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Pulmonary function in coal workers with Caplan's syndrome and non-rheumatoid complicated pneumoconiosis

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Constantinidis, K, Musk, A W, Jenkins, J P R, and Berry, G (1978). *Thorax*, **33**, 764–768. **Pulmonary function in coal workers with Caplan's syndrome and non-rheumatoid complicated pneumoconiosis.** This retrospective study compares the pulmonary function of 24 coal workers with Caplan's syndrome with that of 36 subjects with non-rheumatoid progressive massive fibrosis (PMF). Allowing for differences in radiographical category, age, years worked underground, and smoking, obstruction to air flow as reflected in the one-second forced expiratory volume, the vital capacity, and the ratio of residual volume to total lung capacity, was significantly less in subjects with Caplan's syndrome. No significant differences in transfer factor were found. These findings may be explained by the different pathological features of the two entities. Selection bias does not appear to be responsible for the differences observed between the groups, but studies designed to eliminate this would be desirable.

Caplan's syndrome (Caplan, 1953) is customarily distinguished from non-rheumatoid complicated pneumoconiosis or progressive massive fibrosis (PMF) by its characteristic radiographical appearance (with multiple rounded opacities tending to be situated more peripherally throughout the lungs, individually smaller in size than the single opacities of PMF, and usually on a background of less severe simple pneumoconiosis) and by the coexistence of arthritis or other clinical manifestations of rheumatoid disease or the presence of circulating rheumatoid factor (Miall *et al*, 1953). This study was designed to investigate the different effects of the presence of large opacities on lung function between Caplan's syndrome and PMF and to relate these differences to knowledge of the pathology of complicated coal workers' pneumoconiosis. Although Caplan's syndrome often occurs in the presence of lesser categories of simple pneumoconiosis (Caplan, 1953), simple pneumoconiosis per se has a negligible effect on conventional tests of pulmonary function (Carpenter *et al*, 1956; Morgan *et al*, 1972; Seaton *et al*, 1972) so that differences in function between subjects with Caplan's syndrome and PMF should reflect the differing effects of the superimposed large opacities.

Methods

Coal workers with complicated pneumoconiosis were selected retrospectively on the basis of the appearance of their chest radiographs from referrals to the pneumoconiosis research unit by the Cardiff Pneumoconiosis Medical Panel or by general practitioners over the ten year period to June 1977. Caplan's syndrome was distinguished from PMF by the presence of characteristic radiographical appearances, clinical evidence of rheumatoid disease, and/or positive serology for rheumatoid factor (Rose-Waaler differential agglutination titre $\geqslant 1/32$). Twelve subjects in each of the categories A, B, and C with PMF and 24 subjects with Caplan's syndrome (8 with category A, 12 with B, and 4 with C) were studied.

RADIOGRAPHS

Plain posteroanterior chest radiographs were taken on the day of the performance of pulmonary function tests. Routine procedure required 74 KV, 40 mAs for 0·8 s. The full-sized films were read jointly by two readers, and an agreed classification

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was made (ILO U/C, 1971). They were then read independently by a third reader who confirmed the joint readings.

PULMONARY FUNCTION

Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured with digital bellows spirometer (McDermott and McDermott, 1977). Total lung capacity (TLC), vital capacity (VC), and residual volume (RV) were measured by the helium dilution technique (Cotes, 1975). Transfer factor (T1), transfer factor per unit of alveolar volume (Kco), the diffusing capacity of the pulmonary capillary membrane (Dm), and the volume of blood in the alveolar capillaries (Vc) were measured by the single breath carbon monoxide method (Cotes, 1975) using a Respirameter Mark IV (P K Morgan).

RESPIRATORY SYMPTOMS

The presence of bronchitis and dyspnoea and the smoking and occupational histories were obtained from the 1965 British Medical Research Council questionnaire. Bronchitis and dyspnoea were graded according to the Medical Research Council report (MRC, 1965).

Results

The clinical and radiological characteristics of the subjects from the six categories determined by the type of disease (PMF or Caplan's syndrome) and size of opacities (A, B, or C) were comparable except that those with Caplan's syndrome were on average younger, less dyspnoeic, and had less profusion of small opacities than the PMF cases (table 1).

Table 1 *Clinical and radiographical characteristics of groups*

	Caplan's syndrome			*PMF*		
Radiographical category	A	B	C	A	B	C
No of subjects	8	12	4	12	12	12
Mean age	50·5	54·8	57·5	57·1	58·2	56·3
Mean years underground	27·9	29·3	32·5	33·9	29·6	26·0
Mean dyspnoea grade	2·5	2·6	3·3	3·3	3·4	3·8
Mean bronchitis grade	0·5	0·8	1·2	1·1	0·7	1·3
No of current smokers	8	8	2*	10	8	10
Background of small opacities:						
Mean profusion	2/3	2/3	2/1	2/3	3/2	2/3
Type: No of subjects						
p	2	2	1	6	3	1
q	3	8	3	6	9	11
r	3	1	0	0	0	0
s	0	1	0	0	0	0

*Smoking history not obtained on one subject.

