

# Detection of acute effects of cigarette smoking on airway dynamics:

## A critical and comparative study of pulmonary function tests<sup>1</sup>

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**Sobol, B. J., Van Voorhies, L., and Emirgil, C. (1977). Thorax, 32, 312-316. Detection of acute effects of cigarette smoking on airway dynamics: A critical and comparative study of pulmonary function tests.** In an effort to determine which measure of airway dynamics was the most sensitive to airway obstruction, comparisons were made between a variety of tests. Twenty cigarette smokers were studied both before and immediately after smoking a cigarette. The maximum midexpiratory flow ( $FEV_{25-75}$ ) and the  $FEV_1/FVC$  per cent were abnormal in the largest number of cases. Closing volume was abnormal in only one case. Significant worsening in function after smoking a cigarette occurred in airway resistance and specific conductance. A lesser degree of impairment in airway dynamics was evident from  $FEV_{25-75}$  and first-second expired volume. The closing volume showed no change.

If the early detection of lung disease associated with airways obstruction is to be a feasible undertaking in large groups of asymptomatic subjects, it is important to determine which test or tests are the most sensitive for this purpose. For screening or survey purposes the test must also be non-invasive and fairly rapidly and easily performed. One test which has received enthusiastic endorsement for this purpose has been the closing volume (CV). It fits the criteria mentioned above and is considered superior to standard spirometric techniques by a variety of workers (McCarthy *et al.*, 1972; Buist *et al.*, 1973; Buist and Ross, 1973a, b; Buist, 1973; Devins and Gunn, 1974). However, this view has not been universally held (Gelb and Zamel, 1973; McFadden *et al.*, 1974; Cochrane *et al.*, 1974). In an effort to determine which of the several tests suitable for screening is most sensitive for the detection of airway obstruction, 20 cigarette smokers were subjected to a battery of tests before and after smoking a cigarette.

### Material and methods

All 20 subjects were paid volunteers recruited from personnel within the hospital or from their friends outside the hospital. All but two of the subjects

were currently smoking cigarettes, one was an ex-smoker, and one woman had switched to a pipe. One was five months' pregnant. The number of cigarettes smoked and the duration of smoking among the smokers varied widely—from 5 to 40 cigarettes per day, and from 0.75 to 102 pack years. No effort was made to select subjects on the basis of a history, or lack thereof, of pulmonary disease or respiratory symptoms.

The subjects were requested not to smoke for a minimum of one hour before arrival in the laboratory. Three series of tests were administered before and after the smoking of a cigarette. The order of the tests was determined from a table of random numbers and was the same before and after smoking the cigarette. After administration of the tests the subject was asked to smoke a cigarette which he did in his usual fashion. No instructions were given regarding the number of puffs, depth of inhalation or the like. However, all subjects inhaled. The three tests were then repeated. During the cigarette smoking or before the first series of tests a modified British Medical Research Council questionnaire was administered.

The three tests consisted of the measurement of spirometry, single breath nitrogen washout (closing volume technique), and body plethysmography. Spirometry was performed in the standing position

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with the nose occluded. The spirometer used was a Collins Survey Spirometer with a potentiometer connected to the bell. The potentiometer was connected to a Wang 600 computer via an A-D converter. A permanent graphic record was obtained from the spirometer for each expiratory effort. A minimum of three expiratory efforts properly performed were obtained, the largest two having to agree within 200 ml of each other. For each expiratory effort the computer calculated and printed the value of the forced vital capacity (FVC), the forced expiratory volume (FEV<sub>t</sub>) for 1, 2, and 3 seconds (FEV<sub>1</sub>, FEV<sub>2</sub>, FEV<sub>3</sub>) and the percent of each of the FVC (FEV<sub>t</sub>%, FEV<sub>1</sub>%, FEV<sub>2</sub>%, FEV<sub>3</sub>%), the maximum mid-expiratory flow (FEV<sub>25-75</sub>), and the maximum expiratory flow rate (FEV<sub>200-1200</sub>). In order to determine the rate of flow during the terminal portion of the expiratory effort, two additional measurements were made, the flow rate during the last 10% (to the nearest 100 ml) of the FVC (FVC10%) and the flow rate between the FEV<sub>2</sub> and FEV<sub>3</sub> (FEV<sub>3-2</sub>). Also measured was the total duration (FET) of the largest FVC. The largest FVC was taken as the subject's true FVC. FEV<sub>3-2</sub>, FEV<sub>1</sub>%, FEV<sub>t</sub>%, and FEV<sub>25-75</sub> were taken from this FVC. The largest FEV<sub>200-1200</sub> and FEV<sub>t</sub> were taken to represent the true value.

