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Simple Tests of Ventilatory Capacity in Children with Cystic Fibrosis

Part I: Clinical and Radiological Findings in 85 Patients

Part II: Three-year Follow-up on 50 Patients

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Reports of simple pulmonary function tests in cystic fibrosis first appeared in 1954, when West, Levin, and Di Sant' Agnese showed a characteristic finding in 6 patients, aged 12–16 years, of difficulty in moving air rapidly in or out of the lungs. Cook *et al.* (1957) studied the lung volume in 53 patients, aged 1–31 years, and found that 81% of those diagnosed as having cystic fibrosis were found to have significant alteration in one or more of the measurements made. A further study (Cook *et al.*, 1959) of 64 patients, aged 6–25 years, over a period of three years related clinical evaluation with results of pulmonary function studies. The vital capacity was found to be below normal in all but 10 patients and the residual volumes increased in 28. Their findings showed no obvious trend, and the authors considered that the duration of the study might have been too short. In 1963, Polgar, Chernick, and Toft reported a longitudinal study over a period of 6 months of pulmonary function in 14 children with cystic fibrosis. They concluded that extreme variability was the limiting factor in evaluating patients with cystic fibrosis by pulmonary function tests. A recent study of 20 children by Beier *et al.* (1966) showed a pattern of obstructive pulmonary disease, with evidence of increasing airway obstruction paralleling the increase in clinical severity. Correlation between clinical severity and individual pulmonary function tests was also found.

The prognosis in cystic fibrosis depends almost entirely on the course of the pulmonary lesion. Clinical and radiological assessment of children with cystic fibrosis attending the Queen Elizabeth Hospital shows that a proportion of those treated intensively for lower respiratory infections from an early age is free or almost free from chronic pulmonary disease. The present report concerns an attempt to correlate this clinical impression with simple tests of ventilatory capacity. Serial measurements have been used to assess patients, and will be reported in Part II of this paper.

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Part I: Clinical and Radiological Findings in 85 Patients

Method

Expiratory peak flow rate (PF). This was measured by a Wright Peak Flow Meter. Several trial blows were allowed until consistent reading was obtained, the maximum peak flow rate of five readings being recorded. Values below 100 were checked on the Low Range Peak Flow Meter.

Normal values published by Nairn *et al.* (1961) have been used for comparison.

The results plotted on Fig. 1 showed a similar pattern to the $FEV_{1.0}$. The test has been found useful in the clinic for quick assessment to determine any change in a particular child. No attempt has been made in this study to relate these values to the clinical grouping, and these are not discussed further in this paper.

Forced vital capacity (FVC) and forced expiratory volume at one second ($FEV_{1.0}$). The spirometer used was similar to that described by Bernstein, D'Silva, and Mendel (1952). The light aluminium bell had an inner diameter of 22·4 cm. The airway consisted of a flexible hosepipe (diameter 4·5 cm.) connected to a straight plastic tube mouthpiece (internal diameter 2·4 cm.).

The curves were recorded on a motor-driven kymograph with a speed of 2 cm. per second.

Before starting the tests the standing height was measured. In the previously reported studies of cystic fibrosis (De Toni, 1961; Sproul and Huang, 1964; Doershuk *et al.*, 1965) it has been shown that the majority of children are of short stature. Fig. 2 shows that the heights of the children in this series had a fairly

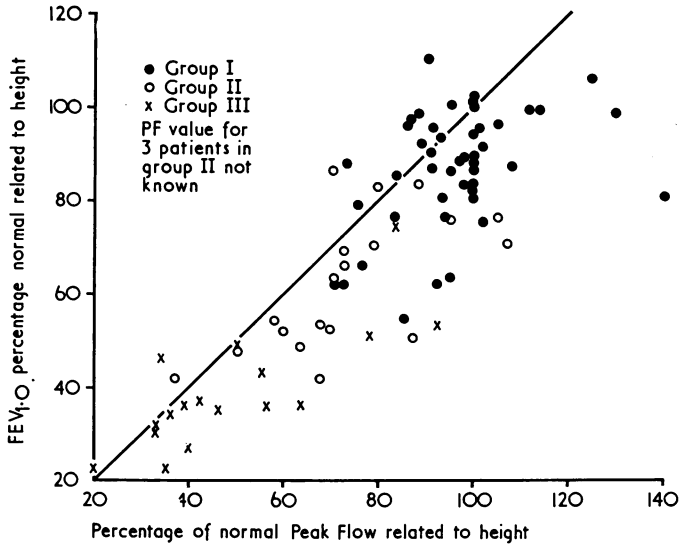

FIG. 1.—*$FEV_{1.0}$ plotted against peak flow.*

normal scatter even among those whose pulmonary function was deteriorating.

The children were then seated in front of the spirometer. They were given instructions and a demonstration of how to perform the test, each child being allowed practice attempts until consistent readings were obtained —the reading being free of artefact and of mistakes as judged by eye. The younger children did not tolerate the nose clip, and after repeating the tests without it, it was found that there was little difference in the results in the majority of children. Thereafter and throughout this study the nose clip was not used. The criticisms of this procedure are appreciated but it was adopted in the interests of obtaining better co-operation at follow-up examinations.

A tracing was made of maximum forced expiration after a full inspiration. The volume of gas expired in the first second of the forced expiration (forced expiratory volume at one second) was measured, the best of three recordings was used, and the value calculated for the FVC and $FEV_{1.0}$. These values were corrected to 37° C.

