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Lung blood flow studies in patients with scoliosis and neuromuscular weakness

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Pulmonary capillary blood flow was measured by the nitrous oxide body plethysmograph technique in 16 patients, 10 of whom had scoliosis and six neuromuscular weakness.

A linear correlation was found between the pulmonary artery to capillary flow conduction time and Pa_{O_2} ($r = +0.85$; $P < 0.001$).

The finding of a reduced flow conduction time and its correlation with the Pa_{O_2} suggests the presence of pulmonary arterial hypertension presumably on the basis of active vasoconstriction.

Chronic hypoxia irrespective of its cause is associated with a characteristic vascular pathology consisting of muscularization of the pulmonary arterioles, absence of medial hypertrophy in the muscular pulmonary arteries, and the presence of longitudinal muscle in the intima of arteries and arterioles (Hasleton, Heath, and Brewer, 1968).

The pathogenesis of cardiorespiratory failure in scoliosis has been described by Bergofsky, Turino, and Fishman (1959); the thoracic deformity leads to compression of the lungs and increases the work of breathing with consequential alveolar hypoventilation. Hypoxaemia so produced may be further increased by venous admixture resulting from inhomogeneity of alveolar ventilation and perfusion (Shaw and Read, 1960) and eventually leads to pulmonary arterial hypertension and right heart failure. This pulmonary arterial hypertension is due to an increased resistance to blood flow through the vascular bed rather than to mechanical obstruction of major blood vessels, to back pressure from the left atrium, or to increases in pulmonary blood flow (Bergofsky *et al.*, 1959).

Lung capillary blood flow can be measured throughout the cardiac cycle using the N_2O-body plethysmograph method (Lee and DuBois, 1955) in which the rate of N_2O uptake from the lungs is recorded continuously using an optical sensor and electropneumatic feedback transducer (Karatzas, Lee, and Stott, 1967). Analysis of the N_2O uptake record provides the following information: (1) mean pulmonary blood flow; (2) the pulmonary artery to capillary flow conduction time, measured from the time of pulmonary valve opening to the foot of the pulmonary capillary flow pulse; (3) the pulsatility of capillary blood flow (ratio of peak to mean flow rates).

Previous work (Reuben, 1970, 1971) has established a close relationship between flow conduction time and mean pulmonary artery pressure and between pulsatility of capillary blood flow and the pulmonary arterial time constant (the product of pulmonary arterial resistance and compliance).

In a series of experiments Reuben, Gersh, Swadling, and Lee (1970) induced hypoxia in animals and produced pulmonary arterial hypertension. Induced hypoxia also caused a significant decrease in pulmonary arterial compliance and pulmonary arterial distensibility while the pulmonary artery to pulmonary capillary flow conduction time was significantly reduced from the control value.

The present paper describes a study of lung capillary blood flow in patients with scoliosis or neuromuscular weakness with particular reference to the effect of hypoxia.

METHODS

Eighteen studies were performed on 16 patients who gave informed consent. The relevant clinical details are listed in Table I; all those patients who had had anterior poliomyelitis had required assisted ventilation during their acute illness.

Patient 5 was studied on three separate occasions: when she was severely hypoxic, a month later following intensive therapy, and, finally, six months later when she had maintained her improvement.

All patients were in sinus rhythm and none had evidence of airways obstruction (Table III).

