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THE EFFECT OF CORTICOSTEROID TREATMENT ON PULMONARY FUNCTION IN SARCOIDOSIS

BY

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Previous studies have shown that pulmonary function in sarcoidosis may be impaired in various ways. The vital capacity and lung volume may be reduced (Bruce and Wassén, 1940; Austrian, McClement, Renzetti, Donald, Riley, and Cournand, 1951), an emphysema pattern with increased residual volume and impaired mixing may be demonstrated (Stone, Schwartz, Feltman, and Lovelock, 1953; Coates and Comroe, 1951), or the diffusing capacity of the lungs may be impaired (Riley, Riley, and Hill, 1952; Marshall, Smellie, Baylis, Hoyle, and Bates, 1958). Now that the effectiveness of corticosteroids in the treatment of sarcoidosis is established, their effect on impaired pulmonary function in this disease becomes of interest, especially as considerable radiographic clearing usually follows this form of treatment. Previous investigations of this problem have been made by Riley *et al.* (1952) in three patients, and by McClement, Renzetti, Himmelstein, and Cournand (1953) in five patients. In the present study 11 patients with pulmonary sarcoidosis have been studied before and during treatment, with special reference to their pulmonary function, chest radiographs, and symptoms.

MATERIAL AND METHODS

The 11 patients studied were all admitted to hospital initially for full clinical investigation along lines reported elsewhere (Smellie and Hoyle, 1957). All were found to have typical clinical and radiographic features of sarcoidosis. Ten had diffuse shadows in the lungs, the eleventh having clear lung fields with clinical evidence of extrapulmonary sarcoidosis: a lung biopsy, however, showed pulmonary fibrosis and non-caseating tubercle follicles. There were typical histological appearances in all biopsies except one, where the liver and conjunctival biopsies were negative, although his disease was typical in all other respects. Pulmonary function tests were performed before and during treatment. The first tests were made in the month before the start of treatment in nine patients, one year before in one and in the remaining patient 10 months after the start of long-term treatment. The second series of tests was made at the time of maximum radiographic improvement; this varied from two to 27 months after treatment began (Table I). The lung volume and its subdivisions were measured, also the mixing efficiency (ME), one second forced expiratory volume (FEV_1), the diffusing capacity for carbon monoxide (Dco), the compliance and the non-elastic resistance (NER) of the lungs. The techniques were mainly those previously described (Marshall *et al.*, 1958). The diffusing capacity was

TABLE I

CLINICAL DATA ON 11 PATIENTS WITH SARCOIDOSIS

Patient No.	Sex	Age (yr.)	Known Duration of Disease (Years)	Biopsy	Interval between Start of Treatment and Repeat Tests (mth.)	Dyspnoea before Treatment	Radiographic Appearances before Treatment
1	M	22	1	–	15	0	Enlarged hilar nodes with nodular infiltration
2	M	39	10	+	5	0	" "
3	F	37	9	+	2	2	Diffuse fine stippling
4	M	57	2	+	3	1	" "
5	F	51	17	+	27	1	Fine " stippling with fibrotic streaks
6	M	49	3	+	3	1	Nodular infiltration
7	F	26	2	+	4	1	Nodular infiltration with fibrotic streaks
8	M	31	6	+	7	1	Enlarged hilar nodes with nodular infiltration
9	F	51	1	+	19	0	Nodular infiltration and advanced fibrosis
10	F	58	5	+	3	2	Clear
11	F	42	5	+	21	1	Nodular infiltration and fibrotic streaks

Dyspnoea grading: 0, Normal exercise tolerance. 1, Dyspnoea on moderate effort, e.g., running for a bus, or inability to climb hills or stairs quickly. 2, Can walk on level without dyspnoea but additional tasks not possible. Can climb one flight of stairs without distress.