Vital capacity (VC). After maximal inspiration the children expired as deeply but not as fast as possible. In health the FVC and VC are equal. This was also found to be so in the present study, except for a few patients with generalized lung disease where the VC was greater than the FVC. This is not discussed in the present study.

The above tests were repeated after the inhalation of 1% isoprenaline sulphate using a Wright's nebulizer, with oxygen flow of 10 l./min. for one minute. Following a rest of two minutes the above tests were repeated.

Values for FVC and $FEV_{1.0}$ in normal British children over 114 cm. in height (Strang, 1959) have been used for comparison. For vital capacity in children with heights lower than this the values for males of Ferris, Whittenberger, and Gallagher (1952), and for females the values of Ferris and Smith (1953) have been used. Values for the $FEV_{1.0}$ are not published by these authors, and for comparative values in the present study the normal $FEV_{1.0}$ has been taken to be 85% of the VC.

The results of FVC and $FEV_{1.0}$ are expressed as

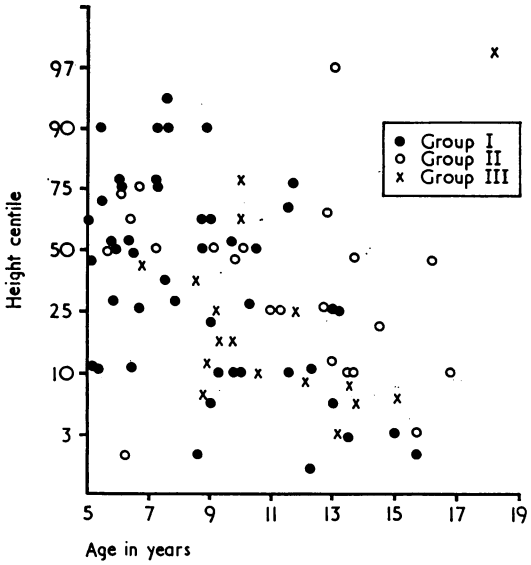

FIG. 2.—*Centile heights of 85 patients. 33 out of the 85 have height above the 50th centile and only 4 below the 3rd centile.*

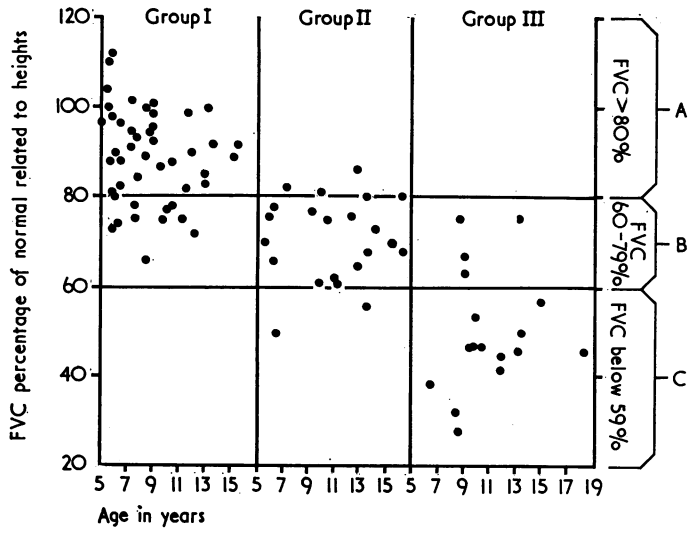

FIG. 3.—*FVC % of normal related to clinical group.*

percentage of predicted normal for height, since height minimizes any differences in growth and nutrition between normal children and those with cystic fibrosis. On the basis of these results the patients were divided into three functional grades (Fig. 3). Grade A: FVC greater than 80% of normal; Grade B: FVC 60–79% of normal; Grade C: FVC 59% of normal and below.

Material

The series included all the children with cystic fibrosis who had reached 5 years of age between December 1963 and March 1967, the diagnosis having been confirmed by analysis of the sweat sodium, a level over 70 mEq/l. sodium being considered diagnostic of cystic fibrosis.

Tests were made on 92 children; 7 were excluded as unreliable results were obtained, and the findings from tests on 85 children are discussed.

The age range was from 5–18¼ years and there were 43 girls and 42 boys. No patient was tested at the time of an acute exacerbation.

These patients have been followed up regularly at a clinic started in the early 1950's. Regular assessment has been made on clinical and radiological findings, the cases being divided into three clinico-radiological groups as previously described (Jackson and Young, 1960; Jackson, 1964).

Clinico-radiological groups

Group I: Good general health. Some may have occasional attacks of bronchitis or short periods with cough and sputum. Chest *x*-ray normal, or there may be a minimal degree of thickened bronchial wall pattern.

Group II: Good general health with respiratory symptoms as above, but chest *x*-ray showing localized change.

Group III: Persistent pulmonary infection with purulent sputum with or without abnormal findings in the lungs on clinical examination, and with or without impairment in general health. Chest *x*-ray showing generalized changes.

Grade A—FVC 80% or more of normal. The results show that 41 of the 85 children had FVC greater than 80% of normal (Table I), the clinical and radiological grouping of these being 36 in Group I and 5 in Group II (see Fig. 3).

Comparison of the percentage normal FVC with the percentage normal $FEV_{1.0}$ shows that in 33 children these values approximated within 5%, of which 2 were in clinico-radiological Group II. Of the remaining 8 children, 5 were from Group I and 3 from Group II. 4 were known to have had an acute episode (that is increase in cough with or without increase in sputum) within the previous 2–3 months, and it is possible there may be some improvement at later testing (Table II).