TABLE I

DIAGNOSTIC AND ANTHROPOMETRIC DATA

Case	Age	Sex	BSA	Scoliosis				Site of Respiratory Muscle Paralysis/ Weakness	Grade of Dyspnoea[1]
				Direction of Convexity	Aetiology	Angle of Curve	Apex of Curve		
1	16	F	1·48	Left	Idiopathic	70	T 12	0	0
2	24	F	1·48	Right	Poliomyelitis	70	T 9	Right side	2
3	35	F	1·72	Left	Poliomyelitis	60	T 12	Right and left side	2
4	15	M	1·52	Left	Idiopathic	40	T 5	0	0
5	28	F	1·28	Right	Poliomyelitis	110	T 4	Right side	3
6	21	F	1·28	Right	Idiopathic	50	T 6	0	1
7	20	M	1·52	Left	Poliomyelitis	65	T 6	Left side	1
8	21	M	1·43	Left	Poliomyelitis	70	T 6	Left side	1
9	27	M	1·66		Poliomyelitis				
10	42	F	1·70	Left	Poliomyelitis	60	T 6	Left side	0
11	40	F	1·57	0	Poliomyelitis	—	—	Bilateral	0
12	36	F	1·38	0	Poliomyelitis	—	—	Bilateral	1
13	34	F	1·65	0	Poliomyelitis	—	—	Bilateral	(Confined to a wheelchair)
14	59	F	1·41	0	Poliomyelitis	—	—	Bilateral	2–3
15	50	F	1·72	0	Poliomyelitis	—	—	Bilateral	1
16	37	M	1·66	0	Muscular dystrophy	—	—	Bilateral	1

[1] 0 No dyspnoea; 1 Dyspnoea with severe exertion; 2 Dyspnoea with moderate exertion; 3 Dyspnoea at rest.

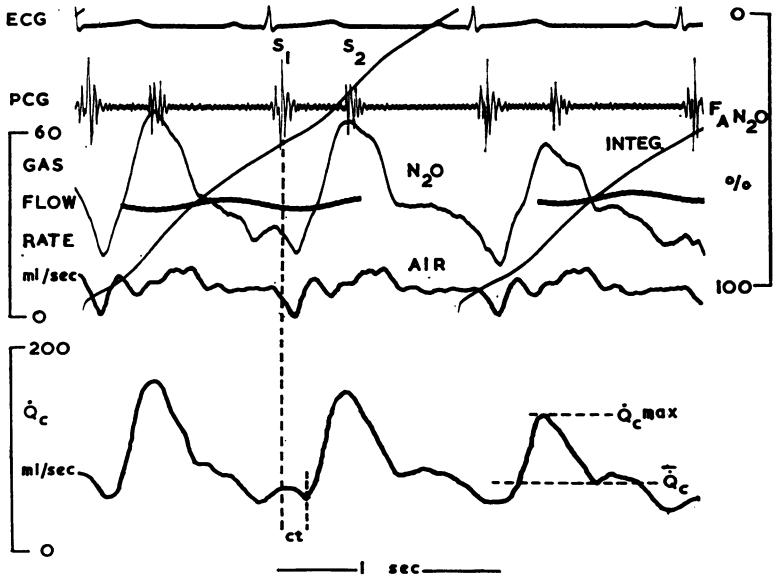

FIG. 1. *Patient 2. Plethysmograph gas flow record. This is a composite figure in which the N_2O trace has been superimposed over the AIR record from a cardiac cycle of equal length and a similar portion of the respiratory cycle. ECG=electrocardiogram (Lead II); PCG=phonocardiogram; N_2O=plethysmograph gas flow record during exhalation, following inhalation of 80% N_2O in oxygen; AIR=plethysmograph gas flow record during exhalation following inhalation of air; $\dot{Q}_c$ represents the algebraic subtraction of AIR from N_2O for one cycle, calibrated in blood flow units; ct=pulmonary artery to capillary flow conduction time. INTEG=the integrated signal of the N_2O flow curve.*

Pulmonary capillary blood flow was measured by the N_2O uptake technique during slow exhalation after a single breath of 80% N_2O in 20% O_2 according to the method of Bosman *et al.* (1964). The plethysmograph optical sensor and electropneumatic feedback system with the relevant calibration details have been previously reported (Karatzas and Lee, 1969). The concentration of N_2O in the expired gas was recorded continuously by an infrared N_2O analyser (Beckman model LB-1) in closed circuit with the body plethysmograph.

Lead II of the electrocardiogram and a high frequency phonocardiogram from the pulmonary area were also obtained.

