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RESPIRATORY FUNCTION AFTER PNEUMONECTOMY

BY

M. B. McILROY AND D. V. BATES

From the Dunn Laboratory, St. Bartholomew's Hospital, London, E.C.1

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After a pneumonectomy which is not combined with or followed by thoracoplasty the volume of the remaining lung is almost invariably greater than before operation. The lung is then said to be " over-inflated " ; but, in spite of this, the patient's respiratory performance may be quite good. Cournand and Berry (1942) carried out the first thorough investigation of the problem of over-inflation, using the ventilatory techniques of study then available. They found evidence of over-inflation of the remaining lung, a condition which they considered to be physiologically undesirable, but, apart from this, changes were few. The oxygen uptake for a given ventilation (O_2/V) was slightly lower than normal, and this change was more marked during exercise: the rate of alveolar clearance of nitrogen was normal, indicating normal gas distribution within the lung, and what dyspnoea there was seemed to be most closely related to a diminution in the " breathing reserve," an index calculated from the maximal breathing capacity and resting ventilation. Eight years later a further study was reported by Cournand, Riley, Himmelstein, and Austrian (1950). The introduction of the technique of cardiac catheterization made it possible to study the changes in the circulation after pneumonectomy, and the techniques developed by Riley and Cournand (1951) enabled the ventilation-perfusion relationships and gas exchange in the lung to be measured. An analysis of extensive data on 16 subjects led to the following general conclusions: (1) The finding of some degree of over-inflation in most of the subjects was confirmed ; (2) the intrapulmonary gas distribution was again found to be normal ; (3) the previous finding of slight resting hyperventilation in relation to oxygen uptake was confirmed, and again noted to be relatively greater on exercise ; (4) the arterial oxygen tension was found to be at the lower limit of normal during exercise ; (5) the pulmonary arterial pressure was reported to be normal at rest and slightly raised on exercise ; (6) in five patients the oxygen-diffusing capacity measured by the technique developed by Riley, Lilienthal, Proemmel, and Franke (1946) was found to be about at the lower limit of the normal range for subjects with two lungs.

These major contributions to the subject have been followed by four other papers of interest. Fowler and Blakemore (1951) studied the effect of pneumonectomy on the respiratory dead space, finding a decrease in some subjects but not in others. Björk and Hilty (1954) measured the arterial oxygen tension after pneumonectomy and reported that it was considerably reduced up to a week after operation. The reason for this was not apparent. Friend (1954) studied 15 men before and at varying times after pneumonectomy. He concluded that, although there was evidence of over-inflation, this had " no demonstrable adverse effect " on ventilation, and that there was no association between over-inflation of the remaining lung and post-operative dyspnoea. It was considered that antecedent bronchitis was the most important factor to be considered in assessing the likelihood of post-operative dyspnoea. Denolin, De Coster, Dumont, and Cantinieaux-Duwaerts (1952) confirmed the finding of a generally normal pulmonary artery pressure after pneumonectomy.

In the last few years two further techniques have been introduced into the study of pulmonary function. First, the measurement of the intra-oesophageal pressure (Dornhorst and Leathart, 1952 ; Fry, Stead, Ebert, Lubin, and Wells, 1952) has enabled measurements to be made of the mechanical aspects of lung ventilation. Secondly, the reintroduction of carbon monoxide to measure the pulmonary diffusing capacity has provided a simple method which can be used at rest and during exercise.

This study of 10 patients after pneumonectomy has been planned with the following questions in mind. Does the presence of over-inflation lead to dyspnoea through changes in the mechanical properties of the lung ? Does the lowering of the diffusing capacity for carbon monoxide (D_{CO}), if present, have any important consequences for the patient ? What is the relationship or distinction between "over-inflation" and "emphysema"? It might be thought that the most satisfactory method of approaching these problems would be by the pre- and post-operative study of a number of patients. Although such a method has advantages, it is not as satisfactory as it might seem, since the pre-operative results may be influenced by such factors as partial bronchial obstruction. This type of difficulty was encountered by Friend (1954) in three of the 15 cases he studied. We have therefore confined our observations to patients studied at least eight months after operation. Every patient had had a pneumonectomy without thoracoplasty for a carcinoma of the bronchus, and all were studied as out-patients.

METHODS

All patients were studied at rest sitting in a chair and during exercise on a motor-driven treadmill. The subdivisions of lung volume and helium mixing efficiency were measured, using the closed circuit method described by Bates and Christie (1950). Measurements of intra-oesophageal pressure were made at the same time, using a long, air-filled balloon (Mead, McIlroy, Selverstone, and Kriete, 1955). The instants of zero air flow at the mouth were recorded on the intra-oesophageal pressure tracing, using the zero flow indicator described by McIlroy and Eldridge (1956). The mechanical properties of the lung were measured from the record of intra-oesophageal pressure and the spirometric tracing obtained during breaths of different depths and at different rates of breathing in order to study the effect of changes in respiratory rate and depth on the compliance of the lung.

