PULMONARY FUNCTION IN BOECK'S SARCOID

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Boeck's sarcoid frequently produces widespread roentgenologic evidence of pulmonary disease without clinical signs or symptoms. Wright and Filley (1) reported normal pulmonary function studies in one such case. Others (2, 3, 4, 5) have reported a variety of effects of more advanced sarcoidosis on pulmonary function. This report is a study of pulmonary function in six cases of Boeck's sarcoid and emphasizes the frequent coincidence of widespread disease without severe functional impairment.

MATERIALS AND METHODS

The six patients included in this report were all young males in Walter Reed Army Hospital. In each instance a positive diagnosis of Boeck's sarcoid was made on histologic material (peripheral lymph node or lung [Case I]), and in each instance exhaustive study ruled out the presence of tuberculosis. The pertinent clinical data are summarized in Table I.

Maximum breathing capacity was determined by having the subject breathe as deeply and as rapidly as possible for 15 seconds through a low-resistance respiratory valve into a Douglas bag. The predicted normal value is based on a formula by Wright (6) which obtains for normal males studied in this laboratory.

Pulmonary ventilation-perfusion studies were performed as outlined by Riley, Cournand, and Donald (7). Fasting subjects lay supine for twenty minutes breathing room air with an indwelling needle in the radial artery, whereupon expired air was collected over a three-minute interval and arterial blood was allowed to flow into a syringe the dead space of which was filled with mercury and a heparin-fluoride mixture. The arterial sample was collected for a 1-minute interval during the middle of the expired air collection and was analyzed immediately for blood gas tensions. Subsequently, the study was repeated during the inhalation of 14 per cent oxygen after a 20-minute interval had elapsed in order to achieve a steady state.

Gas volumes were measured in a Tissot spirometer and corrected to body temperature. Gas composition was measured by the Scholander micro-gas analyzer (8) and duplicates checked within plus or minus 0.03 volume per cent. The RQ of the expired air was calculated from the alveolar equation (9). Arterial pCO_2 and pO_2 were measured by Riley's technique (10) and all duplicate analyses checked within plus or minus 3 mm. Hg. In standardizing this technique a large number of analyses was performed on samples of blood previously equilibrated in a tonometer with gas of known tensions. Agreement was good between blood and gas tensions and there was no need for the correction factors recommended by Riley.

The effective alveolar oxygen tension was calculated from the alveolar equation, substituting arterial pCO_2 for alveolar pCO_2. From a knowledge of the alveolar-arterial oxygen gradient at two levels of oxygenation, the effects of venous admixture and of impaired diffusion on reducing the arterial oxygen tension can be calculated (11, 12). The per cent venous admixture and the oxygen diffusing capacity were calculated from this data by means of charts developed by Riley, Cournand, and Donald (7).

TABLE I

Clinical data on six patients with Boeck's Sarcoid

Case	B.S.A.	Age	X-ray	Symptoms
I	1.85	23	Large, rounded, discrete lesions throughout both lung fields.	Spontaneous pneumothorax on left. No other cardiorespiratory symptoms.
II	1.75	24	Slight hilar adenopathy; generalized hazy infiltration through both lungs.	No cardiorespiratory symptoms. 5-month history of uveitis due to sarcoidosis.
III	1.88	26	Slight hilar adenopathy; generalized hazy infiltration through both lung fields.	9-month history of vague chest pain without cough or dyspnea.
IV	1.70	26	Moderate hilar adenopathy; increased lung markings with slight nodularity.	1-year history of intermittent dry cough and shortness of breath on heavy exertion. Twice treated with cortisone.
V	1.80	22	Marked hilar adenopathy and hazy parenchymal infiltration.	1-year history of progressive exertional dyspnea; 4 months of dry cough.
VI	1.92	26	Hilar adenopathy.	No cardiorespiratory symptoms. Diagnosis made on routine chest X-ray 6 months before study.

Accurate calculation of the oxygen diffusing capacity requires that the effective alveolar-effective capillary oxygen tension gradient be at least 4 mm. Hg. In a study of nine normal individuals in this laboratory a mean diffusion gradient of 1 mm. Hg was found so that the normal diffusing capacity cannot be calculated. A value of 20 has been arbitrarily selected as the low limit of normal for DO_2. Twenty-one normal distribution gradients were measured in this laboratory and the mean gradient was 9 mm. Hg, corresponding to a venous admixture effect of 4 per cent. Similar values for the normal distribution gradient have been reported by Ryan and Hickam (13), Filley, Gregoire, and Wright (14), and Blount, McCord, and Anderson (15). However, Comroe and Dripps (16) and Galdston and Wollack (17) have found no difference between effective alveolar oxygen tension and arterial oxygen tension in normal subjects. In dogs (18) the size of the distribution gradient has been found to vary directly with the magnitude of the alveolar ventilation, and a similar relationship has been found in man (19). This effect is probably due to uneven ventilation which causes different RQs in various parts of the lung and, hence, a gradient between effective alveolar air and arterial blood (18, 20). Thus, the venous admixture effect may vary from 0 to 8 per cent in normal individuals depending upon the nature of the ventilation.

