

Lung function in sarcoidosis

An investigation of the disease as seen at a clinic in England and a comparison of the value of various lung function tests

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A comprehensive series of lung function tests has been carried out on 130 patients with sarcoidosis. Selected results are presented but a full table of analysed results is obtainable on application to the authors. The results are discussed particularly in relation to patients with clear lung fields, to patients with bilateral hilar lymph node enlargement, and with regard to the choice of tests for repeated use in sarcoidosis patients.

The results of lung function tests in sarcoidosis have been reported extensively, the largest series being from the United States (Johns and Ball, 1967; Richert and Klocke, 1966), from France (Basset, Georges, and Turiaf, 1967; Batime *et al.*, 1967), from Germany (Doll, Reindell, Wurm, and Ganz, 1964; Pan, 1964), and from England (Marshall and Karlish, 1967). Although sarcoidosis occurs in all parts of the world (Siltzbach, 1967) the presentation of the disease varies in different countries and in different ethnic groups. The intention of this paper is to present the results of lung function tests in a series of sarcoidosis patients seen in one clinic in England and to consider the relative value of the various tests in sarcoidosis.

MATERIAL

The patients were all seen at the Sarcoidosis Clinic in Reading by one of us (A. J. K.). Pulmonary function tests have been carried out on many other patients with sarcoidosis but in order to avoid distortion of the results as seen in one clinic these have not been included in the series.

The diagnosis of sarcoidosis was confirmed in all cases by tissue biopsy, Kveim test, or both methods. Of 300 patients diagnosed in the Reading clinic during the years 1958-69, 130 had pulmonary function tests and the patients form a representative series as shown in Table I. Only 6 of the 130 patients had clear chest radiographs at the time of diagnosis but by the time of testing their number had increased to 19.

METHODS

Lung volumes, forced expiratory volumes, the mechanical properties of the lungs, blood gas analyses,

TABLE I
DISTRIBUTION OF PATIENTS IN THE RADIOLOGICAL STAGES OF SARCOIDOSIS

Stage at Diagnosis	Pulmonary Function Group (130 patients) %	Sarcoidosis Clinic (300 patients) %
0	4.6	7.7
1	46.9	54.6
2	21.5	21.0
3	26.2	16.0
4	0.8	0.7

Stage 0: chest radiograph clear
Stage 1: bilateral hilar lymphadenopathy
Stage 2: B.H.L. and lung mottling
Stage 3: lung mottling only
Stage 4: lung mottling with fibrosis

and the single breath diffusing capacity for carbon monoxide were carried out by standard methods. The exercise test was walking on a treadmill for five minutes. The degree of exercise selected was influenced by the age and apparent fitness of the patient. At the end of exercise the patients were asked if they felt short of breath, and the degree of dyspnoea, if present, was recorded as slight, moderate or severe, according to the degree of distress apparent to the observer (R. M.).

The results of the tests have been analysed according to the radiological grading of the sarcoidosis (stage 0—chest radiograph clear; stage 1—bilateral hilar lymphadenopathy; stage 2—bilateral hilar lymphadenopathy and lung mottling; stage 3—lung mottling only; stage 4—lung mottling with fibrosis). Normal values for lung volumes were calculated by the equations of Needham, Rogan, and McDonald (1954). These predicted volumes, corrected to BT_{PS}, agree well with results on normal subjects in this laboratory. Normal values for the single breath diffusing capacity for CO were calculated by the equations of Ogilvie, Forster, Blakemore, and Morton

(1957), Williams, Seriff, Akyol, and Yoo (1961), and McGrath and Thomson (1959). Normal values for lung compliance and non-elastic resistance are based on the results of Marshall (1957).

RESULTS

The statistical analysis of the results of all the tests on 130 patients is presented in a table obtainable on application to the authors. Selected results are shown in Figure 1.

