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DYNAMIC SPIROMETRY STUDIES IN PATIENTS WITH LUNG DISEASE

By

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GENERAL INTRODUCTION

In 1919 *Strohl* (84)² emphasized the usefulness of *forced expiratory spiograms* for evaluating ventilatory incapacity. *Tiffeneau* and *Drutel* 1948 stressed the importance of the one second volume of the forced vital capacity, called "Capacité Pulmonaire Utilisable a l'Effort" (90). Since then, different parts of forced expiratory as well as inspiratory spiograms have been studied by various workers (9, 21, 35, 38, 49, 52, 56). For clinical purposes the forced one second volume (FEV_{1.0}) and the forced vital capacity (FVC) seem to be suitable volumes for revealing obstructive and restrictive impairment of pulmonary ventilation, even though other segments of the forced spiogram have been proposed (25, 31, 32, 40, 87). Obtaining smooth and reliable spiograms was made easier after the introduction by *Bernstein et al.* of a spirometer well suited for measuring rapid volume changes (9).

In the present series of papers are reported studies with low resistance spirometers on normal subjects and patients with broncho-pulmonary disease. Dynamic ventilatory parameters will be related to each other and to static lung volumes. The following items will be discussed:³

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² Reference after article no. VI.

³ For terminology see page 330.

- a) Variability of $FEV_{1.0}$ and FVC,
- b) Comparison between different types of slow vital capacity measurements,
- c) Comparison between slow and forced vital capacity,
- d) Comparison among three methods of computing the $FEV\%$, i.e., the fraction of vital capacity expired in one second,
- e) Comparison between ventilatory capacity obtained from forced expirograms and from maximal voluntary ventilation (MVV) at various frequencies,
- f) Relation between Wright's "Peak Expiratory Flow" (PEF) and $FEV_{1.0}$ or maximal voluntary ventilation at rate 40/minute (MVV_{40}),
- g) Variability of PEF in normal and bronchitic subjects,
- h) The value of PEF in pharmacological tests,
- i) Relation between $FEV_{1.0}$ and $FEV\%$ and static lung volumes,
- j) Forced expiratory and inspiratory capacities are compared in normals and in different patient groups.
- k) The discriminatory power to detect drug induced airway constriction was compared for $FEV_{1.0}$, $FIV_{1.0}$, PEF and MMF (Maximal Midexpiratory Flow).

The relation between $FEV\%$ and the nitrogen gradient obtained with the single-breath nitrogen test (53) has been dealt with in an earlier publication (58).

TERMINOLOGY

a) *Spirometric volumes.*

The terminology of dynamic lung volumes recommended by British physiologists is used (39). From a forced expiratory spirogram (FES) the one second volume ($FEV_{1.0}$) was calculated, as well as the forced vital capacity (FVC). The maximal $FEV_{1.0}$ expressed in per cent of the FVC of the same spirogram was termed $FEV\%$. If this FVC was more than 5 % lower than the maximal volume, the $FEV_{1.0}$ was expressed in per cent of the maximal FVC.

From a forced inspiratory spirogram (FIS) the one second volume, ($FIV_{1.0}$),

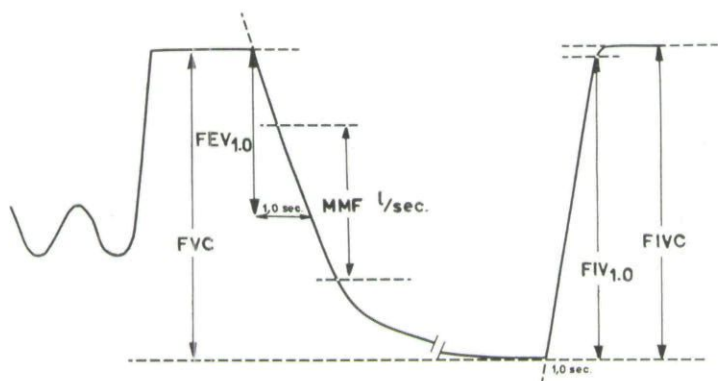


Fig. 1.