The diffusing capacity of the lung for carbon monoxide (D_{CO}) was measured by the method described by Bates, Boucot, and Dormer (1955). A tracing of intra-oesophageal pressure was obtained at the same time and the instants of zero air flow at the mouth recorded, using a capacitance manometer. Expired air was collected for one minute at rest and on exercise, and the mean tidal volume determined from the volume of the expired air and the respiratory rate. The mechanical work done on the lung during inspiration, the compliance of the lung, and the mean inspiratory resistance were measured by the simplified method (No. 1) described by McIlroy and Eldridge (1956). The expired air collected during exercise was analysed for oxygen and carbon dioxide content by Haldane analysis in duplicate. The oxygen saturation was measured, using an ear oximeter. The calibration of the oximeter had previously been checked against arterial blood analysed by the van Slyke method.

PROCEDURE

REST.—After swallowing the oesophageal tube the subject breathed oxygen from the spirometer in the lung volume circuit, and a spirometric tracing was obtained. After a period of quiet breathing, the vital capacity was measured on three occasions, the intra-oesophageal pressure and the points of zero air flow being recorded at the same time.

The effect of changes in the respiratory rate on the compliance of the lung was then investigated, the subject being instructed to breathe first more slowly and then more rapidly than normal. No attempt was made to control the respiratory rate accurately, but the patient was encouraged to keep the tidal volume constant. Finally the patient was asked to hold his breath at the end of a normal inspiration. In the subjects who did not close the glottis, a record of the static end-inspiratory intra-oesophageal pressure was thus obtained. The measurements of the mechanical properties of the lung during normal quiet breathing were repeated during the estimation of the diffusing capacity at rest.

EXERCISE.—The subject walked on the treadmill at a grade of 1 in 50 for approximately six minutes. The speed of the treadmill was gradually increased to a rate which the patient said was the maximum he could comfortably maintain for several minutes. No attempt was made to increase the severity of exercise to reach the limit of respiratory performance. The diffusing capacity and the mechanical properties of the lung were measured between the fifth and sixth minutes of exercise.

CRITICISM OF METHODS.—The technique of measuring the mixing efficiency using the closed circuit helium method takes no account of respiratory dead space, and any diminution of the volume of this space might cause a rather higher estimate of the mixing efficiency than was actually present. The method of measuring the pulmonary diffusing capacity has been shown to be satisfactory in normal subjects, and, except in the presence of grossly uneven gas distribution in the lungs, may be expected to give reliable results in patients with one lung. It may be questioned whether the measurement of intra-oesophageal pressure in patients who have had one lung removed can be expected to reflect the intrathoracic pressure accurately. No attempt has been made to compare intra-oesophageal and intrapleural pressures in such patients for obvious reasons, and the validity of the pressure measurements is thus open to doubt. It was found, however, that the pressure records obtained did not differ technically from those obtained in patients with two lungs, except that oesophageal contractions occurred rather more frequently. The only evidence to support the assumption that the intra-oesophageal pressure accurately reflected the intrapleural pressure in these patients is that the analysis of the mechanical properties of the lung based upon intra-oesophageal pressure records fits well with independent findings, such as the lung volume and the radiological evidence of the degree of over-inflation of the lung. A study of the accuracy of the simplified method of measuring the mechanical properties of the lungs has been reported by McIlroy and Eldridge (1956). While the measurements of

TABLE I

CLINICAL DETAILS OF 10 PATIENTS AFTER PNEUMONECTOMY

No.	Name	Age	Height (cm.)	Weight (kg.)	Body Surface Area (sq. m.)	Side of Operation	Time of Study Post-operatively	Dyspnoea		Bronchitis		Radiological Inflation
								Before	After	Before	After	
1	S.P.	39	169	60	1·7	R	11 months	±	+	+	++	Moderate over-inflation
2	A.McI.	41	177	78	1·9	R	9 ,,	0	+	0	±	Normal
3	H.B.	43	173	71	1·8	L	10 ,,	±	+	±	±	,,
4	R.F.	49	185	63	1·8	R	10 ,,	0	++	0	±	Bronchitic changes
5	F.S.	50	182	81	2·0	R	9 ,,	0	+	0	0	Normal
6	T.E.	53	164	73	1·7	L	8 ,,	0	+	0	0	,,
7	E.A.	54	174	62	1·7	R	8 years	0	+	0	++	Very over-inflated
8	W.R.	54	173	70	1·8	R	2½ ,,	0	+	0	0	,, ,,
9	E.R.	61	162	57	1·5	L	9 months	0	++	0	0	Moderate over-inflation
10	G.C.	63	167	75	1·8	R	11 ,,	+	++	0	0	Normal

compliance and work by this method are reasonably accurate, the values for mean inspiratory resistance are probably too high, particularly at rest.

