared with the weight of the right ventricle. P pulmonale was present in 16 patients of whom four (cases 4, 50, 72, and 80) did not have right ventricular hypertrophy.

Five patients showed no P pulmonale on the electrocardiogram but, of these, four had enlarged right ventricles at necropsy. Changes consistent with right ventricular hypertrophy in the chest leads were shown on 13 electrocardiograms, and only two of these (cases 9 and 50) did not have enlarged right ventricles. Of the eight patients who did not have electrocardiographic changes of right ventricular hypertrophy, three had normal right ventricular weights (cases 15, 72, and 74) and the remaining five did have an increased right ventricular weight.

Chest radiographic changes were also compared with the findings in the lungs and heart found at necropsy. Emphysema was diagnosed on 15 radiographs, and all of these patients had pathological evidence of emphysema. However, there were two cases (21 and 30) in which 21% and 35% of emphysema respectively was present at necropsy and there were no significant signs of emphysema in the radiographs. Thirteen patients had radiological evidence of enlargement of the right ventricle and, of these, 10 had increased right ventricular weights and three had normal weights (cases 9, 50, and 74). Three patients (cases 20, 27, and 34) had no radiological evidence of right ventricular enlargement but had an increased right ventricular weight at necropsy.

Twenty of the 21 patients had histological evidence of acute bronchitis and bronchiolitis at necropsy. Only case 27 did not show this change. Pneumonia was present histologically in four cases (50, 51, 73, and 80). There was histological evidence of pulmonary thromboembolism in five cases (19, 20, 50, 66, and 70) out of the 21 (24%).

DISCUSSION

Several studies have attempted to divide patients with obstructive airways disease into two distinct groups (Ogilvie, 1959; Richards, 1960; Fletcher *et al.*, 1963; Burrows *et al.*, 1964; Briscoe and Nash, 1965). One type, referred to as type B by Burrows *et al.* (1966), is said to have severe right ventricular failure, polycythaemia, and severely altered blood gases and is predominantly bronchitic. The other type, called type A, does not usually have right ventricular failure, polycythaemia or grossly disturbed blood gases and is predominantly emphysematous. Most of these studies did recognize that not all cases could be fitted into these two distinct groups, and several more recent studies have questioned whether this simplified division into two groups has any merit (Martin, Katsura, and Cochran, 1970; Park *et al.*, 1970; Thurlbeck *et al.*, 1970; Anderson *et al.*, 1973). All the patients in the present series were bronchitics and would thus fall into either type B or X of the original Burrows classification. However, 15 of these patients had radiological evidence of emphysema, which is supposed to be a feature of type A disease. All the patients had severely disordered blood gases, but as these estimations were performed during the terminal phase of the disease, this measurement of respiratory failure is probably an indication of airways inflammation and blockage by mucous plugs rather

than the nature of the disease in the steady state. Eight of these patients did not have polycythaemia which is stated to be relatively common in the type B disease, and also eight of the patients had never been in heart failure before the terminal episode. All the patients had significant amounts of emphysema pathologically, a feature in Burrows classification of type A disease. The present series of patients do not appear to fit easily into the previously described groups, either clinically or pathologically. It has been suggested that heart failure is more common in obstructive airways disease when emphysema is slight (Burrows *et al.*, 1966), and also that right ventricular failure is related to predominantly centrilobular rather than to panlobular emphysema (Heath *et al.*, 1968). Neither of these findings is confirmed in the present study from which it appears that the amount and type of emphysema are not related to the presence or absence of right ventricular failure. The group with right ventricular failure in the present study did die at a significantly younger age than the group without failure, although there was no difference in the total duration of the illness, and this confirms the finding of Bishop (1973) that right ventricular failure carries a poor prognosis in obstructive airways disease. The mean length of time that patients survived in right ventricular failure was three years in the present study and this is similar to the findings of Ude and Howard (1971), who noted that 68% of patients died within five years of the first attack of failure, and Bishop (1973) who found that 77% of patients with heart failure were dead within four years.

A considerable group of patients die from chronic airways obstruction without developing pulmonary hypertension or right ventricular hypertrophy (Bishop, 1973), and this study has shown no quantitative clinical or pathological difference, other than the size of the heart, between this group and those who do develop right ventricular failure.

Fulton (1953) suggested that the rate of progression of the disease may be of major importance, as patients may die from airways obstruction before they have time to develop cardiac changes. No evidence of this is found in the present series of patients as the length of history of chest disease was not significantly different in those with and without failure nor was there a difference in the severity of the lung disease. As there is no fundamental difference in the nature or extent of the lung disease in those who die of heart failure and those who do not, the finding

of Lindsay and Read (1972) that there is a spectrum of vascular responsiveness in the pulmonary vessels to alveolar hypoxia is of interest. Patients with chronic airways obstruction who respond to the hypoxic stimulus develop pulmonary vessel contraction and eventually pulmonary hypertension, whereas non-responders do not behave in this manner and do not develop an elevated pulmonary artery pressure.