The dead space was calculated from the Bohr equation (9) and, in normal people, occupies less than 30 per cent of the tidal volume. The relative size of the dead space is also dependent upon the nature of the ventilation and may be increased up to 40 per cent of the tidal volume if the breathing is rapid.

RESULTS

The results of these studies are summarized in Tables II and III. Spirometry was performed on all patients, and in none was there evidence of respiratory obstruction.

Case I was entirely asymptomatic. Six months before the time of the study he had a spontaneous pneumothorax, following which chest X-ray showed extensive parenchymal involvement with many large rounded densities scattered through both lung fields. Five months before study lung biopsy revealed granulomatous disease consistent with Boeck's sarcoid. Chest X-ray was unchanged at the time pulmonary function studies were performed and the studies were entirely normal.

Case II had no cardiorespiratory symptoms, although X-ray revealed moderate hilar adenopathy and slight generalized parenchymal infiltration. The venous admixture effect was at the upper limits of normal, and other studies were entirely normal.

Case III reported no cardiorespiratory symptoms other than a nine-month history of vague chest pain. X-ray revealed slight hilar adenopathy and a diffuse, hazy parenchymal infiltration. Ventilatory function was normal, but the patient exhibited hyperventilation at rest. Since this was

TABLE II

Gas exchange data

Case	Inspired oxygen tension $P_{I_{O_2}}$ *mm. Hg*	"Effective" alveolar oxygen tension $P'_{A_{O_2}}$ *mm. Hg*	Art. P_{O_2} $P_{a_{O_2}}$ *mm. Hg*	Art. P_{CO_2} $P_{a_{CO_2}}$ *mm. Hg*	Expired P_{CO_2} $P_{E_{CO_2}}$ *mm. Hg*	Ventilation *L./min.* BTPS $\dot{V}_E$	Resp. rate f	Oxygen consumption *ml./min.* STPD $\dot{V}_{O_2}$	Respiratory quotient R
I	148	93	88	41	30	2.62	7	243	.70
	100	56	55	39	28	3.48	10	236	.87
II	148	99	88	38	26	4.35	14	305	.74
	96	52	48	37	26	4.25	12	280	.81
III	148	94	87	41	20	4.87	21	293	.71
	96	54	44	38	21	5.07	16	262	.90
IV	148	98	87	39	28	2.92	8	218	.73
	101	60	55	36	27	3.17	10	199	.86
	150	96	83	38	25	3.07	8	232	.66
	102	62	55	33	17	4.81	11	198	.81
V	150	102	77	34	13	6.72	40	281	.65
	98	60	48	34	15	6.89	34	253	.87
VI	149	93	89	39	20	3.95	17	263	.65
	101	58	53	38	22	4.38	19	254	.86

TABLE III

Summary of ventilation, distribution, and diffusion data

Case	Maximum breathing capacity *L./min.* BTPS		Vital capacity *Liters* BTPS		Ratio of dead space to tidal volume	Ratio of venous admixture to total blood flow	Oxygen diffusing capacity of the lungs *cc./min./mm.Hg*
	Obs.	Pred.	Obs.	Pred.	$V_D/V_T \times 100$	$\dot{Q}va/\dot{Q}t \times 100$*	D_{O_2}
I	185	185	5.0	4.6	22	3	Normal†
II	179	184	5.6	4.4	21	6	Normal
III	168	181	3.4	4.7	37	4	15
IV	136	181	4.0	4.3	18	6	Normal†
	136	181	3.8	4.3	25	8	14
V	138	184	3.0	4.5	40	14	15
VI	139	181	5.4	4.8	28	2	18

* Calculations are made with an assumed A-V difference of 25 per cent saturation.

† If the $P^eA_{O_2} - Pa_{O_2}$ gradient is less than 4 mm. Hg during 14 per cent O_2 breathing D_{O_2} is represented simply as "Normal."

not present on exercise, it probably was of functional origin rather than due to the pulmonary disease. This patient showed a slightly diminished diffusing capacity and a large dead space without abnormal venous admixture. In the absence of seriously impaired diffusion or blood-gas distribution the increase in relative dead space may be attributed to the hyperventilation.

Case IV gave a one-year history of intermittent cough and dyspnea on heavy exertion for which he had twice received five-week courses of cortisone therapy, one year and nine months before studied. X-ray revealed hilar adenopathy and increased lung markings with nodularity. The data obtained on two occasions, separated by a ten-day interval, are both included in the tables. Maximum breathing capacity was reduced, although vital capacity was normal. The dead space was not increased but the venous admixture effect was at the upper limit of normal and the diffusing capacity at the lower limit of normal.

Case V gave a one-year history of exertional dyspnea which was accompanied more recently by a slightly productive cough. X-ray revealed marked hilar adenopathy and generalized hazy infiltrations of the lung parenchyma. He showed abnormality in all functions measured with reduced MBC and vital capacity, hyperventilation at rest and on exercise, diminished diffusing capacity, a large venous admixture effect and a large dead space.

