PULMONARY FUNCTION STUDIES IN SARCOIDOSIS [1]

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In spite of a considerable literature on sarcoid disease, very little has been written concerning alterations in pulmonary physiology produced by this condition. Baldwin, Cournand, and Richards (1) recently reported studies of pulmonary function in various fibroses of the lungs, including two proven and three presumed cases of sarcoid. However, no patient was included in their study if the residual volume of the lungs exceeded the predicted normal value.

We have had the opportunity of studying pulmonary function in a group of ten patients with sarcoidosis. The clinical manifestations of the disease included involvement of lymph nodes, lungs, liver, skin and bone. The diagnosis was confirmed in each case by biopsy of a lymph node or cutaneous lesion. All had negative tuberculin skin test. Eight had demonstrable involvement of the lungs or of mediastinal lymph nodes (see Table I). We are presenting the data obtained on these to illustrate a pattern of pulmonary impairment that may be found in this disease.

METHODS

Pulmonary function studies were performed on each patient when first seen and, in five patients, were repeated two months later. The following measurements were made:

1. Arterial blood was obtained with the patient at rest, breathing room air. Arterial pH was measured at 37° C. in a Cambridge closed glass electrode. The CO_2 content of whole blood was measured and CO_2 pressure was calculated (2). Arterial O_2 content and capacity were measured (2) and O_2 saturation was calculated after making appropriate corrections (3).

2. Intrapulmonary distribution of inspired O_2 was studied by the single breath technic described by Fowler (4) and Comroe and Fowler (5) using the Lilly nitrogen and flow meters (6, 7). Data were derived from analysis of curves obtained from a single maximal expiration following a single maximal inspiration of O_2. Studies of intrapulmonary gas mixing were also made by the technic of Cournand and his associates (8), *i.e.*, measurement of the N_2 concentration in an alveolar gas sample delivered at the end of a seven-minute period of O_2 inhalation.

3. Vital capacity, inspiratory capacity (maximum volume of gas that can be inspired from resting expiratory level, and expiratory reserve (maximum volume of gas that can be expired from the resting expiratory level) were measured separately on a Benedict-Roth spirometer; the maximum of three trials was recorded. Functional residual capacity (FRC—sum of RV and expiratory reserve) was determined by the open circuit method of Darling, Cournand, and Richards (9). Residual gas volume (RV) and total capacity (TC) were calculated from the above values.[2] Maximal breathing capacity per minute (MBC) was determined by maximal voluntary hyperventilation for 15 seconds through low resistance valves and wide tubing. The expired gas was collected in a compensating Tissot spirometer of 140 L capacity. The maximum of three attempts was recorded. Respiratory rate, depth, and minute volume were measured while the resting patient breathed through a mouthpiece and valves into the Tissot spirometer.

All gas volumes were corrected to 37° C. 760 mm. Hg, saturated with water vapor. Predicted values for maximal breathing capacity were based on the regression formula of Baldwin, Cournand, and Richards (11). The predicted values for lung volumes were derived from a composite summary of the literature, in which height and weight were the important variables.

RESULTS

The results of the pulmonary function tests are presented in Tables II–IV.

A. Patients with hilar and mediastinal adenopathy. In three patients (O. H., B. S., and I. W., Table I), radiologic studies demonstrated that the intrathoracic lesions were confined largely to enlargement of the hilar and mediastinal lymph nodes. In these, the physiological findings were essentially within the normal range except for a slightly reduced MBC in patient I. W. and low arterial O_2 saturation in patient O. H.

B. Patients with parenchymal involvement of the lungs. Five such patients were studied. Vital

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[2] The terminology used in this paper is that proposed by Pappenheimer (10).

TABLE I

Clinical data upon patients with sarcoidosis

Patient	Sex	Age	Ht.	Wt. (*lbs.*)	S.A.	Radiologic evidence of pulmonary disease	Symptoms related to respiratory disease
O.H.	M	17	5′7″	127	1.67	Mediastinal and hilar adenopathy, plus slight, diffuse reticulation in lung fields	None
B. S.	F	24	5′6″	127	1.63	Mediastinal and hilar adenopathy	None
I. W.	F	29	5′8″	176	1.93	Mediastinal and hilar adenopathy	None
S. F.	F	58	5′3″	170	1.84	Linear densities, chiefly in lower thirds, both lungs	Mild dyspnea on exertion
M. M.	F	44	5′5″	127	1.63	Flocculent and linear densities in upper and lower thirds right lung and upper third left lung	None
G. O.	F	33	5′3″	100	1.47	Extensive densities in upper third of each lung	None
E. S.*	F	26	5′1″	84	1.36	Flocculent and linear densities entire left and lower half right lung. Huge cyst in upper right lung enlarging over several years	Dyspnea on exertion
J. W.	F	28	5′2″	103	1.49	Widespread flocculent and linear densities distributed uniformly throughout both lungs	Dyspnea on exertion

* Died following an intrabronchial hemorrhage 10 months after studies were performed.

capacity was reduced significantly in three of the five; this was due largely to a diminution in the inspiratory capacity. Total lung capacity was less than the predicted normal value only in patient J. W. In all five, residual volume was increased markedly; it varied from 160% to 331% of the predicted normal value. The RV/TC ratios were all abnormally high, 30% to 65%. The FRC was also greater than normal in all. Thus the lungs were in a hyperinflated state at the end of both a forced and a normal expiration. All five had evidence of impairment in the mechanics of breathing; the MBC was 56% to 74% of expected normal values.