The mean values of pulmonary function, corrected to age 55 years and height 1·70 m (Cotes, 1975) are shown in table 2 for each group of subjects. This table suggests that subjects with Caplan's syndrome have less obstruction to airflow as measured by spirometry and lung volumes and a tendency to a larger transfer factor than subjects with PMF of the same radiological category. The statistical significance of these apparent differences was explored by multiple regression technique. There was no evidence that the differences in lung function between Caplan's syndrome and PMF were dependent on the category of pneumoconiosis since there was no significant interaction between category and type of disease for any index of pulmonary function. The data are therefore consistent with the differences in lung function between Caplan's syndrome and PMF being independent of categories A, B, or C.

The mean differences in pulmonary function

Table 2 *Mean values of lung function indices**

	Caplan's syndrome			*PMF*			*Within group standard deviation*
	A	*B*	*C*	*A*	*B*	*C*	
No of subjects	8†	12	4	12‡	12§	12‖	
FEV_1 (l)	2·62	2·24	2·28	1·93	1·76	1·14	0·59
FVC (l)	3·85	3·71	3·45	3·13	3·08	2·63	0·68
FEV/FVC (%)	67·9	59·8	64·2	58·7	54·1	42·5	11·7
TLC (l)	6·56	6·27	5·89	6·15	5·69	5·50	0·93
VC (l)	4·18	3·84	3·71	3·51	3·32	2·97	0·67
RV (l)	2·33	2·39	2·15	2·67	2·43	2·54	0·77
RV/TLC (%)	35·0	38·0	37·4	42·4	44·4	47·1	9·8
T1 (mmol min^{-1} kPa^{-1})	8·53	7·07	6·93	7·36	6·64	6·21	2·0
Kco (mmol min^{-1} kPa^{-1} l^{-1})	1·35	1·21	1·20	1·26	1·21	1·12	0·31
Dm (mmol min^{-1} kPa^{-1} l^{-1})	16·2	12·0	13·0	15·3	12·7	10·3	5·1
Vc (ml)	60·4	55·6	40·9	53·1	36·6	45·0	25·6

*Standardised to age 55 years and height 1·7 m.
†Only 6 subjects for Dm and Vc.
‡Only 11 subjects for Dm and Vc.
§Only 11 subjects for Dm.
‖Only 11 subjects for Vc.

Table 3 *Effects of disease type and category. (Estimate of effect[1] ±SE)*

	Caplan	Category B	Category C
FEV1 (l)	0·70±0·16***	− 0·28±0·18	− 0·67±0·20**
FVC (l)	0·70±0·18***	− 0·09±0·20	− 0·48±0·23*
FEV/FVC (%)	10·40±3·20**	− 6·50±3·60	−12·90±4·00**
TLC (l)	0·48±0·25	− 0·39±0·28	− 0·64±0·31*
VC (l)	0·62±0·18**	− 0·26±0·20	− 0·53±0·22*
RV (l)	− 0·23±0·20	− 0·11±0·23	− 0·13±0·26
RV/TLC (%)	− 7·50±2·60**	2·50±2·90	4·10±3·20
Tl (mmol min^{-1} kPa^{-1})	0·75±0·54	− 1·05±0·61	− 1·33±0·68
Kco (mmol min^{-1} kPa^{-1} l^{-1})	0·05±0·08	− 0·09±0·09	− 0·15±0·10
Dm (mmol min^{-1} kPa^{-1} l^{-1})	0·60±1·40	− 3·40±1·60*	− 4·60±1·80*
Vc (ml)	10·10±7·10	−11·10±8·10	−10·90±9·10

*P < 0·05; **P < 0·01; ***P < 0·001.
[1]For instance, on average the FEV_1 of Caplan cases was 0·70 l higher than of PMF cases after allowing for differences between categories; and categories B and C are 0·28 and 0·67 l respectively less than category A after allowing for difference between disease types.

between subjects with Caplan's syndrome and those with PMF (measured as "effect" of disease type) and between categories of disease (measured as "effect" of disease category) are shown in table 3. Pulmonary function in subjects with Caplan's syndrome was significantly different from those with PMF for FEV_1, FVC, FEV/FVC, VC, and RV/TLC. There was a significant effect of disease category for FEV_1, FVC, FEV/FVC, TLC, VC, and Dm.

The associations of the lung function indices with type and category of disease were further explored for modification of effect by age, years worked underground, smoking, and profusion of small opacities. FVC was negatively correlated with age in addition to the reference effect of age; allowing for this additional age effect reduced the Caplan effect from 0·70 l to 0·62 l. RV/TLC was positively correlated with age in addition to the reference effect; allowing for this the Caplan effect is still significant (−5·9±2·5%). The average TLC for current smokers was 0·68 l greater than for the remainder and allowing for this the Caplan effect was reduced to 0·45 l. Thus it is seen that allowing for these variables made no difference to the interpretations provided by table 3. Since the variables elaborated in table 1 may constitute confounding factors or reflect selection bias we additionally examined the way in which differences in the prevalence of dyspnoea and bronchitis would affect the size of the effects in table 3 attributable to disease type and category. Allowing for the combined effects on pulmonary function results of age (above the reference effect), years underground, profusion of small opacities, and smoking, together with dyspnoea and bronchitis, resulted in a reduction of the magnitude of the Caplan effect, but the differences between Caplan's syndrome and PMF remained statistically significant for FEV_1, FVC, FEV/FVC (table 4).