The pattern of instantaneous pulmonary capillary blood flow was derived from the N_2O uptake in the manner previously described (Karatzas and Lee, 1969).

The patients were trained to perform the respiratory manoeuvres repeatedly in an identical manner and to maintain constant air flow during slow exhalation.

Pulmonary artery to capillary flow conduction time was measured as the time from the third major vibration of the first heart sound (indicating pulmonary valve opening) to the foot of the capillary flow pulse (Fig. 1). The normal range in this laboratory is 120–180 msec. In patients in sinus rhythm no difficulty is encountered in delineating the foot of the pulmonary capillary flow pulse, and measurements made by different observers usually agreed within 10 msec.

The pulsatility index of capillary blood flow was calculated as the ratio of peak to mean flow rates. Normal in this laboratory is 1·8–2·0:1.

Lung function tests were performed on the same day as the plethysmograph studies. These included: (1) forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) using a Med-Science Wedge spirometer which had a digital readout; (2) total lung capacity (TLC) using the nitrogen washout technique; (3) arterial blood was drawn anaerobically from the brachial artery and blood gas tensions were measured with Radiometer electrodes and corrected for elapsed time and temperature according to the nomogram of Kelman and Nunn (1966); (4) expired air was collected over a 5-minute period and analysed for oxygen and carbon dioxide tensions. The ratio of physiological dead space to tidal volume (V_D/V_T) was calculated from the arterial blood and expired air carbon dioxide tensions (Comroe *et al.*, 1962); (5) the degree of venous admixture was calculated assuming an arterial-mixed venous oxygen extraction of 4·5 ml/100 ml.

RESULTS

Table II summarizes the results of the lung capillary blood flow studies. Figure 2 is a graph of pulmonary artery to capillary conduction time plotted against PaO_2. The relationship is a linear one and demonstrates that those patients with the lowest PaO_2 have the shortest flow conduction time. The regression equation obtained was:

$$CT = 1{\cdot}47\ PaO_2 - 15{\cdot}39$$

Correlation coefficient $= +0{\cdot}85$; $P < 0{\cdot}001$.

The results of the lung function studies are summarized in Table III.

TABLE II

N_2O-PLETHYSMOGRAPH RESULTS

Case	Heart Rate (beats/min)	Pulmonary Blood Flow (l./min)	Pulmonary Artery-Capillary Flow Conduction Time (msec)	Pulsatility Index
1	90	6·1	126	1·9
2	96	2·8	105	2·4
3	72	4·1	85	1·9
4	72	5·8	104	2·1
5a	96	2·0	60	1·7
	94	2·7	80	1·7
	90	2·9	75	1·8
6	92	2·5	140	2·4
7	96	2·5	125	2·1
8	72	3·2	110	2·0
9	96	3·3	112	2·0
10	80	6·4	137	2·0
11	72	4·3	100	2·0
12	80	4·0	120	2·2
13	120	2·5	99	2·1
14	100	3·2	70	1·8
15	100	5·6	125	2·0
16	80	3·0	120	2·0
Mean ± S.E.	89 ± 13	3·80 ± 1·5	104·3 ± 23·7	2·0 ± 0·2

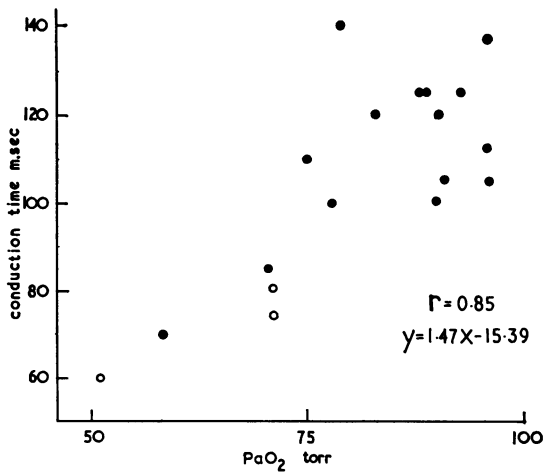

FIG. 2. *Relationship between pulmonary artery to capillary flow conduction time (ordinate) and PaO_2 (abscissa). Each point on the graph represents the average data for each patient. The three open circles represent the findings in patient 5 on three separate occasions.*