The single breath nitrogen washout for the determination of the CV and CV/VC×100 (CV/VC) and the slope of the alveolar plateau was performed with the subject seated and the nose occluded. It was performed by the resident gas technique, the subject starting with an expiration to residual volume, inhaling 100% oxygen to total lung capacity, and then exhaling at a rate of 200 to 400 ml per second to residual volume. Expired nitrogen was analysed by means of a mass spectrometer (Medspect). Volume was determined by means of a rolling seal spirometer (Cardiopulmonary Instruments) and both were plotted on an X-Y plotter (Hewlett Packard). The flow output of the spirometer was connected to a meter which indicated the rate of flow. The subject watched the meter during expiration and maintained his expiratory flow at the desired level by this means. Curves obtained with flow rates which were higher than specified or erratic were discarded. Two properly performed efforts where the vital capacities agreed within 5% of each other were obtained. CV and CV/VC were determined from the larger of the VCs. The point at which phase III ended and phase IV began was identified by drawing a line of best fit along the alveolar plateau, noting the point at which the line

departed from the plateau in an upward direction for the last time.

Plethysmography was performed by standard techniques (DuBois *et al.*, 1956a; DuBois *et al.*, 1956b) with modification (Sobol, 1969). Airway resistance (R<sub>aw</sub>) and functional residual capacity (FRC) were measured and specific conductance (SG<sub>aw</sub>) calculated. The volume used for the SG<sub>aw</sub> was the volume at which R<sub>aw</sub> was measured (V<sub>tg</sub>) and not the FRC. The series of tests took about 20 minutes. The post-cigarette series was more rapid because the subject was familiar with the procedures. The total time spent in the laboratory usually did not exceed an hour.

The limits of normal for the tests used were previously determined on normal subjects in this laboratory. The values for spirometric functions (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>%, FEV<sub>25-75</sub>) have been published (Sobol *et al.*, 1973). The limits of normal for plethysmographic functions in this laboratory are: R<sub>aw</sub> ≤ 2.0 kPa l<sup>-1</sup> s<sup>-1</sup> and for SG<sub>aw</sub> ≥ 0.155 s<sup>-1</sup> kPa<sup>-1</sup>. No values for the limits of normal for the other functions tested are available in this laboratory. The limits for CV/VC were taken from Buist *et al.* (1973). The Student *t* test was used to determine the significance of differences before and after cigarette smoking.

## Results

There were 13 women and 7 men. They averaged 30 years of age with a range of 19 to 60. Fourteen of the subjects were below the age of 30 and half were 25 or less. Although subjects were not chosen with respect to clinical lung disease, there was a high incidence of respiratory symptoms among them. Six subjects gave a history of shortness of breath while hurrying on the level or walking up a slight hill, and one subject stated that she had shortness of breath while walking with others on the level. Two subjects had a chronic cough and one had sputum production. Five gave a history of wheezing and one said she had asthma. Three said they had chronic bronchitis or episodic bouts of bronchitis. One subject said that she had infrequent episodes of allergic bronchospasm and she was having an attack during this study. In all, only one half of the subjects were entirely free of respiratory complaints.