RESULTS

Table I summarizes the physical characteristics and clinical details of the subjects studied. The 10 patients, all men, ranged in age from 39 to 63: in seven the pneumonectomy was right-sided. Only the oldest patient (G. C., No. 10) complained of definite dyspnoea before operation, though two others (H. B., No. 3, and S. P., No. 1) said that they had noticed some dyspnoea a year or so before the operation. It will be noticed that all the patients said they were more short of breath after operation than before, but in only three (R. F., No. 4, E. R., No. 9, and G. C., No. 10) was dyspnoea severe enough to interfere with normal activities. One or two said that their breathing was still improving after the operation. Pre-existing bronchitis was thought to have been worsened by one patient (S. P., No. 1), and others had noticed some bronchitis after operation which had not been present before (A. McI., No. 2, R. F., No. 4, and E. A., No. 7). The chest radiographs showed that the lung in two patients was very over-inflated and in two was moderately so. In Table II the subdivisions of lung volume and mixing efficiency are shown. Tables III and IV show the results of the measurements of the mechanical properties of the lung and gas diffusion at rest and on exercise. It will be seen that the mean inspiratory resistance in all patients was greater than normal.

In Fig. 1 the pressure volume diagram of the lung is shown for each patient. The points were obtained from breaths of different sizes up to the inspiratory capacity. A normal curve for two lungs and an estimated normal curve for one lung are shown for comparison. The end expiratory pressure level is shown for each patient. It will be seen that in about half the patients the compliance of the lung as shown by the slope of the line was less than that expected for one normal lung. In most cases the compliance of the lung decreased more rapidly than normal as lung volume increased.

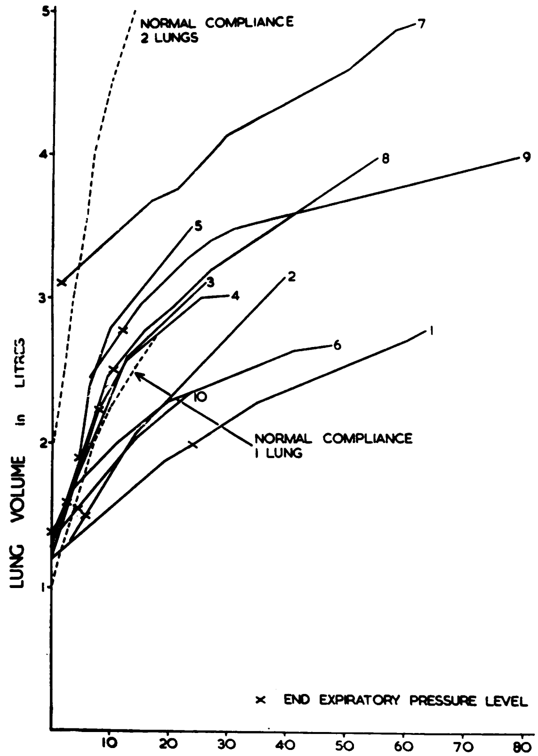

FIG. 1.—Pressure volume diagram of the lung in 10 patients after pneumonectomy. The numbers refer to individual patients in Table I.

TABLE II

SUBDIVISIONS OF LUNG VOLUME AND GAS MIXING EFFICIENCY

No.	Name	V.C.	I.R.V.	E.R.V.	Ratio I.R.V./E.R.V.	F.R.C.	Rd.C.	$\frac{\text{Rd.C.}}{\text{T.L.C.}}\%$	M.E.%
Normal mean values for one lung		1·75	1·30	0·45	2·9	1·75	1·30	42	54
1	S.P.	1·74	0·86	0·88	0·98	1·86	0·98	57	57
2	A.McI.	1·86	1·60	0·26	8·1	1·37	1·11	37	48
3	H.B.	2·14	1·68	0·46	3·65	1·44	0·98	32	74
4	R.F.	1·78	0·84	0·94	0·89	2·16	1·22	41	47
5	F.S.	1·94	1·74	0·20	8·70	1·89	1·69	54	52
6	T.E.	1·55	1·34	0·21	6·40	1·31	1·10	41	41
7	E.A.	2·47	1·51	0·96	1·57	3·10	2·13	47	43
8	W.R.	2·61	1·51	1·10	1·37	2·38	1·28	33	67
9	E.R.	2·24	1·47	0·77	1·91	2·55	1·78	44	48
10	G.C.	1·03	0·76	0·27	2·8	1·54	1·27	55	33

V.C. = vital capacity. I.R.V. = inspiratory reserve volume. E.R.V. = expiratory reserve volume. F.R.C. = functional residual capacity. Rd.C. = residual capacity. T.L.C. = total lung capacity. M.E.% = helium mixing efficiency (%).

In Fig. 2 the compliance of the lung is plotted against respiratory rate. There was no evidence that the compliance of the lung decreased as the patient breathed more rapidly. The results obtained are to some extent affected by differences in tidal volume at different respiratory rates, but indicate that the distribution of ventilation in patients with one lung remains normal, a conclusion confirmed by the normal values for mixing efficiency (Otis, 1956).

Fig. 3 shows the mechanical work done on the lung during inspiration plotted against the minute volume at rest and during exercise. It will be seen that the respiratory work done on exercise was greater than normal, even when the lung was not over-inflated, and greatly increased in the patients with an over-inflated lung.

Fig. 4 shows the relationship between the exercise-diffusing capacity and the functional residual capacity in the patients investigated and in a group of younger normal subjects. It is clear that, although in some patients (S. P., No. 1, A. McI., No. 2, H. B., No. 3, and T. E., No. 6) the diffusing capacity was normal for the reduced lung volume, in others it was lower than would have been predicted from the functional residual capacity.