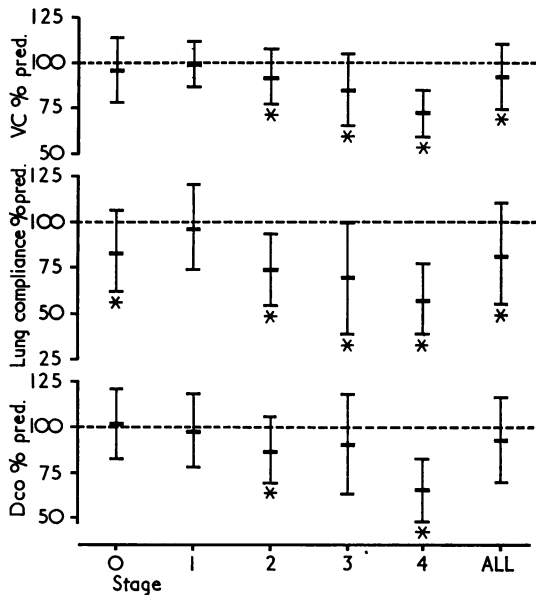


FIG. 1. Vital capacity, lung compliance (percent of normal predicted from the patient's expected functional residual capacity), and diffusing capacity (predicted from the equation of Williams *et al.* (1961)) in the different stages of sarcoidosis. Mean values and one coefficient of variation. * indicates that the mean is significantly different from normal.

DISCUSSION

PATIENTS WITH CHEST RADIOGRAPHY SHOWING CLEAR LUNG FIELDS Of the 19 patients in stage 0 at the time of the lung function tests seven were known to have had previous lung infiltration (stages 2 and 3) and 12 were not known to have lung involvement (seven of the 12 had been in stage 1). Only one patient, previously in stage 3, had a diffusing capacity significantly below normal but four had a low compliance. Of these four, two were known to have had previous lung

changes. These patients illustrate the difficulty in detecting residual fibrosis on the chest radiograph.

STAGE 1 In patients with stage 1 disease the results of lung function tests were essentially normal. Of the 44 patients in stage 1, two had a diffusing capacity below normal. Two had a low FEV% and one patient had a lung compliance at the lower limit of normal. These results differ from those of Sharma, Colp, and Williams (1966), who found much more severe changes in stage 1 disease. The difference in the two series may be due to the more acute disease studied in the American series or to a different type of sarcoidosis in the Negro races. In this series 15 patients had had evidence of stage 1 disease for less than 2 months and six for less than one month, and in these patients the results of their lung function tests were also normal. Six patients are known to have had hilar node enlargement for more than two years and in these too the lung function was essentially normal.

DURATION OF DISEASE AND LUNG FUNCTION A previous report (Marshall and Karlish, 1967) showed that both lung compliance and diffusing capacity decreased with increasing duration of the disease. This was in agreement with the findings reported in 28 patients by Ting and Williams (1965). Examination of the values in the patients with lung infiltration in this larger series shows no significant correlation between either compliance or diffusing capacity (expressed as percentage of predicted by the equation of Williams) and the apparent duration of the disease (compliance *v.* duration, $r = +0.0199$, S.E. 0.1374; diffusing capacity *v.* duration, $r = 0.1503$, S.E. 0.1241). The diffusing capacity expressed as the percentage of predicted from the equation of Ogilvie *et al.* (1957) shows a closer correlation ($r = 0.2451$, S.E. 0.1241, $0.1 > P > 0.05$) but this is biased by the failure of the prediction formula to take into account the natural decrease of diffusing capacity with age.

DYSPNOEA An attempt was made to assess dyspnoea by considering as dyspnoeic those patients who appeared to be slightly dyspnoeic with a minute volume of less than 30 litres/min or moderately dyspnoeic with a minute volume of less than 50 litres/min (see Methods). Although 60 of the 130 patients had complained of shortness of breath at some stage of the disease only 27 showed dyspnoea as assessed by the above standards, and 10 of these had not given a history of shortness of breath (Table II). It is interesting

TABLE II
NUMBER OF PATIENTS WITH DYSPNOEA AS ASSESSED ON TREADMILL

	Stage of Disease					All
	0	1	2	3	4	
History of shortness of breath	4	1	5	4	3	17
No history of shortness of breath	1	7	1	1	0	10
						27

that eight patients with stage 1 disease had apparent dyspnoea on exercise and seven of these had not previously complained of shortness of breath.

CHOICE OF LUNG FUNCTION TESTS A fairly large number of tests was done on these patients, including blood gas studies and the measurement of the mechanical properties of the lungs using an oesophageal balloon. An analysis of the value obtained from the tests is useful in deciding on a limited number of tests for follow-up of the patients. The full range of tests comprising lung volume measurements, FEV, single breath diffusing capacity, blood gas studies, oesophageal pressure measurements, and an exercise test occupy one to one and one-half hours of the patient's time and about two to three hours of the technician's time. Advantages in reducing the number of tests are to reduce the time required, both for patients and technicians, to avoid the need for medical assistance—e.g., for arterial puncture, and to avoid the repeated use of procedures which patients dislike, such as arterial punctures and swallowing an oesophageal balloon.