Forced expiratory spirogram (FES) and forced inspiratory spirogram (FIS).

the forced inspiratory vital capacity (FIVC), and the ratio $FIV_{1.0}/FIVC \times 100$ (FIV%) were calculated, Fig. 1.

The vital capacity performed by slow breathing was termed VC.

b) Diagnoses.

The descriptive terminology on "chronic non-specific broncho-pulmonary disease" proposed by British workers at a CIBA symposium 1958 (21) and modified in a symposium on Bronchitis in Groningen 1960 (72) is chiefly followed.

"Chronic Bronchitis (Chr. Br.) refers to a condition with chronic or recurrent cough with expectoration which is not attributable to conditions excluded from chronic non-specific bronchopulmonary disease".

"Generalized airways obstruction is present in subjects with an increase above the normal in resistance to airflow in the bronchial tree, at least on expiration" (72). In the present studies the increased air flow resistance was defined as a decrease below two standard deviations from the mean value of $FEV_{1.0}/FVC$ in a normal population studied in this laboratory by Birath *et al.* (7).

The Generalized Airways Obstruction is classified as reversible (RGAO) or "asthma", partly reversible (PRGAO), or irreversible (IGAO).

"Irreversible generalized airways obstruction is present in subjects in whom this obstruction has been present for more than one year, and in whom it is unaffected by bronchodilator drugs" (72). When the question of reversibility of the airways obstruction was not clear by reason of faulty information or lack of tests, the term Generalized Chronic Airways Obstruction (GCAO) was used, then including the two last terms listed above (PRGAO and IGAO).

Emphysema was considered to be a diagnosis defined anatomically. In life irreversible or partly reversible airways obstruction are fundamental for the diagnosis (72).

I. *Variability of Forced Expiratory Volumes*

The variation of the $FEV_{1.0}$ and the FVC within individuals in two separate series of FES were analyzed in terms of change within the series and between the two series. The study was made in order to evaluate within a series a possible systematic change. This is of importance when comparing initial values with post drug values in pharmacological tests.

MATERIAL

In the normal group 4 females and 7 males participated. They were doctors, medical students and laboratory workers. All were without signs of cardiac or pulmonary disease as judged from roentgenograms and history. The mean age was 26 years, the range being 22 to 35 years.

The patient group consisted of 2 females and 13 males. The diagnoses are reported in Table 1. The mean age was 54 years, the range 35 to 67 years.

TABLE 1
Patient group.

Chronic Bronchitis	
Without airways obstruction	4
With airways obstruction	
partly or totally reversible	5
irreversible	3
Irreversible Generalized Airways Obstruction	3
(bronchiectasis 1, tbc 1)	
	Total: 15

METHOD

Spirometers. Spirometers built at the hospital according to the description by *Bernstein et al.* were used (9). Patients with tuberculosis and patients with nonspecific disease used different spirometers. The transparent perspex bells weighed

For terminology see page 330.
References after article no. VI.

about 200 grammes. The tubing from the spirometer to a rubber mask had an inner diameter of 5 cm. The lateral pressure at the mouth during a forced expiration with a flow rate of about 7 litres/second was below 1 mm of mercury. The spirograms were recorded with ink on a kymograph paper moving with a speed of 50 mm/second during the FES, or 5 mm/second during slow breathing or maximal voluntary ventilation test. The volume factors of the spirometers were about 0.05 litre ATPS/mm deflection. One of the spirometers was identical with that used by *Birath et al.* when obtaining normal values at this laboratory (10).

Procedure. Sitting at the spirometer the subjects were instructed how to perform the tests: to keep the mask tight to the face, and to blow through the open mouth. Each recording was started with a few quiet breaths, after which the FVC were performed. The subjects were told to make a maximal inspiration followed by a momentarily started maximally forced expiration, which was continued as long as the test conductor, a welltrained female laboratory assistant, could see any increase of spirometer volume. The interval between the spirograms was at least one minute.

Two separate series of FES were performed. The time lapse between the series varied in the normal group from 1 week to 5 months; in the patient group it was about one week. All the normal subjects made eight FES in each series; the patients performed five.