TABLE III
RESULTS OF LUNG FUNCTION STUDIES

Case	FVC (l.)	FVC % predicted	FEV_1 %	TLC (l.)	TLC % predicted	VD/VT %	QS/QT %	Pao_2 (torr)	$Paco_2$ (torr)
1	3·12 (4·20)[1]	74	90	4·13 (6·23)	66	39	6	89·0	39·4
2	0·88 (3·89)	23	100	2·13 (6·00)	36	44	4	90·0	38·2
3	2·57 (3·49)	74	78	4·16 (5·64)	74	40	6	70·5	44·7
4	2·86 (4·45)	64	90	4·79 (5·39)	80	36	3	96·1	40·3
5	0·83 (2·93)	28	—	2·13 (4·23)	50	45	23	51·3	52·2
	1·04	36	86	2·14	47	49	14	71·0	57·8
	1·03	36	—	2·14	47	50	12	70·0	53·0
6	1·60 (3·14)	51	100	2·93 (4·51)	65	61	5	92·6	35·2
7	1·81 (4·68)	39	80	3·48 (5·82)	60	55	9	78·4	50·0
8	2·52 (3·76)	67	92	4·09 (4·84)	84	33	4	96·2	39·2
9	1·93 (5·08)	38	78	3·59 (6·75)	53	54	5	82·8	48·8
10	1·09 (2·50)	44	86	4·12 (4·30)	95	43	5	95·5	45·6
11	3·52	—	90	5·5	—	47	6	79·2	36·7
12	2·86 (3·14)	91	78	4·60 (4·6)	100	43	6	95·9	34·8
13	0·74 (3·19)	23	84	2·32 (4·63)	50	64	11	78·0	48·4
14	0·84 (2·88)	29	80	3·71 (4·46)	83	76	26	58·1	62·5
15	2·51 (2·95)	85	74	4·62 (4·46)	103	48	8	88·1	37·9
16	1·66 (5·08)	33	65	3·8 (6·75)	56	55	3	88·0	41·0
Mean±S.E.	1·82±0·90	49·1±22·2	84·4±9·2	3·57±1·05	68·0±19·9	49·0±10·6	8·6±6·5	81·7±13·3	45·7±8·2

[1] Predicted values given in parentheses based on age and height (Cotes, 1968).

DISCUSSION

Our results show a linear relationship between the pulmonary artery to capillary flow conduction time and the PaO_2; those patients with the shortest conduction times had the severest degree of hypoxaemia. The flow conduction time depends on the distensibility of the pulmonary arterial system and we believe that the shortened conduction time found in these patients is due to reduced arterial distensibility. Reuben (1970) has demonstrated a close correlation between the pulmonary artery to capillary flow conduction time and the mean pulmonary arterial pressure in patients with valvular heart disease and also in patients with normal pulmonary arterial pressures. The relationship was an inverse curvilinear one; patients with the severest degree of pulmonary arterial hypertension had the shortest flow conduction time. It is possible that decreased pulmonary arterial distensibility in the absence of pulmonary arterial hypertension is due to vasomotor activity of the smooth muscles of the pulmonary arteries.