TABLE III

PHYSICAL MEASUREMENTS AND GAS DIFFUSION AT REST

No.	Name	Minute Vol. (l./min.)	Respiratory Rate per min.	Compliance (l./cm.H_2O)	Mean Inspiratory Resistance (cm.H_2O/l./sec.)	Inspiratory Work (kg.m./min.)	End Expiratory Level (cm.H_2O)	O_2Hb Saturation (%)	Diffusing Capacity $D_{CO}II$ (ml. CO/min./mm.Hg)
1	S.P.	6·4	16	0·029	8·1	0·49	−24·2	97	4·9
2	A.McI.	13·5	27	0·058	4·6	0·86	−5·8	95	7·4
3	H.B.	6·0	14	0·110	2·8	0·25	−2·9	97	7·3
4	R.F.	11·7	26	0·051	4·6	0·76	−7·8	97	9·4
5	F.S.	8·3	14	0·096	7·5	0·44	−4·5	97	7·0
6	T.E.	12·9	19	0·042	8·0	1·66	−0·2	97	9·8
7	E.A.	10·0	20	0·041	14·3	1·33	−1·3	—	5·9
8	W.R.	8·6	12	0·050	11·2	0·72	−10·5	97	10·7
9	E.R.	11·1	22	0·031	11·9	1·17	−12·1	97	6·1
10	G.C.	10·0	27	0·045	6·7	0·67	−4·4	—	5·4
Normal values (two lungs)				0·12–0·33	1·5–4·0	0·2–0·5	0 to −5	97	Mean 17·0 Range 10·0 to 25·0

TABLE IV

PHYSICAL MEASUREMENTS AND DIFFUSION DURING EXERCISE

No.	Case	Exercise (m.p.h.)	Mean Volume (l./min.)	Respiratory Rate per Minute	Compliance (l./cm. H_2O)	Mean Inspiration: Respiration (cm.H_2O/l. sec.)	Inspiration at Work (kg.m./min.)	End Expiratory Level (cm. H_2O)	O_2 Uptake (l./min.)	O_2 V	O_2Hb Saturation (%)	Diffusing Capacity	
												$D_{CO}II$	Predicted ½ Normal
1	S.P. (a)	2	14·0	17	0·018	2·1	4·78	−23·0	0·74	5·3	93	14·4	14
	(b)	3	16·8	19	0·025	2·7	4·22	−14·0	0·72	4·3	93	Not measured	14
2	A.McI.	2	22·0	35	0·035	5·8	3·22	−8·7	0·90	4·1	98	9·0	11
3	H.B.	2½	24·2	20	0·066	4·2	3·21	0	1·19	4·9	95	18·3	12
4	R.F.(a)	1	21·6	36	0·052	5·0	1·95	−8·7	0·64	2·95	97	11·2	17
	(b)	2	33·8	49	4·040	4·4	4·35	−4·7	0·88	2·6	91	5·1	17
5	F.S.	2	25·3	27	0·068	5·3	2·84	−0·7	0·95	3·75	97	9·9	15
6	T.E.	1	23·9	32	0·048	6·8	3·19	−3·3	0·95	3·9	97	12·8	11
7	E.A.	1½	22·9	30	0·039	6·4	3·4	−1·7	0·84	3·7	—	7·5	17
8	W.R.	2	20·9	13·5	0·068	7·5	3·5	No record	1·09	5·2	96	14·8	16
9	E.R.	¾	24·1	34	0·021	8·9	6·12	−17·7	1·20	4·9	97	12·9	17
10	G.C.	¾	21·7	35	0·031	7·4	3·09	−6·5	0·48	2·2	—	8·0	12

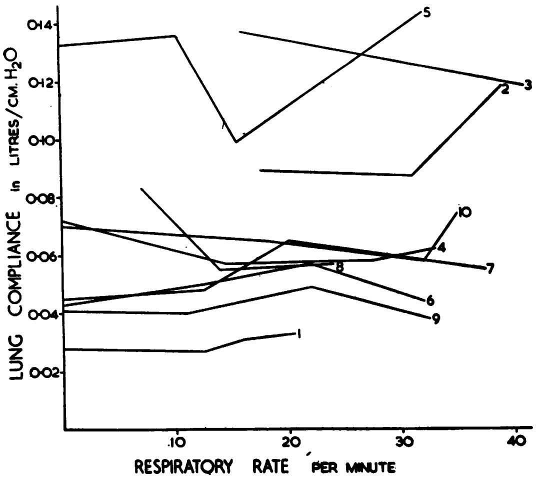

FIG. 2.—Graph showing the effect of respiratory rate on lung compliance. There is no evidence of a consistent reduction in compliance at increased respiratory rates.