Calculations. The expired volumes were measured with a transparent plastic ruler giving an error of measurement of about 0.5 mm. This means for a volume of 1 litre an error of 3 %, for 3 liters 1 %. The first deflection from the maximal inspiratory plateau was considered to be the beginning of the forced expiration. The volumes on the ruler were read in "litres BTPS"¹, i.e. here = $\text{ATPS}^2 \times 1.1$. Thus the volumes were not routinely calculated with the use of the actual

¹ Body Temperature and Pressure, Saturated with water.

² Ambient Temperature, Pressure, Saturated with water.

values for barometric pressure and temperature. As the error introduced by temperature variations is small (22), the error was neglected.

Statistics. The mean $\bar{d}$ of difference between pairs was tested against the hypothesis of "no difference" by Students' *t*-test e.g., $t = d/s\bar{d}$. (See Snedecor, G.W., *Statistical Methods*, 1957, Chapter 2). For all such tests a 5 % level of significance was chosen.

In order to find out whether systematic changes in $FEV_{1.0}$ and FVC^1 are present, the following assumptions were set up:

Systematic changes may occur through connection between 1) $FEV_{1.0}$ (FVC) and order of performance (p) or 2) $FEV_{1.0}$ (FVC) and "time lapse" (t). If such connections were present, they were assumed to be linear. Hence a common type of regression analysis was considered suitable with $FEV_{1.0}$ (FVC) as the dependent variable (see Snedecor, G.W., *Statistical Methods*, 1957, Chapter 6.). After calculations of the regression coefficient, they were tested against the "zero hypothesis" of no connection. If any such hypothesis must be rejected (at 5 % level), the opposite hypothesis was accepted, e.g., $FEV_{1.0}$ (FVC) is *not* independent of order of performance (time lapse).

RESULTS

A. Studies in normal subjects

1. Change of volumes within a series.

In the normal subjects the mean values for the two combined series of 8 $FEV_{1.0}$ were: 4.14, 4.29, 4.33, 4.34, 4.33, 4.34, 4.34 and 4.38 litres. Thus there was a trend toward increasing values early in the series. The regression coefficients for $FEV_{1.0}$ related to the order of performance (p) showed a significant increase of the $FEV_{1.0}$, comprising 0.5 % per spirogram. No significant change concerning the FVC was noted within the series.

¹ Identical calculations were made concerning Peak Expiratory Flow in Part II in the series.

TABLE 2
Comparison between the first and last four spirometers within series
of eight measurements.

11 normal subjects.

Subject No. sex		FEV _{1.0}				FVC			
		Series: I		II		I		II	
		Mean values of spirometers number:							
		1-4	5-8	1-4	5-8	1-4	5-8	1-4	5-8
1	F	2.95	3.04	3.16	3.18	3.52	3.58	3.89	3.87
2	F	3.44	3.46	3.58	3.64	3.56	3.57	3.82	3.74
3	F	3.99	3.94	3.96	4.03	4.66	4.48	4.63	4.59
4	F	3.67	3.79	3.84	3.82	3.74	4.05	4.11	4.09
5	M	4.95	5.05	4.87	4.82	6.14	6.13	5.97	5.88
6	M	4.09	4.25	4.64	4.78	4.89	5.03	5.45	5.59
7	M	5.15	5.18	5.16	5.07	6.26	6.42	6.45	6.30
8	M	4.73	4.07	4.03	4.10	4.58	4.39	4.34	4.37
9	M	4.10	5.22	4.96	5.14	5.88	6.14	5.91	6.11
10	M	4.53	4.57	4.53	4.59	5.29	5.27	5.26	5.20
11	M	5.06	5.06	5.00	5.05	5.48	5.37	5.35	5.24
Mean		4.23	4.33	4.34	4.38	4.93	4.95	5.02	5.00
SD		0.70	0.74	0.66	0.66	0.98	1.00	0.91	0.91
Coeff. of var. %		16.5	17.2	15.2	15.1	19.8	20.6	18.1	18.3

In Table 2 are shown the individual mean values of the FEV_{1.0} and FVC for the *first four* and *last four spirometers* in each series. The difference between the FEV_{1.0} no. 1-4 and FEV_{1.0} no. 5-8 was slightly less in the second series than in the first one. The difference between the mean values no. 1-4 and no. 5-8 was below 3 % in both series. The difference between paired values was not significant. The FVC values were almost identical in the two compared parts.