Clinical and experimental studies have demonstrated a close correlation between hypoxia and pulmonary arterial hypertension. This correlation has been found in normal people living at high altitude (Peñaloza, Sime, Banchero, and Gamboa, 1963) or when rendered acutely hypoxic (Fishman, Fritts, and Cournand, 1960) as well as in patients with emphysema (Whitaker, 1954) and scoliosis (Bergofsky *et al.*, 1959). There is evidence that hypoxic pulmonary arterial hypertension is reversible (Whitaker, 1954; Bergofsky *et al.*, 1959; Peñaloza *et al.*, 1963). Such reversibility due to improved oxygenation is, we believe, reflected by our patient 5, whose flow conduction time lengthened from 60 to 80 msec when the PaO_2 was raised from 52 to 70 torr with vigorous therapy. This finding is in keeping with the results of Bergofsky and his colleagues, who lowered the mean pulmonary artery pressure from 52 to 18 mmHg in a scoliotic patient by positive pressure ventilation.

Three scoliotic patients (2, 4, and 8) had a shortened flow conduction time (105, 104 and 110 msec respectively) despite normal blood gas tensions. Hanley, Platts, Clifton, and Morris (1958) demonstrated a raised pulmonary artery pressure in the absence of hypoxia in one scoliotic patient while the pulmonary vessels of two of their patients dying from 'kyphoscoliotic heart disease' did not show the histological changes commonly associated with severe pulmonary arterial hypertension. Bergofsky and his colleagues (1959) also found a raised pulmonary artery pressure in the absence of hypoxia in certain scoliotics, although when hypoxia was present the pulmonary arterial hypertension was always more severe. These authors suggested that 'compression, diminution in distensibility and distortion of the pulmonary vessels due to the small deformed lungs may produce a raised pulmonary arterial pressure'. It is interesting to note that our three patients (2, 4, and 8) did not have a great reduction in their total lung capacity (66, 89, and 84% of predicted normal respectively). However, it is possible that the distensibility of the vessels may have been altered by the distortion of the lungs.

Lung capillary blood flow is pulsatile with each

heart beat (Lee and DuBois, 1955). Karatzas and Lee (1970) have shown that in patients with valvular heart disease the pattern of capillary blood flow is influenced by both pulmonary arterial and venous resistance as well as heart rate. Studies of the effect of acute hypoxia on the capillary flow profile in dogs have shown that there was no significant difference between values of the pulsatility index of the control state and hypoxia (Morkin, Levine, and Fishman, 1964; Reuben *et al.*, 1970).

The pulsatility index of capillary blood flow in our patients was normal. We believe that this was because the reduction in pulmonary arterial distensibility (as indicated by the reduced flow conduction time) compensated for the raised pulmonary vascular resistance (which we did not measure but assumed was present) and so maintained a uniform time constant. This uniformity of the time constant explains the finding of a normal pulsatility index (Reuben, 1971).

Wasserman, Butler, and Van Kessel (1966) and Karatzas and Lee (1969) showed an inverse relationship between pulsatility of capillary blood flow and heart rate. However, normal pulsatility was maintained up to rates of 100 beats per minute. Only one of our patients had a rate greater than 100 (120 per minute) and she maintained a normal pulsatility. No measurement of pulmonary venous pressure was made in any of our patients; however, from the work of Bergofsky *et al.* (1959) it is unlikely that it would be raised in these patients.

Abnormal ventilation-perfusion relationships will clearly affect the accuracy of the N_2O plethysmograph method when used for estimating the pulmonary blood flow. This would explain the low values found in some of our patients. Bergofsky did not find any extraordinary increases in pulmonary blood flow at rest which could account for a raised pulmonary arterial pressure in his group of scoliotic patients.

We conclude that in our patients the reduced pulmonary artery to capillary flow conduction time and normal pulsatility of capillary flow is due to pulmonary arterial hypertension and reflect the vasoconstrictive effects of hypoxia on their pulmonary arterioles. The N_2O plethysmograph technique could prove a useful non-invasive method for studying the severity of such changes and in assessing the response to treatment.

We wish to thank Professor Duthie for allowing us to study patients who were under his care. We are indebted to Mrs. E. Wheeler, Mr. T. Stallard, Miss C. Ranson, and Dr. B. Hasleman for technical assistance and to Dr. G. de J. Lee who allowed us to use the facilities of his laboratory.

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