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TABLE II

RESULTS OF PULMONARY FUNCTION TESTS ON 11 PATIENTS WITH PULMONARY SARCOIDOSIS

Subject	Interval between Tests (mth.)	FRC (ml.)			VC (ml.)			IC (ml.)			Mixing Efficiency (%)			Compliance (l./cm.H_2O)			NER (cm.H_2O l./sec.)			FEV_1 (l.)		
		Before	After	% Difference	Before	After	% Difference	Before	After	% Difference	Before	After	% Difference	Before	After	% Difference	Before	After	% Difference	Before	After	% Difference
1	15	3,630	3,843	+6	6,510	6,840	+5	4,650	4,778	+3	82	70	−15	0·189	0·208	+10	3·03	1·88	−38	4·60	4·80	+4
2	7	2,830	1,762	−38	3,600	3,825	+6	3,101	3,335	+8	96	80	−17	0·151	0·121	−20	3·00	3·40	+13	2·79	2·42	−13
	8		2,030	−28		3,830	+6		3,068	−1												
3	15	1,415	1,406	−1	2,122	2,305	+9	1,408	1,720	+22	40	45	+12	0·051	0·061	+20	5·04	4·52	−10	1·81	1·52	−16
4	3	2,813	2,798	−1	3,352	3,945	+18	2,006	2,837	+42	61	61	0	0·186	0·158	−15	4·10	2·30	−44	2·58	2·65	+3
5	17	3,490	3,070	−12	2,923	2,990	+2	1,462	2,234	+53	55	63	+15	0·116	0·175	+51	1·92	2·69	+40	2·17	2·33	+7
	28		2,305	−34		2,910	0		2,365	+62		30	−45								2·29	+5
6	7	3,605	3,818	+6	3,335	3,823	+15	2,058	2,540	+23	57	66	+16	0·127	0·168	+32	3·30	2·70	−16	1·65	2·29	+5
7	4	2,792	3,075	+10	2,485	2,943	+18	1,499	1,954	+30	79	75	−5	0·192	0·090	−53	1·80	3·10	+72	2·27	2·61	+15
8	9	2,460	2,430	−1	2,694	3,379	+25	1,830	2,570	+40	42	55	+31	0·090	0·069	−23	2·65	2·23	−16	1·92	2·21	+15
9	19	1,714	1,879	+10	2,620	2,779	+6	2,224	2,269	+2	58	32	−45	0·085	0·071	−16	5·13	5·30	+3	1·85	1·85	0
10	3	3,948	4,060	+3	1,585	1,847	+20	1,363	1,512	+15	22	19	−14	0·059	0·044	−25	7·43	4·90	−34	0·71	0·58	−18
	6		4,089	+4		1,657	+8		1,243	−9		22	0								0·79	+11
11	23	2,490	2,468	−1	2,420	3,020	+25	1,606	2,083	+29	72	64	−11	0·079			4·24			2·36	2·50	+6

TABLE III

RESULTS OF PULMONARY FUNCTION TESTS ON 11 PATIENTS WITH PULMONARY SARCOIDOSIS

Subject	Rest											Exercise										
	Min. Vol. (l.)		Oxygen Utilization (ml./l. Ventilation)			Steady State Dco (ml./min./mm. Hg)			Single Breath Dco (ml./min./mm. Hg)			Treadmill Speed (m.p.h.)	Min. Vol. (l.)		O_2 Uptake (ml./min.)		Oxygen Utilization (ml./l. Ventilation)			Steady State Dco (ml./min./mm. Hg)		
	Before	After	Before	After	% Difference	Before	After	% Difference	Before	After	% Difference		Before	After	Before	After	Before	After	% Difference	Before	After	% Difference
1	17·54	11·67	1·73	2·73	+57	27·5	22·0	−20	35·8	39·8	+11	3	27·3	21·6	1,526	1,274	5·59	5·89	+5	38·7	41·0	+6
2	5·47	5·28	5·00	5·08	+2	21·4	21·9	+2	32·0	30·0	−6	3	31·2	23·4	1,520	1,446	4·88	6·19	+27	25·3	28·5	+13
3	9·70	5·27	—	3·65	—	5·5	7·5	+36	—	10·0	—	2	22·6	15·1	390	536	1·74	3·55	+104	6·0	9·1	+52
4	11·62	10·50	2·44	2·11	−13	16·8	19·2	+14	21·4	24·7	+15	3	24·9	23·5	960	990	3·86	4·42	+14	16·0	19·8	+24
5	13·7	8·03	—	2·80	—	4·1	7·5	+83	—	10·8	—	1½	27·1	22·8	870	639	3·25	2·80	−14	5·3	9·4	+73
		8·02		2·84	—		7·1	+73		7·8	—	1½		29·6		884		2·98	−8		7·7	+45
6	8·24	6·13	3·26	4·75	+46	12·3	11·2	−9	18·4	12·1	−34	3	22·2	29·6	880	930	3·96	3·13	−21	15·3	12·9	−16
7	4·75	4·22	5·58	5·33	−4	17·9	17·5	−2	20·2	17·8	−12	3	21·2	15·9	953	957	4·50	6·01	+33	21·2	21·5	+1
8	8·15	8·32	3·33	3·54	+6	7·7	6·9	−10	13·4	11·9	−11	1¼	19·9	18·2	795	757	4·00	4·17	+4	9·8	10·6	+8
9	10·10	8·50	—	3·92	—	8·1	10·2	+26	—	14·0	—	¾	13·8	13·6	780	693	4·70	5·10	+7	8·7	12·6	+45
10	6·40	7·40	3·67	3·58	−2	—	11·0	—	23·0	20·7	−10	¾	11·3	13·3	575	800	5·07	4·58	−10	14·4	11·3	−21
		5·71		4·37	+16		13·8	—		18·2	−21	¾		11·1		607		5·47	+8		13·5	−6
11	7·00	4·74	—	5·57	—		21·2		—	—	—	1	13·8	15·6	660	773	4·74	4·96	+5		24·4	

measured both by the "steady state" (Bates, Boucot, and Dormer, 1955) and by the single breath (Ogilvie, Forster, Blakemore, and Morton, 1957) techniques. Nine patients were treated with prednisone in doses of 20 to 30 mg. daily, and this was maintained at least until the pulmonary function tests had been repeated. Two others had cortisone. Dyspnoea was assessed clinically according to the patients' accounts of their exercise tolerance (Marshall *et al.*, 1958), irrespective of the result of the pulmonary function tests.