The results of these studies can best be appreciated if the patients are grouped together for purposes of discussion :

NO EVIDENCE OF OVER-INFLATION.—In two patients, H. B., No. 3, and F. S., No. 5, the results in all the measurements were within the expected normal limits for a man with one lung. In these two men, therefore, over-inflation of the lung was minimal. Both patients were more short of breath after operation than they had been before. It must be remembered that during exercise these men were ventilating at a rate of about 25 l./min. This would be equivalent to a total ventilation of 50 l./min. if both lungs were contributing ; thus, as far as the remaining lung is concerned, the ventilation for a given amount of exercise is doubled. As a result the intra-oesophageal pressure swing is about twice that in a patient with two lungs and the compliance is necessarily reduced ; furthermore, the mean inspiratory resistance is increased due to the greater air flow through the bronchial tree of the remaining lung. These factors probably account for the complaint of some dyspnoea. Patient H. B., No. 3, had the highest diffusing capacity on exercise in the series, whereas in patient F. S., No. 5, the value was slightly lower than expected.

OVER-INFLATION OF LUNG AND NORMAL GAS DIFFUSION.—Three patients came into this category, S. P., No. 1, W. R., No. 8, and E. R., No. 9. Radiological evidence of over-inflation was present in all three patients. The principal findings in this group were as follows:

(*a*) The vital capacity was within the predicted normal range, but the I.R.V./E.R.V. ratio was lower than normal.

(*b*) The functional residual capacity was grossly increased in W. R., No. 8, and E. R., No. 9, and probably increased in S. P., No. 1, in view of this man's small stature.

(*c*) The Rd.C./T.L.V.% was normal in W. R., No. 8, and E. R., No. 9, and slightly increased in S. P., No. 1.

(*d*) There was a decreased compliance of the lung (increased stiffness), especially in patient S. P., No. 1. This was associated with a raised respiratory rate in W. R., No. 8, and E. R., No. 9. In all three, the end expiratory level was much lower than normal.

(*e*) The resting diffusing capacity was about half the value for a normal man in patients W. R., No. 8, and E. R., No. 9, and slightly lowered in S. P., No. 1.

(*f*) On exercise, the decreased compliance of the lung was most evident in the two patients with the lowest intra-oesophageal pressure. The ventilation equivalent (O_2/V) was normal, and the exercise D_{CO} was about normal for one lung. It is of interest that a normal exercise D_{CO} was found in the patient with the most negative and expiratory pressure level (S. P., No. 1).

In this group of patients, therefore, there was evidence of considerable over-inflation of the lung

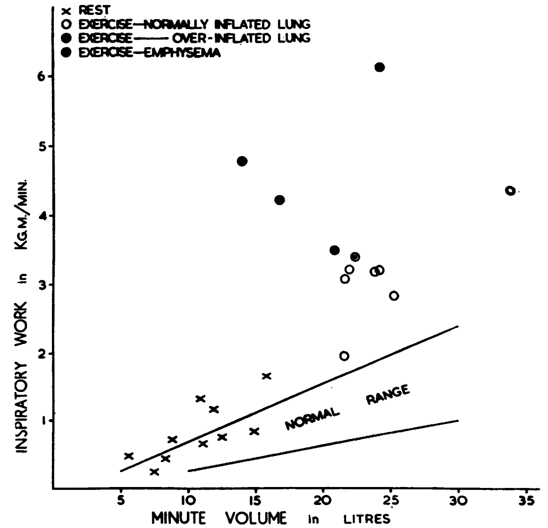

FIG. 3.—Graph showing the mechanical work done on the lung during inspiration plotted against minute volume in litres. It can be seen that work is greater than normal even if the lung is not over-inflated and is further increased in patients with an over-inflated lung.

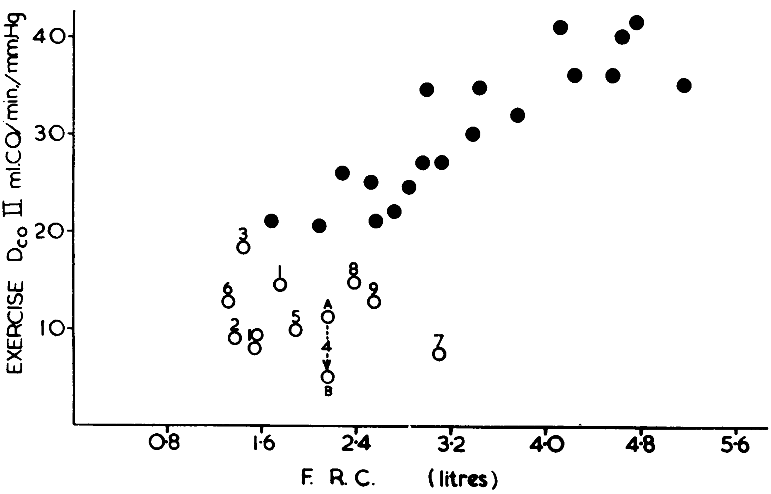

FIG. 4.—Graph showing the diffusing capacity for CO on exercise plotted against the functional residual capacity in litres. ● Young normal subjects (Bates and others, 1955). ○ Patients after pneumonectomy. The numbers refer to individual patients in Table I. In patients 3, 6, 1, and 2 the D_{CO} is about normal in relation to the F.R.C. In patients 7 and 9 it is rather lower. The change in patient 4 from A to B is commented on in the text.

as judged by the lung volume and pressure measurements, but with the maintenance of good gas diffusion. Since the loss of gas-diffusing surface relative to the lung volume (F.R.C.) is one of the most distinctive features of emphysema, it may be said that these patients have overdistension of the lung without, as yet, emphysema.