Grade B—FVC 60–79% of normal. There were 29 children with FVC between 60 and 79% of normal. 10 were in clinico-radiological Group I. Of these, 5 had had infections within the previous 2–3 months, and in all these the FVC rose to 80% or over after inhalation of 1% isoprenaline, though there was not such a marked improvement in the $FEV_{1.0}$. Of the other 5 who had no such recent infection, 3 showed some improvement of results after the inhalation of isoprenaline. These results indicate that there was some degree of variable airway obstruction in this group of patients.

TABLE I

Relation of Clinico-radiological Grouping to % Normal FVC in 85 Children with Cystic Fibrosis

FVC	80% or More Grade A	60–79% Grade B	Less Than 59% Grade C
Clinico-radiological Group I	36	10	0
Clinico-radiological Group II	5	15	2
Clinico-radiological Group III	0	4	13
Total	41	29	15

TABLE II

Comparison between FVC % and $FEV_{1.0}$% in 41 Grade A Children

Patients' Initials	FVC % Normal	$FEV_{1.0}$ % Normal	Comment
Grade A: 33 Patients with FVC > 80% and $FEV_{1.0}$ within 5%			
J.H.	100	98	
T.H.	84	87	
Y.U.	100	102	
V.G.	92	89	
J.L.	87	82	
C.F.	92	97	
C.W.	94	95	
P.C.	86	86	
L.C.	88	87	
N.D.	90	92	
K.D.	99	104	
G.S.	91	90	
A.U.	88	87	
G.G.	97	96	
M.S.	81	80	
C.H.	98	96	
N.O.	95	95	
A.O.	82	87	
I.S.	83	80	
M.W.	99	103	
K.G.	89	88	
J.E.	101	99	
G.A.	97	98	
A.G.	80	85	
J.G.	100	100	
D.M.	105	110	
C.K.	93	89	
E.G.	90	88	
T.G.	96	94	
S.K.	94	89	
F.B.	88	93	
A.M.	81	83	Group II
A.P.	82	87	Group II
Grade A: 8 Patients with FVC > 80% but $FEV_{1.0}$ differs by more than 5%			
E.F.	111	91	Infection within 2–3 months
C.C.	112	99	Infection within 2–3 months
F.McD.	95	83	Infection within 2–3 months
S.S.	101	93	Infection within 2–3 months
D.M.	82	76	
J.T.	86	76	
S.S.	80	70	Group II
R.B.	80	65	Group II

TABLE III

Response to Inhalation of Isoprenaline in 10 Children with Cystic Fibrosis

Patients' Initials	FVC % Normal	After Isoprenaline FVC % Normal	$FEV_{1.0}$ % Normal	After Isoprenaline $FEV_{1.0}$ % Normal
J.MD.	73	—	83	—
T.A.	75	—	79	—
J.G.	72	77	62	71
*S.G.	74	80	76	90
K.M.	78	80	62	69
*J.M.	78	85	54	73
*R.C.	75	80	62	70
*D.G.	77	87	75	81
*M.G.	67	80	65	76
W.O'T.	67	73	72	81

* Recent infection.

The detailed results showing response to inhalation of isoprenaline in the 10 children in clinico-radiological Group I are set out in Table III.

Of the 19 remaining Grade B patients, 15 were in clinico-radiological Group II, and 4 in Group III. A comparison of the FVC and $FEV_{1.0}$ shows that in only 5 did these values approximate to within 5%. In none did the FEV value show significant change after the inhalation of isoprenaline (Table IV).

Grade C—FVC 59% of normal and below. Of the 15 patients with FVC below 59% of normal, all but 2 were in clinico-radiological Group III. The 2 patients in Group II (localized lesion on *x*-ray) had both had lobectomies, which would result in some reduction in lung volume. The majority of

TABLE IV

Grade B: Patients in Clinico-radiological Groups II and III

Patients' Initials	FVC % Normal	$FEV_{1.0}$ % Normal	Comment
W.J.	78	76	Group II
S.K.	70	70	Group II
P.J.	73	49	Group II
J.G.	68	48	Group II
S.S.	70	52	Group II
W.D.	61	54	Group II
D.A.	66	70	Group II
W.S.	76	69	Group II
W.W.	76	63	Group II
D.G.	75	65	Group II
A.S.	77	83	Group II
L.F.	62	48	Group II
J.D.	68	48	Group II
J.R.	65	42	Group II
C.C.	61	53	Group II
C.A.	67	49	Group III
N.S.	75	51	Group III
M.B.	63	52	Group III
K.P.	76	74	Group III

TABLE V

Grade C—FVC Below 59% of Normal

Patients' Initials	FVC % Normal	$FEV_{1.0}$ % Normal	Comment
P.S.	56	43	Group II
S.F.	54	52	
C.C.	46	30	
N.C.	32	22	
J.M.	28	27	
L.B.	38	36	
M.F.	50	36	
A.W.	57	34	
S.D.	45	31	Group III
K.G.	47	37	
S.C.	47	35	
L.D.	46	35	
S.C.	54	43	
D.B.	47	36	
S.P.	46	22	

these Grade C patients showed a much greater reduction in the $FEV_{1.0}$ values than in FVC. 6, all of whom had $FEV_{1.0}$ below 40% of normal, have died. Inhalation of isoprenaline made no appreciable difference to the $FEV_{1.0}$ values in this group, indicating fixed airway obstruction (Table V).