All had definite abnormality in the distribution of inspired gas to the alveoli as judged by the single breath analysis (5), even though pulmonary nitrogen elimination was normal in all five as judged by the Cournand seven-minute test (8). This emphasizes the greater accuracy and reliability of the single breath test as a measure of the uniformity of distribution of inspired gas. The reasons for this are presented elsewhere (5); hyperventilation during the seven-minute test was probably suffi-

TABLE II

Arterial blood measurements

Patient	O_2 cont.	O_2 cap.	O_2 satur.	CO_2 cont. (wh. bl.)	CO_2 cont. (plasma)	CO_2 pressure	pH	Total Hb	Hematocrit
	vol. %	*vol. %*	*%*	*vol. %*	*vol. %*	*mm. Hg*		*grams*	*%*
O. H.	17.2	18.2	92.3	50.1	59.8	40.5	7.41	13.6	46
B. S.	16.9	17.4	96.7	50.9	60.5	39.0	7.44	13.0	42
I. W.	14.5	15.1	96.2	54.0	62.4	42.2	7.41	11.3	35
S. F.	18.9	19.8	95.5	37.8	46.2	29.2	7.45	14.8	43
M. M.	13.7	14.3	96.1	47.2	53.9	40.0	7.38	10.7	35
G. O.	14.7	15.3	96.0	48.5	56.2	38.2	7.42	11.4	34
E. S.	13.0	14.0	93.5	41.9	47.9	30.0	7.45	10.5	36
J. W.	17.0	17.9	95.1	44.0	51.6	41.0	7.34	13.4	—

TABLE III

Lung volumes in patients with pulmonary sarcoidosis

Patient	Vital cap. (cc.)			Insp. cap. (cc.)			Exp. res. (cc.)			Resid. vol. (cc.)			Total cap. (cc.)			% RV/TC	FRC		
	Obs.	Pred.	%	Obs.	Pred.	%	Obs.	Pred.	%	Obs.	Pred.	%	Obs.	Pred.	%		Obs.	Pred.	%
*O. H.	4,020	4,270	94	2,715	3,435	79	1,595	835	191	915	1,070	86	4,935	5,340	93	19	2,510	1,905	132
*B. S.	3,165	3,340	95	2,230	2,505	89	1,025	835	122	1,080	835	129	4,245	4,175	102	25	2,105	1,670	125
*I. W.	3,000	3,460	88	2,050	2,615	79	1,010	845	120	1,000	870	115	4,000	4,330	92	25	2,010	1,715	117
S. F.	2,420	2,560	95	2,000	1,920	104	500	640	78	2,150	900	239	4,570	3,460	132	47	2,650	1,540	172
M. M.	2,350	3,320	71	1,720	2,490	69	760	830	92	2,310	1,020	226	4,660	4,340	107	50	3,070	1,850	166
G. O.	2,990	3,220	93	1,960	2,415	81	1,530	805	190	1,290	805	160	4,280	4,025	106	30	2,820	1,610	175
E. S.	1,420	3,160	45	1,020	2,370	43	685	790	87	2,650	800	331	4,068	3,960	103	65	3,335	1,590	209
J. W.	1,090	2,860	38	630	2,145	29	480	715	67	1,220	715	171	2,310	3,575	65	52	1,700	1,430	118

* Pulmonary disease limited primarily to mediastinal and hilar adenopathy.

cient to mask the presence of the poorly ventilated areas, clearly revealed by the single breath.

Only one patient, E. S., had pulmonary insufficiency at rest for the oxygenating mechanism; none had insufficiency so far as CO_2 elimination was concerned. None had disabling dyspnea. Apparently breathing could still be increased, without severe discomfort, sufficiently to arterialize the venous blood.