Results

Table I contains some clinical data on the 11 patients. The results of the pulmonary function tests made before and during treatment, and the percentage difference between these measurements, are recorded in Tables II and III. The percentage differences which we considered significant were (*a*) greater than 10% for functional residual capacity (FRC), vital capacity (VC), and FEV_1; (*b*) greater than 25% for compliance and NER; and (*c*) greater than 25% for Dco. These estimates of significance are approximate and are based on the degree of variation found in repeat tests on normal subjects. The significant changes are recorded in Table IV, together with the changes in the chest radiographic appearances and dyspnoea. A check of the significance of a change is provided when two or more tests measure the same function: thus an increased vital capacity should be accompanied by an increased compliance, the single breath and steady state Dco results should be altered to approximately the same extent, and a change in FEV should be accompanied by an inverse change in NER.

Pulmonary function was initially normal in five of the 11 patients (Cases 1, 2, 4, 7, and 11). Case 11 has been included because the only abnormal tests were a high NER in the presence of a normal FEV_1. During treatment the vital capacity increased significantly in three of these five but without an accompanying increase in lung compliance. Six patients had abnormal function before treatment and an impaired diffusing capacity, and three had changes in the mechanical properties of the lungs. After treatment the diffusing capacity improved significantly in three of the six, although not enough to give a normal result. The mechanical properties of the lungs likewise remained abnormal although improved in isolated tests.

TABLE IV

SIGNIFICANT CHANGES IN PULMONARY FUNCTION TESTS, IN RADIOGRAPHIC APPEARANCES, AND IN DYSPNOEA

Subject	FRC	VC	Compliance	NER	FEV	Dco	Radiographic Clearing	Dyspnoea
1				+			++	
2	Reduced				−		+	−
3					−	+	0	+
4		+		+			++	0
5	,,		+	−		+	0	0
6		+	+			−	++	+
7		++	−	−	+		+	+
8		+					++	+
9						+	+	−
10		+		+	+			0
11		+					+	+

−=Worse. +=Improved. ++=Considerably improved. 0=No change.

The changes in the main subdivisions of pulmonary function may be summarized as follows:

Functional Residual Capacity.—Four patients had reduced FRC, which was not increased by treatment. Three patients had an increased FRC, and in only one was it reduced by treatment and even then not to normal.

Vital Capacity.—Three patients had a low vital capacity initially. In all three there was an increase with treatment though in no case to normal. Another three patients had an increase in their VC, the initial result being in the normal range.

Forced Expiratory Volume.—Six patients had a reduced FEV, and this was increased in three with treatment, two of these reaching a normal result.

Compliance.—This was reduced in three patients, in whom it did not increase with treatment.

Non-elastic Resistance.—This was increased in five patients, of whom three improved with treatment, one to normal limits.

Diffusing Capacity for Carbon Monoxide.—Five patients had a reduced Dco, and in three of them it was increased with treatment, but not to normal levels.

Reduction of the radiological shadows in the lung fields occurred in nine of the ten patients with initial changes. The tenth had improvement in dyspnoea and diffusing capacity, despite no radiographic improvement, and it is of interest that the other two patients with a significant increase in the Dco during treatment showed only slight clearing. In the whole group of patients, improvement in dyspnoea occurred in five, two of whom had normal function initially. Four of the five had moderate or considerable radiographic clearing with treatment, together with an increase in vital capacity, but no improvement in diffusing capacity.

Discussion

Riley *et al.* (1952) found the vital capacity to be inversely related to the amount of pulmonary

infiltration and considered it to be a sensitive guide to the progress of the pulmonary lesions. Shulman, Schoenrich, and Harvey (1952) observed an increase in vital capacity in all of seven patients treated with corticosteroids. In the present series four of the five patients who showed an improvement in dyspnoea also had an increased vital capacity. In only one of these patients, however, was the compliance increased. This suggests that their improvement in vital capacity and dyspnoea may not be due to improvement in the function of the lungs, but to some other factor such as an increased sense of well-being produced by the corticosteroids.

There was no relationship between improvement in dyspnoea and increased diffusing capacity in our series. Riley *et al.* (1952) and McClement *et al.* (1953) found, as we did, that treatment usually failed to increase the diffusing capacity to normal. This finding supports the view that impaired diffusion in sarcoidosis is due to irreversible changes in the lungs, presumably fibrotic in nature.

We conclude that, in pulmonary sarcoidosis, striking improvement in chest radiographic appearances with corticosteroid therapy may be unaccompanied by improvement in either pulmonary function or dyspnoea.

SUMMARY

Pulmonary function tests were done before and during corticosteroid treatment in 11 patients with pulmonary sarcoidosis. The main disturbance of pulmonary function was an impaired diffusing capacity in six patients which improved partially after treatment in three though without corresponding improvement in dyspnoea. The vital capacity increased with treatment in six patients, but its significance was lessened by the absence of accompanying increase in compliance. These minimal changes in lung function with treatment contrasted with the striking improvement often seen radiographically.

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