The two aspects of pulmonary function which are probably of most importance in sarcoidosis are oxygen uptake by the lung and lung stiffness. It is therefore of interest to see if measurement of blood gases gives useful information additional to that given by the diffusing capacity, and if measurement of lung compliance gives useful information additional to that afforded by the vital capacity.

Blood gas studies were carried out on 109 patients. Twenty-six had a low diffusing capacity (less than 80% of predicted normal) but in only six of these was the arterial oxygen tension below the lower limit of normal (less than 75 mmHg). Eight other patients had an arterial oxygen tension below 75 mmHg, making a total of 14 out of the 109 tested, but seven of these eight

patients had some evidence of uneven distribution of ventilation, either a low FEV%, a high airway resistance or a low gas-mixing efficiency index. Uneven ventilation and/or perfusion reduces the arterial oxygen tension but may give a falsely high value to the single breath diffusing capacity. Fortunately in sarcoidosis uneven ventilation is not common and is probably due in many cases to coexisting chronic bronchitis or emphysema. Changes in arterial oxygen tension may reflect changes in the bronchitis rather than of the sarcoidosis.

The other results derived from blood gas studies, namely the arterial CO₂ tension, the alveolar-arterial oxygen tension difference, and the physiological dead space, gave no information of value additional to that provided by the diffusing capacity.

In the absence of severe airway obstruction the single breath diffusing capacity has been much more useful for follow-up measurements than the results of blood gas studies. The single breath diffusing capacity gives a figure which is reproducible over a period of years in a subject who is not deteriorating. Blood gas studies are influenced by the type of respiration during arterial sampling, and between repeat measurements the alveolar-arterial oxygen tension difference and the physiological dead space may show changes in conflicting directions. For follow-up purposes such changes are more difficult to assess than the single figure of diffusing capacity.

Lung compliance correlates well with vital capacity ($r=0.8025$, S.E. 0.0971) and it is of interest to see if measurement of lung compliance, which requires the swallowing, often unpleasant, of an oesophageal balloon, gives any useful information. The vital capacity was low (less than 80% of predicted) in 29 of the 130 patients. Lung compliance was measured in 23 of these and was low (less than 75% of predicted) in 21. Thus, in sarcoidosis, a low vital capacity usually indicates stiff lungs. On the other hand, a normal vital capacity is frequently seen in patients with a low lung compliance (Table III) probably because

TABLE III
RELATIONSHIP BETWEEN LUNG COMPLIANCE AND VITAL CAPACITY IN 110 PATIENTS

	No. with Compliance (relative to predicted) of:		
	< 75% 42	< 60% 27	< 50% 14
No. (%) of these with normal vital capacity (> 80% pred.)	21 (50)	10 (37)	4 (29)

increased muscular effort is able to compensate for increased stiffness of the lungs. Thus the vital capacity is a less sensitive measure of increased lung stiffness than measurement of lung compliance, but for repeated measurements the vital capacity may be adequate. In 32 patients the measurement of lung compliance and vital capacity was repeated at a later date (Fig. 2). In most

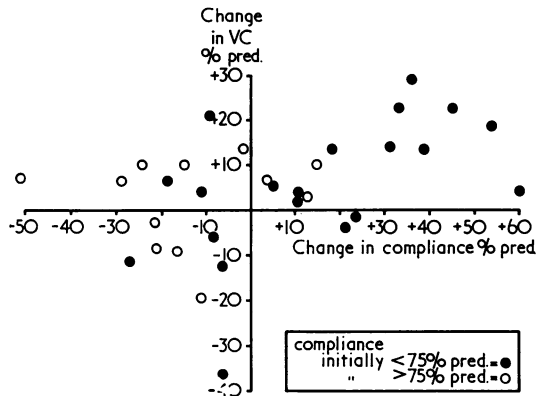


FIG. 2. Change in vital capacity and lung compliance between repeat measurements on 32 patients. Points in the upper right and lower left quadrants indicate that the changes in vital capacity and compliance are in similar directions.

of the 20 patients who had a low initial compliance a change in vital capacity was a good indication of the direction of the change in compliance. While an initial measurement of lung compliance is desirable the measurement of vital capacity is adequate for follow-up purposes.

To summarize, most of the information useful in the follow-up of patients with sarcoidosis can be obtained from the vital capacity, the single breath diffusing capacity, and a forced expiratory volume, the latter giving an indication of airway disease which might coexist with, rather than be due to, the sarcoidosis.

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