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SERIAL MEASUREMENTS OF THE PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE IN A GROUP OF MEN EMPLOYED IN INDUSTRY

BY

J. J. DALY AND J. W. ROE

From the Departments of Medicine and Preventive Medicine, University of Sheffield

Increasing attention has been given to the use of serial measurements of lung function in clinical and epidemiological studies of respiratory disease (Shephard, Turner, Carey, and Phair, 1960; Ashford, Forwell, and Routledge, 1960; Bates, Knott, and Christie, 1956). For such studies it is important to know the reproducibility of the measurements used, and interest in this respect has concentrated on ventilatory function. Though numerous studies have been concerned with defining the factors which influence the pulmonary diffusing capacity (D_{Lco}) (Forster, 1957; Turino, Brandfonbrener, and Fishman, 1959; Ross, Frayser, and Hickam, 1959; Cadigan, Marks, Ellicott, Jones, and Gaensler, 1961), few have attempted to assess its variability over an interval of time in the normal individual. The purpose of the present study was to make serial measurements of D_{Lco} in a group of men working in industry. An attempt was also made to determine whether changes in lung function occurred as a result of exposure to atmospheric conditions existing in the iron-foundry section of the work. The principal contaminants were the pyrolysis products of "core-bond" which is used in casting.

METHODS

Twelve healthy men aged between 33 and 60 years (average 45 years) were studied. Their average height was 67 inches, their average weight 163 lb., and their average body surface area 1.85 sq. m. None had respiratory symptoms. Six of the subjects worked in an iron foundry and the remainder were employed in clerical and other capacities in another department of the same works.

Pulmonary function studies were done on three occasions over a period of three to five weeks; the first two studies were made at the end of a subject's normal working day, and the interval between these was one to two weeks. The final set of measurements in each individual was made at the end of his two weeks' annual holiday but before his return to work.

Functional residual capacity and residual volume were obtained by a closed circuit helium method on each occasion (Gilson and Hugh-Jones, 1949). The forced expiratory volume in 0.75 sec. ($F.E.V._{0\cdot75}$) was measured using a modified form of the apparatus described by Gaensler (Gaensler, 1951), and peak expiratory flow (P.E.F.) was determined with a flow meter (Wright and McKerrow, 1959). Five measurements of $F.E.V._{0.75}$ and P.E.F. were made on each visit, and the mean of the three best efforts was used. The D_{Lco} was determined by a single-breath technique previously described (Ogilvie, Forster, Blakemore, and Morton, 1957). A minimum of two estimates was obtained at each visit. In calculating the D_{Lco} a correction was made for the equilibrium pressure of CO in the blood, which was determined by a rebreathing method (Sjöstrand, 1948).

RESULTS

The table shows the results of measurements of ventilatory function and D_{Lco} with the dates on which they were obtained. The results of the ventilatory measurements and D_{Lco} were within the "predicted" range in all subjects and the ratio of residual lung volume to total lung capacity ranged from 20% to 43%. The changes in measurements between visits were small and did not correlate with the known changes in the environment.

VENTILATORY MEASUREMENTS.—The average coefficient of variation* of $F.E.V._{0.75}$ between visits was 6.3%, with a range of 2.2% to 14.2%, and that of P.E.F. was 6.4%, with a range of 0.8% to 12.8%.

PULMONARY DIFFUSING CAPACITY.—The average coefficient of variation of D_{Lco} between visits was 4.2%, with a range of 0.5% to 6.4%, and that of a single measurement was 6.1%, with a range of 3.8% to 9.5%. The average coefficient of variation between measurements on the same day was 4.3%, with a range of 0.9% to 5.6%.

*Here and elsewhere in this paper the term "average coefficient of variation" should be understood as the root mean square of the coefficients for the 12 subjects.