Discussion

These findings from simple tests of ventilatory capacity in 85 children show that the FVC correlates well with an independent clinical and radiological assessment.

However, some patients who had no cough or sputum and normal chest *x*-rays showed a reduction in the $FEV_{1.0}$ which improved after the inhalation of isoprenaline. A $FEV_{1.0}$ reduced to much greater degree than the FVC is the pattern expected in either bronchial obstruction or diminished elastic recoil of the lungs. A good response to isoprenaline suggests a degree of variable airway obstruction, and this finding in cystic fibrosis may herald an acute or insidious respiratory infection, or may be an indication of generalized bronchial change which cannot be detected in any other way in this disease.

With progression of the disease the FVC diminishes, and the variable airway obstruction seems to become fixed, as shown by some of the patients in Group II. Though the radiological findings in these patients indicate localized disease, the pulmonary function tests show that the $FEV_{1.0}$ is reduced to a greater extent than the FVC, and improvement is less marked after isoprenaline, suggesting that the changes are generalized. The patients with generalized radiological lung changes (Group III) had gross reduction in lung volume, and their response to isoprenaline was completely lost.

The pattern where the $FEV_{1.0}$ and FVC are reduced in proportion is that expected in restrictive lesions in the lungs. It has been shown (Dayman, 1951) that in diffuse airways obstruction there may be gross narrowing or collapse of airways on expiration, and Macklem, Fraser, and Brown (1965) pointed out that the effect of bronchodilator drugs might not be detected by tests involving maximal expiratory effort. It has not been possible to demonstrate if this occurs in this group of patients, but the finding that the VC was greater than the FVC in some patients in Group III supports this view.

Strang (1960) showed that a disproportionate fall of $FEV_{1.0}$ to FVC was less obvious in children with bronchiectasis than in those with asthma. In some cases of bronchiectasis this change was less marked, and in others the $FEV_{1.0}$ and FVC were reduced in equal proportions, and he concluded that many children with bronchiectasis might have diffuse bronchial damage or bronchitis, and measurement of FVC and $FEV_{1.0}$ might show this. The present study shows that children with cystic fibrosis have the same variable pattern in tests of ventilatory capacity as those with bronchiectasis, and that, though clinico-radiological assessment suggests localized disease, this is not always confirmed by pulmonary function tests.

Prolonged ventilatory abnormality, which is presumably associated with bronchial obstruction, may contribute to permanent pulmonary damage, especially if other factors, such as infection, capable of damaging the lung, are added. In cystic fibrosis, bronchial obstruction often occurs at a time when the lung is actively growing, and may result in lung hypoplasia (L. Reid, 1966, personal communication). Therefore, the changes in ventilatory capacity in cystic fibrosis may not be entirely due to the result of chronic infection. Only a long-term study could determine this.

Summary

The results of pulmonary function tests in 85 children with cystic fibrosis are reported.

These results correlate well with clinical and radiological findings. In the 46 Group I children with no clinical symptoms and normal *x*-ray, serial pulmonary function tests might help in diagnosis of insidious infections. 33 out of 85 children had normal pulmonary function with regard to both FVC and $FEV_{1.0}$ for a child of that height, and a further 8 children had normal FVC with slight reduction of the $FEV_{1.0}$.

Part II: Three-year Follow-up on 51 Patients

Initially it had been decided to perform tests of ventilatory capacity at the time of the yearly clinical and radiological assessment. After the first year it became apparent that the results of the tests reflected the changes found on clinical and radiological assessment. Having baseline values for the patients, the decision was then made to repeat tests at the time of acute incidents and after clinical and radiological clearing, as this might give some indication if permanent pulmonary damage had occurred. Later the tests were repeated during the course of respiratory incidents and were found to help in assessing response to treatment.

TABLE VI
Age Range and Clinico-radiological Grouping of 50 Children

Group	No.	Average Age (yr.)	Age Range (yr.)	Male	Female
I	28	8 3/12	4 6/12 to 14 2/12	17	11
II	16	9 10/12	5 to 14 2/12	5	11
III	6	9 5/12	6 9/12 to 13 4/12	2	4
				24	26

Method

The apparatus and method was the same as previously described.

Material

Of the 85 children reported on in Part I, 50 have been followed up for 12–41 months.

The children were grouped according to the clinico-radiological criteria previously described. 28 were in Group I, 16 in Group II, and only 6 in Group III. The average and range for age are shown in Table VI.

Results

The results are recorded as in Part I, Grading A, B, and C on the values of FVC for each of the 3 clinico-radiological groups.

Clinico-radiological Group I—28 patients. The results of the initial pulmonary function tests were: Grade A: FVC greater than 80% in 20; Grade B: FVC 60–79% in 8; and Grade C: FVC below 59% in none.