Case VI had no cardiorespiratory symptoms. Six months before the study, routine chest X-ray showed hilar adenopathy with some nodular increase in lung markings in the perihilar areas. Although his vital capacity was normal, he showed a diminished maximum breathing capacity. Nevertheless, there was no increase in dead space or venous admixture, and diffusing capacity was normal.

DISCUSSION

The abnormalities in pulmonary function in Boeck's sarcoid exhibit great variability. This might be expected from a knowledge of the pathology of the disease. Basically, the lesions consist of granulomata in the alveolar walls with large areas of normal lung interspersed between the diseased tissues, and accumulations of granulomatous lesions in the peribronchial and perivascular areas (21). These granulomata generally become fibrosed, and the extent of the resultant scar tissue determines the effect of the disease on lung function. Patients with peripheral granulomata without scarring and with large areas of normal lung (Case I) may exhibit perfectly normal lung function at rest. Another such case has been reported by Wright and Filley (1), and the only abnormality in that individual was hyperventilation on exercise.

On *a priori* grounds, one would anticipate that extensive scarring of the lung parenchyma would lead to impairment of ventilatory function, hyperventilation at rest, and an increase in the size of the lung dead space. One or more of these findings was evident to a slight extent in Cases III, IV, and VI. In these cases the process had not progressed to the point of significant interference

with the diffusion of oxygen or with the ventilation-perfusion relationship of sufficient area of lung to cause an increase in venous admixture. Similar findings have been observed by others in one patient who had diminished ventilatory function (MBC and vital capacity) and an increased lung dead space but normal resting diffusing capacity and venous admixture (22). Baldwin, Cournand and Richards (5) have included five such cases of Boeck's sarcoid in their group 1 of pulmonary fibrosis.

More extensive involvement of the lungs with the pathologic process leads to generalized pulmonary fibrosis with interference of all phases of pulmonary function. Case V is an example of generalized pulmonary fibrosis with evidence of alveolar-capillary block. In addition to impaired ventilatory function (hyperpnea at rest) and a large dead space, he had a greatly increased venous admixture effect and slightly diminished oxygen diffusing capacity. Reports by others (3, 4) include five more such cases with the manifestations of "alveolar-capillary block."

The presence of granulomata in the hilar lymph nodes and peribronchial areas exerts no effect on pulmonary function unless there is encroachment on the airways. None of these patients demonstrated signs of obstructive disease, although Coates and Comroe (2) reported five out of eight cases of Boeck's sarcoid who showed this type of abnormality.

Thus, the physiologic abnormalities in Boeck's sarcoid would appear to be quite variable but dependent upon the location and the extent of the pathologic process. Peripheral granulomata, even though extensive, may exert no measurable effect on pulmonary function at rest. Accumulations of fibrous tissue around the airways may lead to a predominantly obstructive type of disease. Extensive scarring of the parenchyma may lead to restriction of lung volume, impairment of maximum ventilatory function, increase in the size of the pulmonary dead space, and an augmented venous admixture effect, probably due to uneven ventilation and perfusion of the lung. Finally, diffuse fibrosis may cause impairment of the diffusing capacity of the lungs, either by thickening of the alveolar wall or by reduction in the number of pulmonary capillaries, as discussed by Riley, Riley, and Hill (4). Such effects may occur singly, but in advanced cases they generally occur in combination. In the cases herein reported, no particular combination of defects was obvious, three patients having a single different abnormality. The diffusing capacity in these patients was only measured at rest, and it is quite possible that their maximum diffusing capacities were subnormal, in view of the apparent frequency of "alveolar-capillary" block in this disease. Only two patients experienced exertional dyspnea and in all but Case V the degree of functional impairment was slight despite the presence of large areas of disease evidenced by X-ray.

Finally, a word should be said about therapy with cortisone or ACTH. Although the functional deficit may correlate with the patient's symptoms, one cannot correlate the extent of disease demonstrable by X-ray with the effect of the disease on pulmonary function. Since pulmonary tuberculosis may easily be mistaken for Boeck's sarcoid, and since cortisone and ACTH are considered to exert an unfavorable action on tuberculosis, such therapy should not be considered on the basis of the amount of disease which is demonstrated by X-ray alone. Cortisone and ACTH should be reserved for those cases in which there is evident effect of the disease on pulmonary function.

SUMMARY

Observations are presented of some pulmonary functions in six patients with Boeck's sarcoid. There was little correlation between the degree of roentgenologic involvement and of impaired pulmonary function. Pulmonary function in such patients at rest may be normal despite the presence of large areas of diseased lung by X-ray. Sarcoidosis may cause pulmonary fibrosis with diminished ventilatory function and increased pulmonary dead space. In advanced cases, these abnormalities may be accompanied by impairment of oxygen diffusing capacity and of pulmonary ventilation-perfusion relationships.

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