Before smoking a cigarette the FEV<sub>25-75</sub> was abnormal in six subjects, the FEV<sub>1</sub>% in five, SG<sub>aw</sub> in three, and R<sub>aw</sub> in three. FEV<sub>1</sub> was abnormal in only one case and FVC in none.

The Table lists those functions in which the change after smoking one cigarette was significant

Table Pulmonary function before and after smoking in 20 subjects

Case	FEV <sub>1</sub> *		FEV <sub>25-75</sub> *		FEV <sub>10</sub> %		R <sub>aw</sub> *		SG <sub>aw</sub> *		FRC	
	1	2	1	2	1	2	1	2	1	2	1	2
1	2.98	3.00	3.31	3.72	65	56	1.08	1.55	0.310	0.222	2.5	2.6
2	3.38	3.38	4.41	4.48	188	169	0.93	1.27	0.345	0.205	2.8	3.7
3	2.86	2.95	2.55	2.81	163	169	2.44	3.18	0.155	0.115	2.2	2.5
4	2.66	2.64	3.81	2.95	96	63	0.76	1.30	0.406	0.221	2.8	3.2
5	3.64	3.49	4.72	3.90	43	44	2.25	2.62	0.190	0.158	2.0	2.2
6	3.68	3.66	3.87	3.64	73	38	1.34	1.72	0.218	0.171	3.1	3.2
7	3.97	3.85	3.85	3.41	+	+	0.94	0.87	0.294	0.278	3.1	3.5
8	2.26	2.20	1.21	1.31	50	38	1.11	1.40	0.212	0.173	3.5	3.5
9	2.01	1.94	1.14	1.02	50	44	1.90	2.51	0.140	0.113	3.1	3.3
10	3.47	3.30	3.15	2.56	81	75	0.62	0.69	0.444	0.417	3.3	3.6
11	3.23	3.13	3.50	3.13	87	75	0.83	0.98	0.380	0.297	2.7	2.9
12	3.67	3.63	5.48	5.16	175	144	0.67	0.70	0.413	0.380	3.1	3.2
13	2.99	2.92	2.49	2.36	63	55	1.43	1.79	0.153	0.131	3.8	3.8
14	4.84	4.69	6.58	6.10	69	81	0.74	1.01	0.322	0.246	3.5	3.5
15	4.14	4.08	3.79	3.64	75	81	1.97	2.19	0.123	0.112	3.5	3.6
16	3.13	3.17	2.78	3.04	56	50	0.81	0.69	0.410	0.503	2.5	2.6
17	2.02	2.15	0.97	1.04	48	56	2.58	2.26	0.099	0.108	3.3	3.3
18	3.48	3.36	2.71	2.78	81	50	0.74	0.84	0.374	0.302	3.2	3.2
19	2.82	2.57	3.25	2.70	50	50	1.01	0.95	0.369	0.309	2.5	2.5
20	3.89	3.90	5.23	5.11	88	100	1.13	1.53	0.267	0.221	2.5	2.6
Mean	3.25	3.20	3.44	3.24	84	76	1.26	1.49	0.284	0.237	2.96	3.13
Percentage change	-2		-4		-9		+20		-16		+6	
P	< 0.02		< 0.025		< 0.025		< 0.005		< 0.005		< 0.005	

FEV<sub>1</sub>: forced expiratory volume in one second, litres.

FEV<sub>25-75</sub>: maximum mid-expiratory flow, litres/second.

FEV<sub>10</sub> %: flow in the last 10% of the FVC, ml/s.

R<sub>aw</sub>: airway resistance, kPa l<sup>-1</sup> s<sup>-1</sup>.

SG<sub>aw</sub>: specific conductance, s<sup>-1</sup> kPa<sup>-1</sup>.

FRC: functional residual capacity, litres.

1, 2: before and after smoking a cigarette.

Bold type: beyond the limits of normal.

\*Normal values available in this laboratory. + Record lost; calculation could not be made.