TABLE

F.E.V.$_{0.75}$ AND P.E.F. MEASURED ON THREE SEPARATE OCCASIONS IN 12 SUBJECTS

Subject	Date	D_{Lco} (ml./min./mm. Hg)			Average D_{Lco}	Modified D_{Lco} (Average)	R.V. (l. B.T.P.S.)	F.E.V.$_{0.75}$ (l.)	P.E.F. (l./min.)
H.C.	4/7	17·5	19·9	17·8	18·4	18·3	1·886	1·60	3·95
	13/7	19·3	17·4		18·4	18·0	1·914	2·13	4·67
	4/8	19·8	18·1	17·9	18·6	18·2	1·749	2·25	4·63
C.P.	4/7	35·8	36·9	36·7	36·5	36·0	1·495	3·20	5·33
	13/7	35·2	35·5		35·4	35·0	1·452	3·33	5·62
	28/7	32·7	37·3	33·9	34·6	34·2	1·403	3·25	5·55
R.H.	11/7	22·3	19·4		20·9	20·5	1·818	2·37	5·18
	18/7	21·9	22·3		22·1	21·4	2·004	2·25	5·28
	8/8	21·0	21·2		21·1	20·7	1·530	2·33	5·25
L.H.	12/7	34·1	30·9		32·5	31·7	1·318	2·07	5·03
	20/7	30·7	29·7		30·2	29·5	1·347	2·30	4·90
	8/8	32·5	29·8		31·2	29·1	1·526	2·38	4·93
B.G.	11/7	31·3	29·7		30·5	30·2	2·149	2·98	4·73
	18/7	30·0	31·3		30·7	30·1	2·152	2·67	4·33
	3/8	29·4	27·6	26·9	28·0	27·3	2·245	2·85	5·83
G.K.	7/7	22·4	22·1	24·6	23·0	23·2	2·213	1·70	2·67
	12/7	22·0	20·6		21·3	21·0	1·947	1·50	2·20
	7/8	24·1	23·8	25·3	24·4	23·7	2·432	1·47	2·83
E.J.	3/7	29·8	28·7	28·7	29·1	28·6	1·682	2·40	4·78
	19/7	28·8	31·7		30·3	30·1	2·402	2·18	4·78
	8/8	28·0	29·1		28·6	28·2	2·248	2·15	4·87
E.B.	5/7	23·3	17·8	20·7	20·6	20·7	2·160	1·95	4·78
	10/7	23·9	23·0		23·5	23·4	—	1·60	4·87
	8/8	24·2	23·1		23·7		2·424	1·77	4·75
C.W.	6/7	23·6	22·3	22·7	22·9	22·6	1·977	1·53	2·83
	14/7	22·3	22·1		22·2	21·7	1·659	1·60	2·70
	4/8	20·4	21·9	21·1	21·1	20·7	1·479	1·47	3·05
A.B.	5/7	24·0	22·4	25·7	24·0	23·4	1·801	2·27	4·80
	10/7	22·6	21·3	19·9	21·3	20·9	—	2·05	5·00
	30/7	20·9	21·8	20·4	21·0	20·5	1·796	2·12	5·03
J.J.	3/7	26·4	23·6		25·0	24·9	2·322	3·00	5·30
	19/7	24·3	24·3		24·3	24·6	2·303	2·85	5·65
	3/8	23·5	21·3	20·8	21·9	21·6	2·288	2·88	5·83
E.T.	6/7	32·4	33·5		33·0	32·4	2·615	2·70	4·03
	14/7	31·8	31·7		31·8	31·2	2·549	2·50	5·00
	4/8	29·9	30·3		30·1	29·4	2·509	2·85	4·85

DISCUSSION

Ogilvie, Forster, Blakemore, and Morton (1957) reported that the coefficients of variation of single-breath D_{Lco} on a single day and over an interval in a group of normal subjects were 5.8% and 8.5% respectively. These coefficients are greater than the corresponding values for the present study, but the latter were obtained over a shorter interval of time. Cadigan *et al.* (1961) reported a coefficient of variation of D_{Lco} of 8.9% in 12 normal subjects and noted a close correlation between D_{Lco} and the alveolar volume at which the measurement was made. They concluded that most of the variation in D_{Lco} was attributable to the variation in alveolar volume, and, by controlling the latter, the coefficient of variation of D_{Lco} was reduced to 3.2%. In the present study no attempt was made to control alveolar volume, and there was no consistent relationship between it and D_{Lco}. In only four subjects was there a strong association between alveolar volume and D_{Lco}, as illustrated in Figure 1. In the remaining eight subjects variations in D_{Lco} were unrelated to alveolar volume, as illustrated in Figure 2. These observations do not conflict with the view that D_{Lco} is dependent on lung volume because the changes in alveolar volume in the present study were generally small, being determined by the degree of the individual's effort. The results indicate that in this study alveolar volume was not the only determinant of variations in D_{Lco}.