DISCUSSION

The data obtained in our studies differ strikingly from those reported by Baldwin, Cournand, and Richards (1). Their patients with sarcoidosis had a mean decrease in residual volume and total capacity, whereas ours had no consistent change in total capacity but a marked increase in residual volume. The discrepancy appears to lie entirely in the selection of cases. Baldwin was studying diffuse pulmonary fibrosis specifically, and consequently included in her report only cases that fitted her rigid criteria. On the other hand, we were studying patients who fitted rigid clinical criteria for pulmonary sarcoidosis. The pathological disturbance in all cases of sarcoidosis may well be that of fibrosis, but as Spain (12) has pointed out, fibrotic lesions may occur predominantly in one of five general regions in the lung: bronchiolar, interstitial, intra-alveolar, vascular or pleural. In the cases reported by Baldwin, intra-alveolar or interstitial fibrosis must have been the predominant lesion, leading to obliteration of some functional lung tissue and a decrease in lung volume. In our cases, the fibrosis must have been concentrated around bronchioles or air ducts, so as to produce residual hyperinflation quite similar to that reported by Beale, Fowler, and Comroe (13) in symptom-free patients with chronic

TABLE IV

Alveolar gas uniformity and ventilatory measurements

	Alveolar gas uniformity % N_2	N elim. (9) % N_2	Resp. rate per min.	Resp. depth L/M²	Min. vol. (air) L/M²	Min. vol. (O_2) L/M²	MBC L/M²		
							Obs.	Pred.	%
Normals	1.5 or less	<2.5	16	.22	3.5	3.8			
Patient									
O. H.	1.0	1.5	11	.431	4.73	5.09	98.8	77.6	127
B. S.	1.5	1.0	24	.202	4.90	5.46	62.2	60.3	103
I. W.	1.5	1.0	19	.208	3.99	4.09	38.6	57.5	67
Patient									
S. F.	4.5	1.3	11	.516	5.65	5.27	27.9	43.3	66
M. M.	4.0	1.3	15	.294	4.42	4.47	37.1	50.4	74
G. O.	8.0	1.8	23	.224	5.24	6.25	41.6	55.6	75
E. S.	7.0	1.3	33	.305	10.10	9.94	32.8	58.8	56
J. W.	6.0	1.2	33	.235	7.85	6.04	40.1	57.5	70

asthma. It is likely that the clinical picture of pulmonary sarcoidosis varies sufficiently in different patients and at different stages of the disease that either alveolar fibrosis or bronchiolar fibrosis might occur, each producing a different physiological pattern. In our group, diffuse alveolar fibrosis may have been present in only one patient (J. W.). This one patient was quite similar to the cases of fibrosis reported by Baldwin in that the vital capacity was reduced to a much greater extent than the MBC and the TC was reduced to 65%; however, the patient had an RV 171% of predicted normal, which suggests a mixed picture of alveolar and peribronchiolar fibrosis.

It is possible that the parenchymal disturbance in sarcoidosis may, in some patients and at some stage of the disease, lead to the tearing of alveolar septa and diminution in elasticity that is characteristic of emphysema. We cannot be certain, without histologic studies or measurements of intrapleural pressure, that our patients did not have this destructive type of emphysema. However, we have the impression that our patients differed in several respects from patients with severe enough emphysema to result in residual volumes in the range of 47–65% of TC. Our patients did not have history of chronic cough or asthmatic attacks, elevated alveolar N_2 concentration after seven minutes of inhalation of O_2, decrease in arterial O_2 saturation such as occurs when there is uneven distribution of both blood and air to alveoli,[3] or elevation of arterial pCO_2 such as usually occurs in patients with advanced emphysema. Therefore we believe that the lungs of our patients were hyperinflated primarily because of obstructive lesions rather than because of primary destruction of alveolar septa and diminution in pulmonary elasticity.

Considered alone, pulmonary function studies are not useful in diagnosis of pulmonary sarcoidosis because the pattern may vary widely. However, we have found these studies to be helpful in assessing the type and degree of existing functional abnormality, and in measuring changes in function, whether due to natural evolution of the disease or as a result of therapy. Roentgen examination in this particular group of patients has been unreliable as a guide to functional impairment; we have observed that considerable change may occur both in function studies and in clinical symptoms with little change in the X-ray appearance.

[3] An exception here was patient E. S.; autopsy later revealed that she had distortion and scarring of bronchioles but in addition had many cystic-like areas which had resulted from destruction of parenchymal tissue.

SUMMARY

1. Pulmonary function studies were performed in eight patients with clinical sarcoidosis, confirmed by biopsy.

2. In three of these, the thoracic disease was confined primarily to hilar and mediastinal adenopathy; in these the function studies were essentially normal except for a decrease in maximum breathing capacity in one and a reduction of arterial O_2 saturation in another.

3. In five, the intrathoracic lesions were primarily pulmonary in nature; consistent abnormalities found in these were: (*a*) abnormal intrapulmonary gas distribution as measured by the single breath test; (*b*) increase in the absolute and relative value for residual capacity (residual hyperinflation); (*c*) decrease in maximum breathing capacity.

4. Reasons are presented for attributing these changes to peribronchiolar fibrosis rather than to intra-alveolar or interstitial fibrosis or to emphysema of the destructive type.

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