FVC greater than 80% (Grade A) 20 patients. Of these 20 patients, 13 had a percentage $FEV_{1.0}$ within 5% of their FVC%, and at the end of the study they remained in Group I (Table VII). The remaining 7 patients showed a greater discrepancy between their FVC and $FEV_{1.0}$. Three (Fig. 4 (5) and (13), Fig. 5 (7)) with this discrepancy but with $FEV_{1.0}$ values over 80% of normal, have remained well, and follow-up tests showed FVC and $FEV_{1.0}$ values to approximate within 5%. It is possible that, at the first test, they may not have fully recovered from recent respiratory infection. The

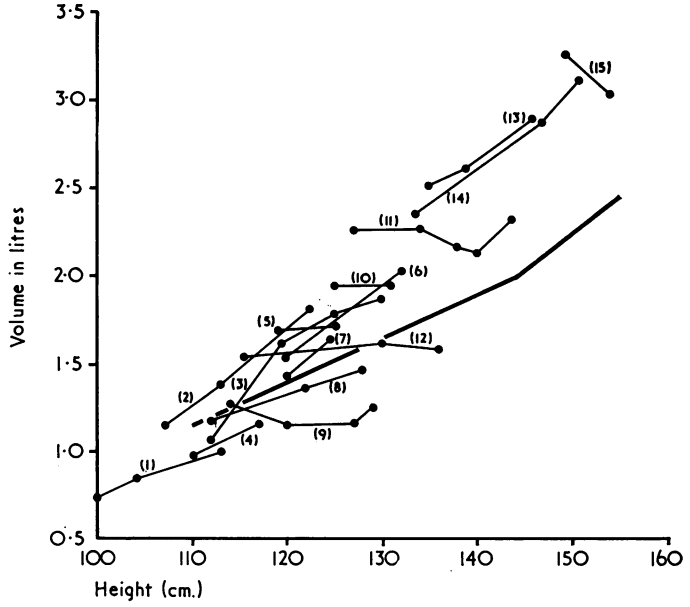

FIG. 4.—*Change in FVC in relation to increase in height. Males remaining in Group I at end of study. Solid black line = FVC (+2SD) (Strang, 1959).*

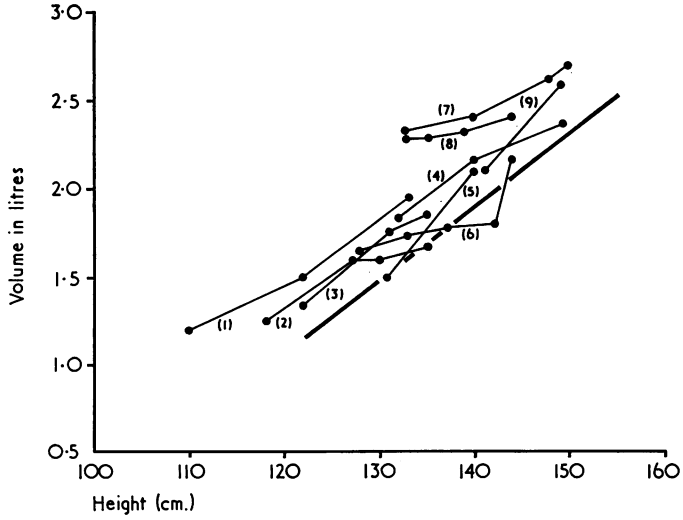

FIG. 5.—*Change in FVC in relation to increase in height. Females remaining in Group I at end of study. Solid black line = FVC (−2SD) (Strang, 1959).*

3-year follow-up of the 4 patients with discrepancy in these values but with $FEV_{1.0}$ below 80% of normal (Fig. 4 (1), Fig. 5 (4) and (6), Fig. 6 (9)) showed each to have had episodes of productive cough and subsequent pulmonary function tests showed the $FEV_{1.0}$ to remain below 80%, with a decrease in the FVC, but only one had developed a persistent localized lesion on *x*-ray (Group II).

FVC 60–79% (Grade B) 8 patients. At the end of the follow-up period 2 of the 8 patients (Table VIII) had both FVC and $FEV_{1.0}$ over 80% of normal, and the values approximate within 5% of

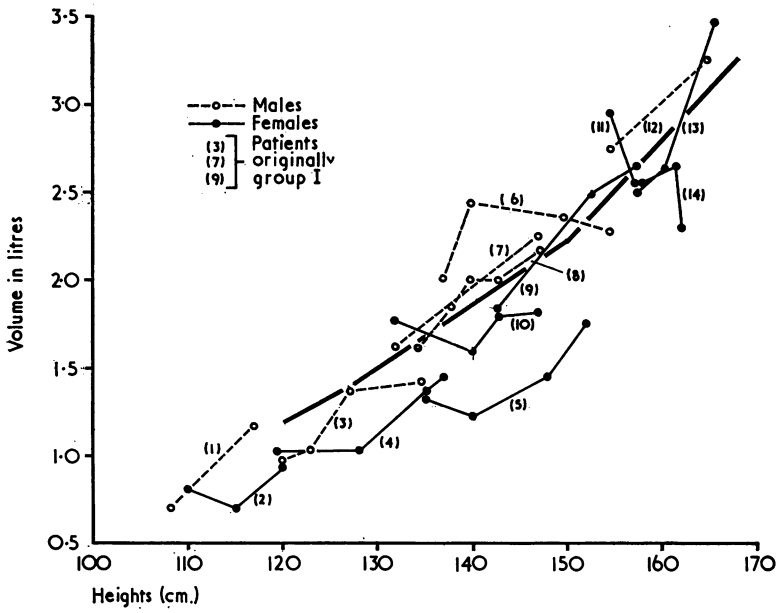

FIG. 6.—*Change in FVC in relation to increase in height. Males and females in Group II at end of study. Solid black line = FVC (−2SD) mean of male and female values (Strang, 1959).*