EMPHYSEMA.—In one patient, whose radiograph showed a very over-inflated lung, the end expiratory pressure was normal and there was a considerable impairment of gas diffusion. This man, E. A., No. 7, was studied eight years after pneumonectomy and had been subject to attacks of winter bronchitis in the past few years. The principal findings were: (*a*) Normal vital capacity but reduced I.R.V./E.R.V. ratio; (*b*) the largest functional residual capacity (3.10 litres) in the series; (*c*) normal Rd.C./T.L.V.% and only very slight lowering of the mixing efficiency; (*d*) a normal end expiratory pressure level with a somewhat reduced compliance; (*e*) on exercise, the diffusing capacity was the lowest in the series; the O_2/V was also much reduced, indicating a higher than normal ventilation for a given oxygen uptake.

These findings show that the lung volume was increased, but, as the end expiratory pressure level was not abnormally low, the lung must therefore have lost its normal elastic recoil, and may be said to show emphysema in the mechanical sense. There was no bronchospasm, and the mixing efficiency was considerably better than in patients with conventional emphysema. The low D_{CO} in this patient indicated a considerable loss of diffusing surface in relation to the F.R.C. Thus, both in mechanical terms and in terms of the diffusing change, this man may be said to have emphysema.

Three patients, A. McI., No. 2, T. E., No. 6, and G. C., No. 10, cannot be placed satisfactorily in any of the three groups above. In A. McI., No. 2, the compliance was lower than normal, and the end expiratory pressure slightly lower than normal. The F.R.C. was normal, as was the mixing efficiency and the diffusing capacity. This patient, therefore, shows very slight evidence of overinflation on the mechanical measurements. In patient T. E., No. 6, a reduced compliance was the only abnormality found. Patient G. C., No. 10, was the oldest in the series. He showed a slight reduction in compliance. The F.R.C. was normal. The diffusing capacity was, however, considerably reduced and the mixing efficiency lowered. The reduced diffusing capacity may have been related to his age, but if the reduced mixing efficiency and D_{CO} be taken as some evidence of emphysema in this man, then this has occurred without any evidence—either radiological or functional—of overinflation.

Two observations were made during the course of this study which merit particular mention. In patient S. P., No. 1, the youngest in the series, there was a great decrease in compliance with no tachypnoea. This presented a striking—and in our experience unique—exception to the general principle that increased stiffness of the lungs is associated with an increased respiratory rate. On reference to the operation note, it was found that this man had had a much more extensive mediastinal dissection than any other in the group, and it seems possible that the pulmonary branches of the vagus nerve to the remaining lung were cut at the operation. It has been suggested (McIlroy, Marshall, and Christie, 1954) that the control of the rate and depth of breathing by which the work of breathing is kept to a minimum is mediated through the Hering-Breuer reflex. This control should be abolished by vagotomy, and the results reported in this patient may therefore constitute the first evidence in man that this hypothesis may be correct. This man also showed another peculiar finding, as, when he increased his rate of walking on the treadmill from 2 m.p.h. to 3 m.p.h., the work of inspiration decreased. This result was explained by the change in respiratory level which occurred. At 2 m.p.h. the end expiratory pressure level was -24 cm. H_2O, while at 3 m.p.h. it was only -16 cm. H_2O. The compliance of the lung in this patient decreased markedly as the lung volume increased, so that by changing to a lower respiratory level he achieved a greater ventilation with a smaller intrathoracic pressure swing.

The results in patient R. F., No. 4, must also be considered separately. This man had a normal vital capacity, but a reduced I.R.V./E.R.V. ratio. The F.R.C. was slightly increased and the mixing efficiency normal. The compliance of the lung was reduced and the end expiratory pressure level slightly lowered. There was therefore slight evidence of over-inflation. He completed the first exercise period at 1 m.p.h. (4a, Table IV) without respiratory distress, and he then did a second period of six minutes at 2 m.p.h. At the end of this period he was moderately dyspnoeic but not very distressed. He had no cough. He sat in a chair for a few minutes and then left the department, without making any comment suggesting respiratory difficulty. Subsequent analysis of the results showed that this second exercise compared with the first had produced a striking series of changes, namely, a higher respiratory rate ; an increased lung stiffness ; a rise in the end expiratory pressure level ; a drop both in the O_2/V and in the arterial oxygen saturation—this last change being the only example of unsaturation seen—and a great drop in the D_{co} from 11.2 to 5.1 ml. CO/min./mm. Hg. All these changes are of the type one might find in pulmonary oedema, and it seems likely that the patient developed subclinical pulmonary oedema. This sequence of events may be related to the observation of occasional " drowned lung " syndromes in the patients mentioned by Cournand and Berry (1942), due to a more severe attack of pulmonary oedema. The possibility that patients after pneumonectomy may develop pulmonary oedema on exercise, without overt clinical evidence of its presence, is of some interest and importance, as it may represent a stage of development of increased transudation of fluid across the pulmonary capillary bed before frank pulmonary oedema develops.