Percentages are the average of the individual changes, not the percent differences of the averages. They are rounded off to the nearest whole number.

at  $P \leq 0.05$ . Plethysmographic functions were most sensitive to the changes produced by cigarette smoke. R<sub>aw</sub> rose 20% on average, and two additional patients became abnormal. SG<sub>aw</sub> also changed significantly; this was due almost exclusively to the change in R<sub>aw</sub> since thoracic gas volume did not change significantly. However, FRC rose significantly.

The measures of expiratory flow showed a significant worsening in the FEV<sub>1</sub>, FEV<sub>25-75</sub>, and FEV<sub>10</sub> % while FEV<sub>2</sub>, FEV<sub>3</sub>, and their percents of the FVC did not change nor did FEV<sub>3-2</sub>. FEV<sub>200-1200</sub> did not quite reach a level of statistical significance,  $P=0.07$ . The alveolar plateau, as determined during the CV manoeuvre, ie, the slope of the best fit line of phase III rather than the delta 750-1250 ml, showed no significant change after smoking. Assuming the delta N<sub>2</sub> % of 1.2%/500 ml as the upper limit of normal (Sobol *et al.*, 1968) to be applicable to the slope of phase III, then three subjects had abnormal N<sub>2</sub> slopes before smoking a cigarette; after smoking the cigarette one subject each got better, got worse, and showed no change. No additional sub-

jects became abnormal after smoking a cigarette.

The CV/VC was abnormal in only one subject (No. 17) before smoking the cigarette, and this subject was in the midst of an attack of allergic bronchospasm. Comparison before and after smoking the cigarette showed an average change in CV of 2 ml and CV/VC of 0.002. In both instances  $P > 0.9$ .

## Discussion

This study again points out the sensitivity of the FEV<sub>25-75</sub> and the FEV<sub>1</sub> % (at least using the criteria for normal previously proposed—Sobol *et al.*, 1973) and the insensitivity of the FEV<sub>1</sub> for the detection of airway obstruction. As one might expect, the sensitivity of these simple measures of flow rate exceeded that of the body plethysmograph. However, what is most striking is the poor sensitivity of the CV and CV/VC. Only one subject was abnormal and no additional subjects became abnormal after smoking a cigarette. As previously suggested, these differences might lie in the sensitivity of the tests themselves or might

be due to the level at which abnormality is set (Sobol, 1976). The latter problem is eliminated when a group of subjects are compared before and after a bronchoconstrictor, in this case cigarette smoke. The sensitivity of the test is then determined by the magnitude of the percent change as well as the statistical significance of the change. When such a comparison is made,  $R_{aw}$  and  $SG_{aw}$  are the most sensitive to increased bronchial obstruction, measures of flow rate also being significant at the 5% level.

$FEV_1\%$ , which is a useful test in the detection of airway obstruction, did not demonstrate significant changes after cigarette smoking. The reason for this is that the percent decline in FVC and  $FEV_1$  was quite similar,  $r=0.77$ , so that there was no significant change in their ratio  $FEV_1/FVC$ . There was absolutely no change in CV and CV/VC. It is likely that closing capacity, although not measured, also did not change. The failure of these tests to reflect the bronchoconstriction evident by other measurements of airway dynamics, particularly  $R_{aw}$ , might suggest that the site of the effects of cigarette smoke is limited to the large airways. However, such a conclusion poses two problems.

It has certainly been widely accepted that early airway obstruction in the small airways is not detectable by the measurement of  $R_{aw}$ . This is due to the fact that only a small portion of the total  $R_{aw}$  is contributed by the small airways and only significant obstruction in these airways would be manifest as an abnormal  $R_{aw}$ . However, there has as yet been no work demonstrating that a change in  $R_{aw}$  in the small airways is not demonstrable statistically. Thus a small change in  $R_{aw}$  as demonstrated in these subjects does not identify the location of the bronchoconstriction and could well represent bronchoconstriction in the small airways.