TABLE VII

Clinico-radiological Group I—Grade A

Patients' Initials	Follow-up (mth.)	Initial		Final		Fig. No. and Patient No.	Comment
		FVC % Normal	$FEC_{1.0}$ % Normal	FVC % Normal	$FEV_{1.0}$ % Normal		
13 Patients with $FEV_{1.0}$ % within 5% of FVC%							
I.S.	37	112	112	83	80	4 (11)	All remain Group I
C.F.	18	107	112	92	95	4 (15)	
J.E.	36	105	105	101	99	4 (2)	
M.W.	38	105	109	99	103	4 (14)	
V.G.	34	102	100	92	89	5 (8)	
N.D.	14	102	100	90	92	4 (10)	
P.C.	24	92	96	86	86	5 (9)	
C.W.	15	92	87	94	95	4 (6)	
S.K.	39	89	84	89	85	4 (3)	
G.S.	12	88	90	91	90	4 (7)	
M.G.	35	84	80	80	83	4 (12)	
S.G.	12	81	84	90	86	4 (4)	
L.C.	18	80	85	88	87	5 (5)	
7 Patients with discrepancy more than 5% between $FEV_{1.0}$ and FVC							
J.G.	34	88	74	72	62	5 (6)	
D.M.	39	90	75	82	76	5 (4)	
D.G.	33	88	55	75	66	6 (9)	Now Group II
W.O'T.	37	80	74	67	72	4 (1)	
K.G.	36	114	100	89	88	5 (7)	? Recent acute episode before initial testing
J.H.	37	104	95	100	95	4(13)	
C.K.	15	100	93	93	89	4 (5)	

TABLE VIII

Clinico-radiological Group I—Grade B: 8 Patients with FVC 60–79%

Patients' Initials	Follow-up (mth.)	Initial		Final		Fig. No. and Patient No.	
		FVC % Normal	$FEV_{1.0}$ % Normal	FVC % Normal	$FEV_{1.0}$ % Normal		
T.G.	41	78	52	96	94	5 (1)	
J.L.	37	77	84	87	82	5 (3)	
K.M.	36	78	67	78	62	5 (2)	
R.C.	37	78	77	75	62	4 (8)	
D.G.	33	76	81	64	59	4 (9)	
S.S.	37	76	67	81	70	6 (7)	Now Group II
G.C.	37	60	45	61	53	6 (3)	Now Group II
L.B.	30	68	62	38	36	—	Died

each other (Fig. 5 (1) and (3)). Three continue to show a marked reduction in the $FEV_{1.0}$ compared with the reduction in FVC (Fig. 4 (8) and (9), Fig. 5 (2)). The pulmonary function testing on one shows no increase in volume with height, and he has developed a persistent productive cough (Fig. 4 (9)).

Two patients with FVC between 60 and 70% have had a downhill course. One died after a subacute illness, and the other has developed a persistent productive cough with localized change on *x*-ray (Fig. 6 (3)).

Clinico-radiological Group II—16 patients (Table IX). At the initial tests the FVC was between 60–79% (Grade B) of normal in 12 patients while in 2 it was above and in 2 below these levels. The group as a whole showed the $FEV_{1.0}$ reduced to a greater degree than the FVC, only 5 out of 16 patients having values that approximated within 5%. 11 patients have remained in Group II during the period of follow-up. 8 of these showed no change in their clinical and radiological findings, of whom 4 showed an increase in FVC and $FEV_{1.0}$ with increasing growth (Fig. 6 (1), (4), (12), and (13)),

TABLE IX

Clinico-radiological Group II—16 Patients

Patients' Initials	Follow-up (mth.)	Initial		Final		Fig. No. and Patient No.	Comment
		FVC % Normal	$FEV_{1.0}$ % Normal	FVC % Normal	$FEV_{1.0}$ % Normal		
R.B.	18	78	68	80	65	6 (12)	Increase in lung volumes
W.S.	13	75	55	75	69	6 (1)	
J.T.	25	72	74	86	76	6 (13)	
L.F.	36	66	57	62	48	6 (4)	
P.J.	18	85	65	73	49	6 (11)	Poor increase in lung volumes
J.G.	30	74	62	68	43	6 (14)	
P.S.	38	64	57	56	42	6 (5)	
S.F.	14	59	58	50	52	6 (2)	
S.S.	36	79	66	66	53	6 (6)	Clinical deterioration
J.R.	35	79	56	73	58	6 (10)	
W.W.	37	72	60	76	63	6 (8)	
Now Group III							
N.S.	40	75	51	56	51		
D.B.	38	72	62	31	27		
Died							
C.C.	6	65	46	46	30		
J.M.	30	73	78	28	27		
N.C.	27	88	86	32	22		

and 4 showed some deterioration on pulmonary function testing (Fig. 6 (2), (5), (11), and (14)). The 3 remaining patients (Fig. 6 (6), (8), and (10)) deteriorated clinically and radiologically, and 2 of them had reduced their FVC and $FEV_{1.0}$ by approximately 15%.

Five patients were no longer in Group II by the end of the study. 2 developed a persistent productive cough, and more than one localized area of disease on *x*-ray (Group III). The results of pulmonary function tests reflect this deterioration. The other 3 patients died. They deteriorated clinically and radiologically, and this was apparent on testing ventilatory capacity, the $FEV_{1.0}$ being reduced earlier and to a greater extent than the FVC.

Clinico-radiological Group III—6 patients (Table X). In 3 the initial FVC was below 59% (Fig. 6) and the $FEV_{1.0}$ approximated within 10% of the FVC value in only 1 patient. 2 patients have maintained a steady state. One developed diabetes in 1965 at the age of 14 years, and from that time deteriorated clinically and radiologically, and also on pulmonary testing. The 3 remaining patients died.