DISCUSSION

It is clear that the absence of one lung may result in very little change in function of the remaining lung. In the case of patient H. B., No. 3, the final result may be said to be first-class. It will be noted from Table I, however, that this man did complain of some dyspnoea after operation, and it is to be presumed that this was due to the fact that the ventilation of the remaining lung was about double that before pneumonectomy for a given level of external work. The high diffusing capacity in this man is a considerable help to him, as there is thus no need for a raised level of ventilation for a given oxygen uptake. Although only 10 patients were studied in this series, it is of interest that the correlation coefficient between the ventilation equivalent (O_2/V) and the D_{co} on exercise is 0.7, which is significant at the 5% level. With so few cases, the importance of this relationship might be doubted, but Cournand and Berry (1942) and Cournand and others (1950) also found a decreased O_2/V in the patients they studied, indicating an excessive ventilation for a given oxygen uptake. Certainly this is the change one would expect to find if the diffusing capacity were reduced, as a higher than normal alveolar oxygen tension would then be required to effect an adequate oxygen transfer. If this relationship can be confirmed in more patients, it will indicate that part of the respiratory drive is being supplied by a lowered arterial oxygen tension, the ventilatory response to this slight reduction being mediated by the same mechanism as in acclimatization to altitude. The idea that this phenomenon may occur in the absence of any demonstrable drop in oxygen saturation seems an interesting one. The work of Björk and Hilty (1954) lends some general support to this idea, since their finding of a consistently low arterial oxygen tension during the week after pneumonectomy might be due to the fact that the necessary ventilatory adjustment or acclimatization has not yet had time to occur.

When over-inflation is present the immediate result is that the lung is ventilated at an abnormally low intrathoracic pressure. This results in a " stiffer than normal " lung as a result of the shape of the pressure-volume curve of the lung. If the lung now loses elasticity, the intrathoracic pressure will rise, the functional residual capacity will increase, and the diffusing capacity will begin to fall in relation to it. This suggested sequence of changes is shown diagrammatically in Fig. 5. Unless chronic bronchitis and bronchospasm have been features of this phase, we may expect this type of " emphysema " to be somewhat different

State of Lung	*Effect*	*Changes in Function Tests*
Removal of one lung Remaining lung not over-inflated	Remaining lung has to double ventilation for given level of external work by the patient. Loss of diffusing surface leads to slight increase in ventilation required for a given oxygen uptake	V.C.: F.R.C.: ½ normal predicted values Rd.C. / T.L.V.%: M.E.%: normal. D_{CO} rest and exercise: ½ normal value. Lung compliance halved. Airway resistance doubled. End expiratory pressure normal. Exercise O_2/V slightly reduced
Overinflation of lung. No other change	More respiratory work is done for a given level of ventilation	V.C.: ½ normal predicted value. Slight fall in I.R.C./E.R.V. ratio. F.R.C. increased. Rd.C./T.L.V.%: M.E.%: normal. D_{CO} rest and exercise: ½ normal value or nearly so in relation to F.R.C. Compliance more reduced. End expiratory pressure more negative. Exercise O_2/V reduced slightly
"Loss of elasticity" in over-inflated lung. Onset of "emphysema"	Loss of diffusing surface necessitates further increase in ventilation for a given oxygen uptake	V.C.: ½ normal or slightly reduced. F.R.C. still further increased. M.E.%: normal initially. D_{CO} falling in relation to F.R.C. Compliance less reduced. End expiratory pressure less negative. Exercise O_2/V more reduced

FIG. 5.—Diagram showing the suggested sequence of changes following pneumonectomy. V.C. = vital capacity. F.R.C. = functional residual capacity. R.D.C./T.L.C.% = residual capacity as a percentage of total capacity. M.E.% = mixing efficiency %. I.R.V./E.R.V. ratio = ratio of inspiratory reserve volume to expiratory reserve volume.

from the classical type secondary to long-standing chronic bronchitis, for gas distribution will be little deranged. It may be objected that the definition of emphysema should not be expanded to include those patients in whom the bronchitis is minimal, but if the destruction of alveolar walls is real it is difficult to know how else they should be classified. Evidence has been presented elsewhere (Bates, Knott, and Christie, 1956) that a falling D_{CO} is the most useful prognostic sign in emphysema, and Shepard and others (1955) have described patients with emphysema in whom the D_{O2} defect was the predominant one and evidence of bronchitis was minimal.

Certain conclusions may be drawn from the data included in this study as to which tests or measurements may be useful in indicating the state of the remaining lung. It is clear that the vital capacity is of no value, but the ratio I.R.V./E.R.V. is generally higher in those whose lung is not over-inflated. The functional residual capacity is of considerable value; it would be enhanced if reliable pre-operative figures were available. The Rd.C./T.L.V.% is useless both in diagnosing over-inflation and in detecting emphysema, though if the changes of emphysema were gross enough it is possible that it might reveal them. The mixing efficiency of the lung remains normal even in the presence of considerable over-inflation, and in the absence of bronchospasm is likely to remain little changed as emphysema develops. This finding is consistent with the absence of any significant change in compliance at different respiratory rates (Fig. 2) (Otis and others, 1956). The measurement of the end expiratory pressure level is probably the best indicator of the presence of over-inflation, particularly when the F.R.C. is also known. The diffusing capacity of the lung is related to the normality of the vascular bed, and the comparison on exercise between the D_{CO} and the F.R.C. is probably the most sensitive indicator of change in the lung of the type seen later as evident emphysema.