2. Variability within each series (8 FES). See Table 3.

a) For the FEV_{1.0} the average individual SD and SE was in series I 0.12 (0.05-0.44) and 0.03 (0.02-0.17) litres, respectively, and in series II 0.08 (0.03-0.18) and 0.03 (0.01-

0.07) litres. The mean individual coefficient of variation was 2.8 % (1.0–8.9) in series I, 1.9 % (0.8–3.4) in series II. The wide range of variation in series I was due to one single subject. (The SD and SE for the two combined series of $FEV_{1.0}$ were 0.16 and 0.04 litres respectively, with a coefficient of variation of less than 4 %).

TABLE 3

Statistical data from two series of $FEV_{1.0}$ and FVC measurements on normal subjects and patients with pulmonary disease.

Mean values from the series and average individual values.

	Forced one second volume				Forced vital capacity			
	Normals		Patients		Normals		Patients	
	Series		Series		Series		Series	
	I	II	I	II	I	II	I	II
<i>Mean value</i> in the series	4.29	4.36	1.55	1.56	4.94	5.00	3.33	3.45
<i>SD</i> of the mean:	0.73	0.66	0.48	0.52	1.00	0.91	0.70	0.62
<i>Coeff. of var.</i>	16.9	17.2	31.1	33.5	20.0	18.0	21.1	18.1
<i>Average individ.</i>								
<i>SD</i> of the mean:	0.12	0.08	0.07	0.08	0.11	0.09	0.22	0.15
<i>SE</i> of <i>SD</i> :	0.050	0.023	0.022	0.020	0.029	0.024	0.071	0.046
<i>Average individ.</i>								
<i>SE</i> of the mean:	0.032	0.032	0.032	0.04	0.042	0.035	0.098	0.065
<i>Average individ.</i>								
per cent:								
<i>Coeff. of var.</i>								
(SD/MV $\times$ 100)	2.8	1.9	4.9	5.5	2.3	1.7	5.4	4.6

b) For the FVC the average individual SD and SE was in series I 0.11 (0.06–0.16) and 0.04 (0.01–0.06) litres, respectively, and in series II 0.09 (0.03–0.17) and 0.03 (0.1–0.06) litres. The mean coefficient of variation was 2.3 % (0.9–3.4) in series I and 1.7 % (0.7–2.9) in series II. (The SD and SE for the two combined series of FVC were 0.15 and 0.04 litres with a mean coefficient of variation of less than 4 %). Thus the variation of $FEV_{1.0}$ and FVC was identical in the present series of eight FES in normal subjects.

3. *Changes of volumes between the series.*

A comparison of mean values between the two series, related to time lapse (t), showed a significant increase in the second series, which was estimated to be 1.9 % of the $FEV_{1.0}$. This effect was accounted for mainly by four subjects out of eleven (UA, RB, GO, BG). The *FVC* also showed a significant increase in the second series, the relative increase being 1.4 %; this was due to four subjects (UA, RB, GO, AÖ), whereas the rest remained unchanged.

B. *Studies in patients*

1. *Changes of volumes within a series.*

No significant relation was obtained in the series of $FEV_{1.0}$. The *FVC*, on the other hand, showed a significant change within the series, comprising an increase of 1.2 % per FES.