Follow-up over 3 years shows that 24 out of 28 patients in Group I remained free of persistent respiratory infection or permanent radiological change on *x*-ray. Results of pulmonary function tests repeated during this period indicate that there was no reduction of lung volume—the mean FVC and $FEV_{1.0}$ for the group changing very little (Table XI).

The follow-up period is admittedly short, and with the many variable factors in this disease a further period of study is necessary.

Patients with localized disease radiologically

TABLE X

Clinico-radiological Group III—6 Patients

Patients' Initials	Follow-up (mth.)	Initial		Final		Comment
		FVC % Normal	$FEV_{1.0}$ % Normal	FVC % Normal	$FEV_{1.0}$ % Normal	
S.D.	15	59	43	45	31	Died
K.G.	34	49	39	47	37	Steady state
S.C.	34	47	41	47	35	Steady state
C.A.	32	62	43	67	42	Died
M.F.	12	68	48	50	36	Died
A.W.	37	71	58	57	34	Diabetes

TABLE XI

Group I: Average Initial and Final Results of Simple Tests of Ventilatory Capacity

	Initial %	Final (% of normal)
Mean FVC	89	85
Mean $FEV_{1.0}$	83	84
	28 patients	24 patients

TABLE XII

Average Initial and Final Results of Simple Tests of Ventilatory Capacity

	Initial %	Final (% of normal)
Mean FVC	72	68
Mean $FEV_{1.0}$	62·5	56
	16 patients	11 patients

(Group II) had a slower rate of increase in volume in relation to height, and some showed a decrease (Fig. 6). The signs of progress of the disease in these patients is insidious, few having acute episodes to herald further deterioration. Clinical and radiological assessment suggests that their status is stationary, but pulmonary function tests show deterioration. The impression gained is that change in $FEV_{1.0}$ value is more significant than change in FVC (Table XII). The follow-up period has not yet been long enough for certainty on this point, being on average 27·5 months.

In some patients forced expiration during routine testing induced paroxysms of cough, and comparison with previous results showed deterioration. It has been realized that as these patients get older they learn to suppress their cough effectively. As non-productive cough may be the first indication of insidious infection, elucidation of this symptom is important. In other patients tests repeated during episodes of infection have helped in the assessment to treatment. These points are illustrated in the records of the following patients (Fig. 7).

J.E., aged 9 years, attended the clinic for a routine check-up when pulmonary function tests showed that forced expiration induced paroxysms of cough. The parents then volunteered that he had been coughing on exercise for a few weeks and chest *x*-ray showed a small lesion at the left apex. At a subsequent attendance pulmonary function had deteriorated further. Antibiotics by aerosol and intensive physiotherapy were, therefore, given, and over the next few weeks the cough cleared and tests of pulmonary function showed improvement.

S.K., aged 8½ years, had also attended for a routine examination at which tests of pulmonary function showed a marked deterioration from his previous values. The parents were reluctant to admit to any respiratory symptoms because of the child's general well-being, but stated that he had been producing a small amount of sputum for 2–3 weeks. Following treatment similar to J.E.'s but as an in-patient, tests of pulmonary function showed improvement.

K.P., aged 9½ years, was referred from another clinic for a course of intensive treatment as an in-patient, having had a productive cough for some months, and an *x*-ray showing generalized changes. The patient was dyspnoeic and very little exertion caused her to cough. Intensive treatment was given as an in-patient. The *x*-ray showed some clearing, and there was marked improvement in pulmonary function over a period of 5–6 months.

Discussion

The value of simple pulmonary function tests in the assessment of pulmonary disease is a much debated topic. Normal values for forced vital capacity and forced expiratory volume have a wide range, and variation from these occasionally

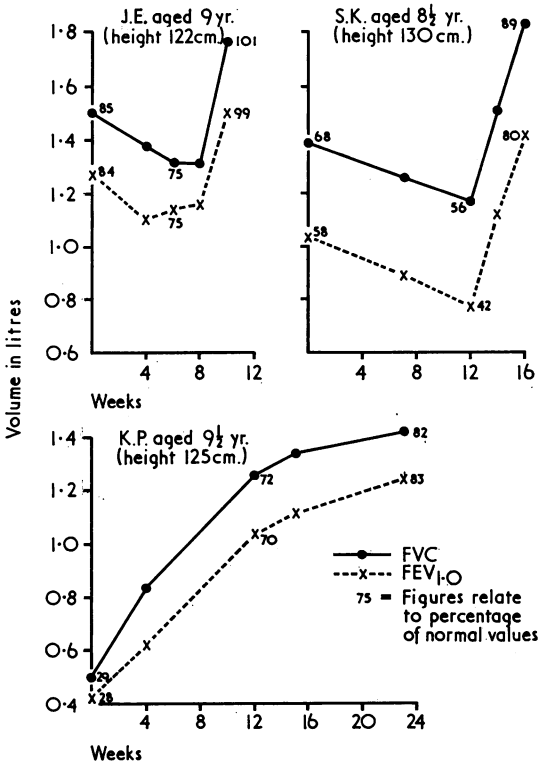

FIG. 7.—*Changes in ventilatory capacity during course of respiratory infection in 3 patients.*

may not be significant. Gross changes in function can be predicted in patients with generalized radiological findings. Pulmonary function tests have been found helpful in assessment of response to treatment and in total assessment of patients with borderline damage on *x*-ray, i.e. some patients in Group I and II. In particular, change in the $FEV_{1.0}$ value has been an indication of the onset of pulmonary incidents. Unfortunately, children under the age of 5 years cannot be assessed in this way, and it is in this young age-group in which it is most difficult to clear pulmonary infection; older children clear by voluntary coughing and deep breathing.