The second problem in locating the site of airway obstruction is the failure of the CV to change. This failure could be ascribed to the fact that cigarette smoke affects the large airways only and CV is sensitive only to small airway obstruction. However,  $FEV_{25-75}$ , which has traditionally been thought to reflect small airway disease, changed significantly. Furthermore,  $FEV_{10}\%$ , used here to measure terminal air flow, also changed significantly. Since terminal airflow is supposed to reflect the status of the small airways there was an indication of small airways constriction. The failure of the CV to detect changes in airway dynamics has been noted before (DaSilva and Hamosh, 1973). However, to date there has been no satisfactory

explanation why this should be so.

In view of the fact that the CV requires more expensive equipment and more precise ventilatory manoeuvres on the part of the patient than the forced expiratory volume, there seems little advantage in its use for screening purposes. The work presented here suggests that, despite all its known drawbacks, spirometry still provides a better, more rapid, and simpler screening technique than the closing volume measurements.

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## References

- Buist, A. S. (1973). Early detection of airways obstruction by the closing volume technique. *Chest*, **64**, 495-499.
- Buist, A. S. and Ross, B. B. (1973a). Closing volume as a simple, sensitive test for the detection of peripheral airway disease. *Chest*, **63**, 295-305.
- Buist, A. S. and Ross, B. B. (1973b). Predicted values for closing volumes using a modified single breath nitrogen test. *American Review of Respiratory Disease*, **107**, 744-752.
- Buist, A. S., Van Fleet, D. L., and Ross, B. B. (1973). A comparison of conventional spirometric tests and the test of closing volume in an emphysema screening center. *American Review of Respiratory Disease*, **107**, 735-743.
- Cochrane, G. M., Prieto, F., Hickey, B., Benatar, S. R., and Clark, T. J. H. (1974). Early diagnosis of airways obstruction. *Thorax*, **29**, 389-393.
- DaSilva, A. M. T. and Hamosh, P. (1973). Effect of smoking a single cigarette on the "small airways". *Journal of Applied Physiology*, **34**, 361-365.
- Devins, G. S., and Gunn, W. S. (1974). Application of a new technique (closing volume) for the early detection of obstructive lung disease in the elderly. *Journal of the American Geriatric Society*, **22**, 72-74.
- DuBois, A. B., Botelho, S. Y., Bedell, G. N., Marshall, R., and Comroe, J. H., Jr. (1956a). A rapid plethysmographic method for measuring thoracic gas volume: a comparison with a nitrogen washout method for measuring functional residual capacity in normal subjects. *Journal of Clinical Investigation*, **35**, 322-326.
- DuBois, A. B., Botelho, S. Y., and Comroe, J. H., Jr. (1956b). A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. *Journal of Clinical Investigation*, **35**, 327-335.
- Gelb, A. F., and Zamel, N. (1973). Simplified diagnosis of small-airway obstruction. *New England Journal of Medicine*, **288**, 395-398.
- McCarthy, D. S., Spencer, R., Green, R., and Milic-Emili, J. (1972). Measurement of "closing volume"

- as a simple and sensitive test for early detection of small airway disease. *American Journal of Medicine*, **52**, 747–753.
- McFadden, E. R., Jr., Kiker, R., Holmes, B., and deGroot, W. J. (1974). Small airway disease. *American Journal of Medicine*, **57**, 171–182.
- Sobol, B. J. (1969). Methods for simplifying constant-volume body plethysmograph. *Journal of Applied Physiology*, **27**, 295.
- Sobol, B. J. (1976). The early detection of airway obstruction: another perspective. *American Journal of Medicine*, **60**, 619–624.
- Sobol, B. J., Emirgil, C., Garcia, F., and Goyal, P. (1968). Tests of ventilatory function not requiring maximum subject effort. I. The single breath nitrogen washout. *American Review of Respiratory Disease*, **97**, 859–867.
- Sobol, B. J., Park, S. S., and Emirgil, C. (1973). Relative value of various spirometric tests in the early detection of chronic obstructive pulmonary disease. *American Review of Respiratory Disease*, **107**, 753–762.

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