2. *Variability within each series (5 FES).* See Table 3.

a) For the $FEV_{1.0}$ the average individual SD and SE was in series I 0.07 (0.02–0.23) and 0.03 (0.008–0.12) litres, and in series II 0.08 (0.02–0.10) and 0.04 (0.01–0.05) litres. The mean individual coefficient of variation was 4.9 % (1.9–13.6) in series I, 5.5 % (2.2–8.1) in series II. (The SD and SE for the combined series of $FEV_{1.0}$ were 0.09 and 0.03 litres, respectively, which means an average variation coefficient of 5.5 % in two combined series of five FES each).

b) For the *FVC* the average individual SD and SE was in series I 0.22 (0.08–0.87) and 0.1 (0.04–0.44) litres, respectively, and in series II 0.14 (0.05–0.30) and 0.06 (0.03–0.15) litres, respectively. The mean coefficient of variation was 5.4 % (2.2–12.5) in series I, and 4.6 % (1.0–8.9) in series II. (The SD and SE for the combined series of *FVC* were 0.22 and 0.07 litres; the mean variation coefficient was 6 %).

3. *Changes of volumes between the series.*

No change with time lapse (t) between the two series could be found for the $FEV_{1.0}$ in pulmonary diseased subjects. The FVC, however, showed a significant increase in the second series, estimated to be 3.5 %.

DISCUSSION

The pattern of a decreasing variability with repetition and a small increase of the $FEV_{1.0}$, FVC or VC values with practice in normal subjects, noted by some authors, was confirmed for the $FEV_{1.0}$ only (30, 80). Peabody and Sturgis did not find any such changes in a long series of VC-spirograms (74). The reason for an increase of volumes within a series may be an improved coordination with training. The trend of a decreasing variation with time speaks in favor of this concept.

The increase of FVC in patients during the series can be interpreted in several ways. An improvement of general condition or a better knowledge of how to perform the test might also here be of importance. The exerted expiratory pressures are maintained for a longer time by subjects with airways obstruction, and this might decrease the pulmonary blood volume or move mucous secretion in the bronchial tree and increase the FVC (2).

The change of forced expiratory volumes with time between the series (t) must be interpreted with caution in patients with bronchitis because of the possible unstable status. The largest change recorded was 3.5 %, which concerned the FVC between the series in the pulmonary diseased group. The small volume differences with time in this study are probably due to a relatively steady state of the bronchopulmonary conditions.

The mean coefficient of variation for both $FEV_{1.0}$ and FVC of less than 3 % in the normal subjects agrees with figures reported in the literature, when the numbers of subjects and spirograms in the series are considered. Thus repeated measurements in normal subjects have given coefficients of varia-

tion between 1.5 and 5 % for both VC, FVC and $FEV_{1.0}$ (29, 31, 32, 75, 77). In spirometry with direct reading, e.g., with timer, the standard deviation seems to become larger (30). For $FEV_{0.75}$, figures as high as 11.5 % are reported (57).

The larger standard deviation obtained in patients was expected. In "cardio-respiratory cripples", Shephard obtained an SD of about three times the values in normal subjects. No significant increase of volumes was observed within the series (82). The larger variation may reflect the effect of pressures during expiration, which tend to collapse airways in diseased lungs. With varying force there will thus be a larger variation of the volumes expelled than in normal subjects. This might also explain the lack of increase of $FEV_{1.0}$ within the series in patients, where an increase of force does not invariably result in a larger expired volume.

SUMMARY AND CONCLUSION

The variability of the forced one second volume ($FEV_{1.0}$) and the forced vital capacity (FVC) in two series of eight spiograms in 13 normal subjects and five spiograms in 15 patients with airways obstruction was studied with low resistance spirometers. The interval between the two series varied in the normal groups between 1 week and 5 months, in the patient group it was about one week.

The normal subjects increased their $FEV_{1.0}$ slightly within the series, the patients did not. There was, however, no statistical difference between the first four $FEV_{1.0}$ compared to the second four $FEV_{1.0}$ in normal subjects. The variation coefficient within normal subjects for $FEV_{1.0}$ and FVC was less than 3 %. In the pulmonary diseased group the corresponding figure was 6 %.

A change of an average $FEV_{1.0}$ or FVC by 10 % in normals or about 15 % in subjects with obstructive broncho pulmonary disease after giving a bronchoactive drug thus can be considered to be significant.

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