Variation in the severity of the pulmonary involvement in cystic fibrosis makes evaluation of methods of treatment and comparison of results difficult. Shwachman and Kulczycki (1958) published a report of a 5-year follow-up of 105 cases showing that more effective antibiotics and supportive therapy resulted in progressive increase in the average age of death. Matthews, Doershuk, and Spector (1967) and Doershuk *et al.* (1965) showed that a prophylactic therapeutic programme to prevent irreversible pulmonary damage could prevent progression of the pulmonary lesion for 3–7 years, and they believed that this period could be extended indefinitely for most children. Therapy which was started after irreversible damage had occurred was able to decrease morbidity and prolong lives, but slow progression of the pulmonary lesion occurred in most of them.

Matthews *et al.* (1967) have made the only comparable observations to those described in this paper. They reported on 20 patients (aged 4½–16 years) with mild pulmonary disease who were followed up for 4¾ years after their previous treatment had been supplemented by sleeping in a mist tent. There was no significant change in the vital capacity for the group as a whole, but the mean residual volume was more abnormal than the VC or FRC which indicated a moderate degree of hyperinflation of the lungs. After the addition of the tent this value decreased towards normal and improvement was maintained. Comparison of these findings and those from the patients in Group I in the present study can be made if the hyperinflation in our patients is assessed by the discrepancy between their FVC and $FEV_{1.0}$ values.

Matthews' second group of patients numbered 16 (aged 5½–28 years), all but 3 of whom had significant pulmonary involvement. This group was followed up for 2½ years. Mild hyperinflation was present despite continuous mist tent therapy, and this increased notably when the tent was removed, with an associated decrease in VC. This group can perhaps be compared with the Group II patients, though Matthews' patients were probably less severely affected than ours, their mean VC being higher. Initially patients in our Group II showed a greater discrepancy between FVC and $FEV_{1.0}$ values than those in Group I, and subsequently the mean values had changed little. There was deterioration in the mean $FEV_{1.0}$ which may indicate increased hyperinflation.

This report of children with cystic fibrosis with follow-up examinations shows in parallel with similar records (Shwachman and Kulczycki, 1958; Matthews *et al.*, 1967; Doershuk *et al.*, 1965) that it is often possible to avoid irreversible pulmonary damage, but that once the damage has occurred it is usually progressive and involves multiple areas of the lungs. Prominence has been given to the place of the mist tent in the treatment of cystic fibrosis, since Matthews *et al.* suggested that patients whose tests showed evidence of airway obstruction might be improved by using the mist tent. The present study shows that without the mist tent, but using intensive treatment for acute respiratory illness and very close clinical follow-up from the time of diagnosis, children presenting without permanent lung damage can remain well and maintain good respiratory function over a period of years. Even those with localized disease on *x*-ray examination may be maintained in good health and full activity for long periods, and deterioration is often slow.

Summary

Serial tests of ventilatory capacity, i.e. Forced Vital Capacity and Forced Expiratory Volume in 1 second were performed on 50 patients with cystic fibrosis during a 3-year period.

Group I: 28 patients with little or no clinical or radiological evidence of permanent damage to the lungs. The majority of pulmonary function testing showed values within the normal range and these values were maintained.

Group II: 16 patients with localized damage on chest *x*-ray showed a greater reduction in the $FEV_{1.0}$ value than in the FVC, and they had a slower rate of increase in lung volume in relation to height than normal, or those in Group I.

Group III: 6 patients with widespread pulmonary involvement showed marked reduction in $FEV_{1.0}$ and FVC values. Improvement and deterioration clinically and radiologically were reflected in results of pulmonary function tests, though they remained grossly abnormal.

During the 3-year follow-up period 7 children

died, the average age being 10 years 10 months, the youngest being 7 years 1 month. Only 1 patient free of chronic pulmonary disease at the onset died.

Serial pulmonary function tests were a valuable aid to clinical assessment, especially in patients with no or very little radiological change—variation from previous values sometimes warning of an insidious respiratory infection and response to treatment of these incidents was noted by follow-up tests.

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Addendum

I am grateful to Dr. M. Alderson for the following statistical comments.

Fitted regression equations for $FEV_{1.0}$ on height are:

(a) Normals (male and female)

$y = 29{\cdot}4\ x - 2124$ $\quad x = 100\ \ y = 816$ $\quad x = 150\ \ y = 2286$

(b) Group I (male and female)

$y = 35{\cdot}2\ x - 3051$ $\quad x = 100\ \ y = 469$ $\quad x = 150\ \ y = 2229$

(c) Group II (male and female)

$y = 27{\cdot}2\ x - 2401$ $\quad x = 100\ \ y = 319$ $\quad x = 150\ \ y = 1679$

(d) Group III (male and female)

$y = 27{\cdot}0\ x - 2747$ $\quad x = 100\ \ y = 47$ $\quad x = 150\ \ y = 1303$

If these are plotted on one graph it will be seen that for any particular value of x (height) the FEV is highest for the normals, then I, II, and lowest for III.

There is no significant difference in the age effect in any of the 4 categories of children (i.e. none of the slopes of the fitted regression lines for the disease groups differ significantly from that of the normal children). The relevant ordering of the position of the lines shows a significant disease effect ($p = 0{\cdot}042$).