The results in this small group of patients suggest certain answers to the three questions posed in the introduction. It seems clear that some dyspnoea is present after operation, even in the absence of evidence of over-inflation of the lung. The mechanism of this is presumably the necessary over-ventilation of the remaining lung. The presence of over-inflation accentuates the dyspnoea by a further reduction in compliance associated with an abnormally high negative end expiratory pressure level. Contrary to the only previously reported measurements, we have found that the diffusing capacity is generally half the value found in normal subjects, which is to be expected in view of the dependence of this measurement of the blood surface area of the lungs. This reduction in available diffusing surface necessitates an increased ventilation for a given oxygen uptake, reflected by a lowered ventilation equivalent for oxygen. This decreased ventilation equivalent was noted by Cournand and Berry (1942) and by Cournand and others (1950). The results in this study suggest that there is a clear distinction between over-inflation and emphysema. Over-inflation results in an increased lung volume with a low intrathoracic pressure level and normal gas diffusion. Emphysema, on the other hand, is characterized by an increased lung volume with a normal intrathoracic pressure level and impaired diffusion.

The investigations carried out on each patient took about one hour, and the calculations required approximately the same length of time. The only inconvenience to the patient was the swallowing of an oesophageal tube, which, though uncomfortable, is no worse than a Ryle's tube to swallow.

It is clear that pulmonary function studies such as these can give information about the state of the patient's lung of direct clinical value and obvious research interest. A carefully planned and systematic study of a much larger number of patients would throw a great deal of light, for instance, on the effect of other surgical procedures on the chest at or after pneumonectomy: it would also enable more definite conclusions to be reached regarding the occurrence and nature of emphysema in these patients.

SUMMARY

Pulmonary function has been studied in 10 patients after pneumonectomy for bronchial carcinoma. The subdivisions of lung volume and the mixing efficiency have been measured and the mechanical properties of the lung and the diffusing capacity for carbon monoxide studied at rest and during exercise.

In every patient the compliance of the lung and the diffusing capacity were reduced and the inspiratory resistance increased. In six patients with little or no evidence of over-inflation of the lung or emphysema, the changes in pulmonary function were similar to those expected with a halving of the amount of lung tissue available for respiration.

In three patients with radiological evidence of over-inflation of the lung there was a much reduced compliance, a low intra-oesophageal pressure, and a normal diffusing capacity.

In one patient, studied eight years after operation, the findings were interpreted as showing emphysema of the remaining lung.

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REFERENCES

Bates, D. V., and Christie, R. V. (1950). *Clin. Sci.*, **9**, 17.

—— Boucot, N. G., and Dormer, A. E. (1955). *J. Physiol. (Lond.)*, **129**, 237.

—— Knott, J. M. S., and Christie, R. V. (1956). *Quart. J. Med.*, **25**, **137.**

Björk, V. O., and Hilty, H. J. (1954). *J. thorac. Surg.*, **27**, 455.

Cournand, A., and Berry, F. B. (1942). *Ann. Surg.*, **116**, 532.

—— Riley, R. L., Himmelstein, A., and Austrian, R. (1950). *J. thorac. Surg.*, **19**, 80.

Denolin, H., De Coster, A., Dumont, A., and Cantinieaux-Duwaerts, S. (1952). *Acta cardiol. (Brux.)*, **7**, 261.

Dornhorst, A. C., and Leathart, G. L. (1952). *Lancet*, **2**, 109.

Fowler, W. S., and Blakemore, W. S. (1951). *J. thorac. Surg.*, **21**, 433.

Friend, J. (1954). *Lancet*, **2**, 260.

Fry, D. L., Stead, W. W., Ebert, R. V., Lubin, R. I., and Wells, H. S. (1952). *J. Lab. clin. Med.*, **40**, 664.

McIlroy, M. B., and Eldridge, F. L. (1956). *Clin. Sci.*, **15**, 329.

—— Marshall, R., and Christie, R. V. (1954). Ibid., **13**, 127.

Marshall, R., Stone, R. W., and Christie, R. V. (1954). Ibid., **13**, 625.

Mead, J., McIlroy, M. B., Selverstone, N. J., and Kriete, B. C. (1955). *J. appl. Physiol.*, **7**, 491.

Otis, A. B., McKerrow, C. B., Bartlett, R. A., Mead, J., McIlroy, M. B., Selverstone, N. J., and Radford, E. P. (1956). Ibid., **8**, 427.

Riley, R. L., and Cournand, A. (1951). Ibid., **4**, 77.

—— Lilienthal, J. L., Proemmel, D. D., and Franke, R. E. (1946). *Amer. J. Physiol.*, **147**, 191.

Shepard, R. H., Cohn, J. E., Cohen, G., Armstrong, B. W., Carroll, D. G., Donoso, H., and Riley, R. L. (1955). *Amer. Rev. Tuberc.*, **71**, 249.