It has been pointed out previously that D_{Lco} decreases with an increase in breath-holding time (Ogilvie *et al.*, 1957). Variation in breath-holding time was not an important factor in the present investigation because the range in any individual did not exceed 3 seconds. Jones and Meade have provided evidence that the differences in inspiratory time and the time taken for expiration of the alveolar sample are factors influencing the reproducibility of the measurement (Jones and Meade, 1961). They calculated a "modified breath-holding time" and the reproducibility of measurements of D_{Lco} in a normal individual was improved by the use of this modification. The D_{Lco} was recalculated from the results obtained in the

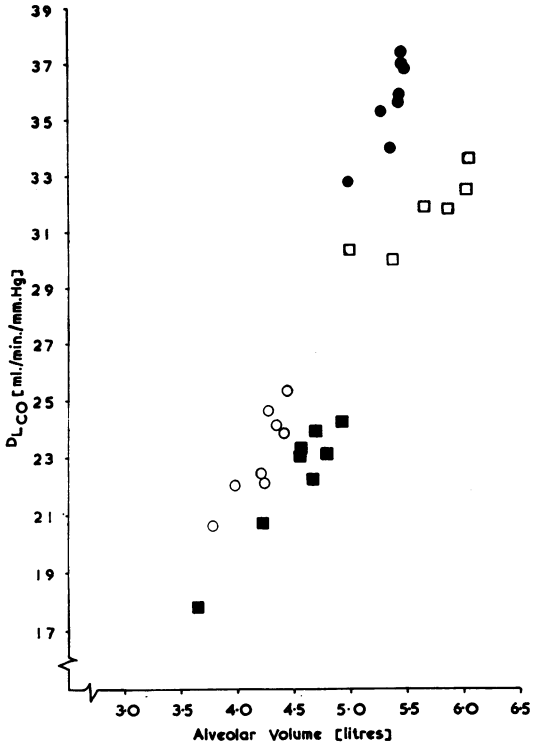

FIG. 1. *Diffusing capacity plotted against alveolar volume for four subjects in whom these variables were strongly associated. The values for each subject are represented by symbols of a different shape.*

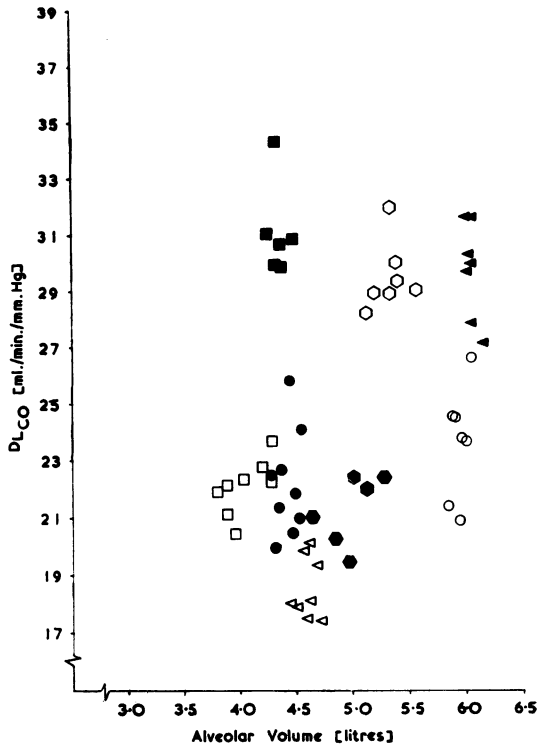

FIG. 2. *Diffusing capacity plotted against alveolar volume for eight subjects in whom these measurements were not associated. The values for each subject are represented by symbols of a different shape.*

present study using the modified breath-holding time, and the values may be compared with those obtained by the conventional method (see table). In most subjects the modified values are lower but the overall scatter was not reduced. No measurements were made using early alveolar samples, as described by Jones and Meade (1961).

A disadvantage of the single-breath technique for measuring D_{Lco} is that the residual volume is separately determined. Changes in the residual volume greater than 100 ml. did occur in eight subjects. The average coefficient of variation for the 12 subjects was 7.4%, which is in agreement with the reports of other workers (Rahn, Fenn, and Otis, 1949 ; Comroe, Forster, DuBois, Briscoe, and Carlsen, 1955).

Previous investigators have reported an influence of atmospheric changes on CO uptake in subjects with chronic respiratory disease (Shephard *et al.*, 1960). The present study offered an opportunity of assessing the effect of a contaminated industrial environment on lung function inasmuch as half the subjects worked in a foundry and all were studied before and after their annual two weeks' holiday. There was no evidence that the changes in environment influenced the measurements as judged by a comparison of the results in the two groups of subjects. This does not exclude the possibility that changes in D_{Lco} or ventilatory function may occur either during acute exposure to conditions existing in the foundry or over a longer period of time than was used in the present study.

SUMMARY

Estimates of ventilatory function and single-breath D_{Lco} were made on three separate occasions at intervals of one to three weeks on 12 normal men, of whom six were employed in an iron foundry.

The average coefficient of variation of $F.E.V._{0.75}$ between visits was 6.3%, that of P.E.F. 6.4%, and that of D_{Lco} 4.2%. The reproducibility of D_{Lco} was not improved by the use of a modified breath-holding time.

There was no consistent difference between the changes in lung function occurring in the six foundry workers and those occurring in the other men.

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