The pattern of functional abnormalities associated with Caplan's syndrome in comparison with PMF is indicative of less obstruction to airflow as indicated by higher values of FEV_1, FVC, VC, FEV/FVC, and lower values of RV/TLC. There is no evidence of less disturbance of gas transfer in Caplan's subjects. The differences in FEV_1, FVC, and FEV/FVC persist when maximum adjustment is made for possible confounding variables and selection bias.

Table 4 *Effects of disease type after allowing for multiple variables and factors[1]. (Estimate of effect ±SE)*

	Caplan effect
FEV[1] (l)	0·57±0·19**
FVC (l)	0·53±0·21*
FEV/FVC (%)	8·20±3·90*
TLC (l)	0·37±0·27
VC (l)	0·39±0·21
RV (l)	−0·05±0·22
RV/TLC (%)	−3·50±2·80
Tl (mmol min^{-1} kPa^{-1})	0·05±0·61
Kco (mmol min^{-1} kPa^{-1} l^{-1})	−0·05±0·10
Dm (mmol min^{-1} kPa^{-1} l^{-1})	−0·60±1·60
Vc (ml)	−2·00±8·30

[1]Caplan effect after allowing for effects of age (above the reference effect of age), years spent underground, profusion of small opacities, smoking habits, dyspnoea, and bronchitis.
*P < 0·05; **P < 0·01.

Discussion

Previous studies (Gilson *et al*, 1955; Cochrane and Higgins, 1961; Hyatt *et al*, 1964) have shown that differences in pulmonary function exist between categories of complicated pneumoconiosis, and we found similar trends that were statistically significant for FEV_1, FVC, FEV/FVC, TLC, Vc, and Dm. In addition, however, the results show that our subjects with Caplan's syndrome had a larger vital capacity and less airflow obstruction than those with PMF of the same radiographical category. There may be several reasons for this.

(1) PMF is predominantly situated in the upper zones and occurs more centrally in the lung (Kilpatrick *et al*, 1954). Resulting distortion of the adjacent large airways that may result in obstruction to air flow is likely to be greater than in Caplan's syndrome, where the lesions tend to be distributed throughout the lung in more peripheral locations, away from the central structures (Caplan, 1953).
(2) The lesions in PMF affect the adjacent lung to a greater extent than in Caplan's syndrome; scar emphysema is more apparent in association with PMF lesions than with Caplan's lesions (Gough *et al*, 1955).
(3) On whole lung sections PMF is usually accompanied by more extensive focal emphysema in the lung than is Caplan's syndrome. This may be independent of the number of coal nodules that are present. Although category of simple pneumoconiosis has little effect on pulmonary function Ryder *et al* (1970) have shown that the extent of focal emphysema on whole lung sections is related to the degree of premortem ventilatory impairment. However, differences in the extent of emphysema between subjects in this study do not appear a likely explanation in view of the similarities in gas transfer between the groups.
(4) The lesions in Caplan's syndrome tend to be small and multiple, and the opacities in PMF tend to be large and single. The volume occupied by five separate lesions each of 1 cm diameter is 2·6 ml, and a single spherical lesion of 5 cm diameter occupies a volume of 65·4 ml. Both appearances would radiographically be at the upper limit of category A complicated pneumoconiosis, which depends only on the combined diameter of the lesions—a linear dimension. The discrepancy for categories B and C, that are identified on an area basis, would be less. This volume effect may contribute to the differences in VC observed.
(5) It is conceivable that selection bias in a study of this design could contribute to the differences in pulmonary function between the groups if there was a tendency for subjects with Caplan's syndrome to be referred for study on the basis of the appearance of their routine chest radiographs or the onset of arthritic symptoms and subjects with PMF because of respiratory symptoms. In our analysis we stratified the data by radiographical category of complicated pneumoconiosis, and we examined the effects of the presence of bronchitis and dyspnoea on the results, although bronchitis and dyspnoea may be regarded as manifestations of disease rather than as causes of changes in pulmonary function. It is not surprising that the Caplan effect was reduced by allowing for differences between the groups in prevalence of these respiratory symptoms. Despite this adjustment, evidence of airflow obstruction remained significantly less in the subjects with Caplan's syndrome. This suggests that bias due to the selection of subjects with PMF because of the presence of respiratory symptoms does not account for the differences in the results. The evidence does not indicate that the possibility of selection bias should alter our interpretations of the differences in pulmonary function between subjects with Caplan's syndrome and subjects with PMF.

The results of this study suggest that in coal workers with complicated pneumoconiosis the magnitude of impairment of pulmonary function is less in subjects with Caplan's syndrome than in subjects with PMF of the same radiological category. Several explanations are offered for this, but the implication is that the current radiographical classification of complicated pneumoconiosis excludes some of the information that is required.

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