It has been stated that polycythaemia is more common in the 'bronchitic' type of patient who has cardiac failure than in the 'emphysematous' patient without failure (Ogilvie, 1959; Burrows *et al.*, 1964). This is not confirmed in the present series where there was no significant difference between the number of patients with polycythaemia in the right ventricular failure group and the non-failure group. Nor was there a difference in the degree of polycythaemia, as measured by the haemoglobin and packed cell volume, between the two groups. These haematological measurements were made during the terminal phase of the illness, and this may reflect the effects of a recent severe hypoxic episode as well as long-standing moderately reduced oxygen levels. There was no confirmation of the finding of Millard and Reid (1974) of a relationship between the weight of the right ventricle and the packed cell volume.

This study has shown a good correlation between the presence of clinical right ventricular failure and right ventricular hypertrophy at necropsy. Other studies (Thurlbeck *et al.*, 1970; Watanabe, Mitchell, and Renzetti, 1965) have noted similar correlations but, as in these series, there are exceptions. Three cases were present in which the right ventricle was enlarged but the patients had not been in clinical right ventricular failure. It appears from the present series that patients in right ventricular failure have developed an enlarged right ventricle but that some patients may develop right ventricular hypertrophy without subsequent heart failure (Thomas, 1972).

The electrocardiographic changes correlated reasonably well with the necropsy findings in the right ventricle. The presence or absence of P pulmonale proved to be a correct index of the presence or absence of right ventricular hypertrophy in 13 out of 21 cases (62%), and similarly electrocardiographic signs of 'right ventricular hypertrophy' in the chest leads were correct in 66% of cases. This degree of accuracy in the electrocardiographic detection of an enlarged right ventricle is similar to that of other studies (Fulton, 1953; Rees, Thomas, and Rossiter, 1964;

Padmavati and Raizada, 1972). Cases where the electrocardiographic changes and the right ventricular weight do not correspond may well be due to the fact that overdistension of the right ventricle may cause changes in the electrocardiogram although there is no increase in the weight of the ventricular muscle (Burrows *et al.*, 1964).

The radiographic diagnosis of emphysema proved to be accurate when compared to the necropsy findings, and in only two cases where there was a significant amount of emphysema at necropsy were radiological changes absent. In severe degrees of emphysema radiology has been shown to be a useful indicator of the presence of the disease (Thurlbeck, 1963; Burrows *et al.*, 1966), but it is less reliable when only small amounts of emphysema are present (Thurlbeck *et al.*, 1970). In the present series, where all the patients had severe airways obstruction, this high incidence of radiological emphysema would be expected due to overinflation of the lungs.

The radiographic estimation of the presence or absence of right ventricular enlargement was correct in 11 out of 17 cases (65%) in the present study. There were three false positives and three false negatives in the series when the radiographic changes were compared to the actual weight of the right ventricle. Previous studies have shown a similar number of inaccuracies in chest radiographic estimation of the size of the right ventricle (World Health Organisation, 1961; Thurlbeck *et al.*, 1970) and much of this is due to the increase in the radiographic size of the right ventricle being caused by dilatation rather than hypertrophy (World Health Organisation 1961; Cullen *et al.*, 1970).

This study has also shown the possible importance of an episode of acute infection in the airways in precipitating death in patients with chronic airways obstruction. Only one of the patients in the series did not have acute bronchitis histologically at necropsy. Pneumonia, however, was not a particularly common event in the present series. The importance of infection and its association with episodes of heart failure, in chronic airways obstruction, was pointed out by Fulton (1953) and Simpson (1958), and both these authors stressed the point that this terminal infection may be overlooked by the clinician as the temperature of the patient is often normal. This proved to be the case in the present series where the clinicians stated that there was no evidence of acute respiratory infection during life in the majority of the patients. Episodes of acute

bronchitis may precipitate right ventricular failure (Simpson 1958; Sweet *et al.*, 1961) but in the present series it was present equally in the patients with and without right ventricular failure.

Pulmonary thromboembolism contributed to the death of five patients in the present series (24%) but did not cause death in any of them. Few studies of the incidence of thromboembolic disease in chronic airways obstruction have been done but this percentage is similar to that of 29 found by Thurlbeck *et al.* (1970).

The finding of left ventricular hypertrophy at necropsy in patients with chronic airways obstruction has been noted by several authors (Michelson, 1960; Fluck, Chandraseker, and Gardner, 1966; Williams *et al.*, 1968; Fishman, 1971; Edwards, 1974). The left ventricular weight was greater than normal in 10 patients in the present series but in only one of these was the increase great enough to be called true left ventricular hypertrophy. All except one of the patients who had enlarged left ventricles were in the group with right ventricular failure. These patients also had right ventricular hypertrophy, and this confirms previous findings of a correlation between the size of the right and left ventricles (Boushy *et al.*, 1971; Edwards, Heath, and Harris, 1971). As muscle bands extend around both ventricles, hypertrophy of one is thought to cause concomitant hypertrophy of the other.

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