

# Evaluation of the Forced Oscillation Technique for the Determination of Resistance to Breathing

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**ABSTRACT** Total respiratory resistance ( $R_T$ ) was measured by the application of a sine wave of airflow to the mouth at the resonant frequency of the respiratory system. The mean respiratory resistance of 42 normal subjects, measured at a mean functional residual capacity of 3.3 liters, was  $2.3$ ,  $SD \pm 0.5$ , cm  $H_2O$ /liter per sec, and the resonant frequency was between 5 and 8 cycle/sec. The airway resistance measured in these same subjects with the body plethysmograph at a mean panting thoracic gas volume of 3.5 liters was  $1.3$ ,  $SD \pm 0.3$ , cm  $H_2O$ /liter per sec. Total respiratory resistance was found to vary inversely with lung volume ( $V$ ) measured plethysmographically; prediction formulae for normal subjects based on this relationship are:  $R_T$  (mean)  $= 7.1/V$ ,  $R_T$  (range)  $= 4.0/V$  to  $11.6/V$  where  $V$  is in liters and  $R_T$  is in cm  $H_2O$ /liter per sec. When these criteria were applied to subjects with thoracic disease the following results were obtained: 17 subjects with obstructive lung disease all had elevated total respiratory resistance; 9 subjects with diffuse lung disease without airway obstruction all had normal respiratory resistance; all but 1 of 5 obese subjects and all but 2 of a heterogeneous group of 9 subjects without airway obstruction had normal respiratory resistance. Failure to take lung volume into account resulted in a considerable decrease in the ability to discriminate between obstructive and nonobstructive

lung disease on the basis of the forced oscillation test. The resonant frequency of the respiratory system of patients with obesity or nonobstructive lung disease was similar to that obtained in the normal group; accurate evaluation of resonant frequency in subjects with obstructive lung disease was frequently not possible. The combined resistances of lung, thoracic wall and abdominal tissues were found to account for less than 43% of the total respiratory resistance in normal subjects and were only slightly increased by the presence of obesity, restrictive diseases of the thoracic wall, and hyperinflation of the thorax. The forced oscillation method is potentially of value in the study of resistance to breathing of patients who cannot undergo body plethysmography, such as acutely ill, anesthetized, or unconscious subjects. Accurate evaluation of  $R_T$  requires an independent measure of lung volume as well as careful attention during measurements to the airflow rate, phase of respiration, and the adequacy of cheek compression and laryngeal relaxation.

## INTRODUCTION

Spirometry, the method most widely used to evaluate the increased resistance to breathing that occurs in obstructive lung disease, is dependent upon subject effort and its results may be affected by factors other than changes in airway resistance. The state of the airways may be assessed more objectively by the direct measurement of airway resistance with the body plethysmograph (1) or the measurement of pulmonary resistance with an

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*Received for publication 12 February 1968 and in revised form 8 May 1968.*

esophageal balloon (2). However, technical difficulties frequently preclude the routine clinical use of these more objective methods. The technique of forced oscillations originally described by DuBois, Brody, Lewis, and Burgess (3) estimates total respiratory flow resistance and has proven useful in the study of resistance to breathing of animals and normal human subjects (3-6). It has recently been suggested that this method may be applicable as a routine diagnostic tool or as a screening test to detect subjects with emphysema (7). However, there has been no critical evaluation of the use of this technique in subjects with known airway obstruction or other types of lung disease. In order to provide this critical assessment, we have used the method of forced oscillations to evaluate total respiratory resistance in patients with a variety of pulmonary or thoracic wall abnormalities and have compared the results with values obtained in the same subjects with the body plethysmograph. An additional objective of this study was to provide an evaluation of the tissue resistance (lungs and chest wall) in subjects with various thoracic diseases.

## METHODS

**Subjects.** The 42 control subjects consisted of 40 healthy laboratory personnel and two subjects who were studied while hospitalized for arteriosclerotic peripheral vascular disease. The subjects were not trained before the day of the experiment but several had had previous experience with the tests. None of this group had a history of pulmonary abnormality although 13 regularly smoked cigarettes; the age range was 18-79 yr with five subjects over 60-yr old; 25 of the group were male; all were thought to be of normal weight. An additional subject (A1) was rejected as normal and placed in the patient group because of elevated airway resistance. The remainder of the 43 patients were selected on the basis of the clinical diagnosis and the results of routine studies performed in the clinical pulmonary function laboratory at the Hospital of the University of Pennsylvania or Philadelphia General Hospital.

**Theoretical aspects.** When a sine wave of airflow ( $\dot{V}$ ) is applied to the tracheobronchial air column, the resultant transthoracic pressure ( $P$ ) changes are related to the total impedance ( $Z$ ) of the respiratory system:

$$P = Z \dot{V}. \quad (1)$$

Impedance is the vector sum of the effective resistance ( $R$ ) and the effective reactance ( $X$ ); the latter in turn is the sum of a component ( $X_M$ ) related to respiratory inertance and a component ( $X_C$ ) related to respiratory compliance. In a simple system, the magnitude of  $X_M$  is

directly proportional to frequency ( $f$ ) while the magnitude of  $X_C$  is inversely proportional to frequency:

$$\begin{aligned} X_M &= 2\pi f M \text{ and} \\ X_C &= -1/(2\pi f C) \end{aligned} \quad (2)$$

where  $M$  is inertance and  $C$  is compliance. Therefore, as the sine wave frequency is increased,  $X_M$  increases while  $X_C$  becomes closer to zero.  $X_C$  and  $X_M$  are  $180^\circ$  out of phase because the pressure drop due to compliance is proportional to volume (the integral of flow) and the pressure drop due to inertance is proportional to acceleration (the derivative of flow). Consequently, there is a frequency at which  $X_C$  and  $X_M$  will be of equal magnitude and opposite sign. At this frequency, called the resonant frequency ( $f_R$ ), the pressure change during the induced cycle will depend only upon the flow resistance and the rate of flow. This frequency is recognized by the zero phase angle between pressure and flow.

In contrast to the simple system just described, the lungs are a complex arrangement of many parallel branches each containing resistance, inertance, and compliance; further complexity is introduced by the chest compliance and compressibility of gas in the airways and alveoli. In the case of normal lungs, the parallel lung pathways probably have similar mechanical properties and similar phase relationships between pressure and flow. In addition the impedance of the cheeks over the range of frequencies considered is high compared with the impedance of the remainder of the system. Therefore, the impedance of the normal lung at the resonant frequency should approximate the true resistance (3). With diseased lungs, on the other hand, the properties of the parallel branches may differ and the above simplifications are not valid. In this case, the effective resistance, when the output pressure and flow are in phase, is composed of the "true resistance" plus an "in phase" portion of the reactance. Also in the presence of elevated lung resistance (e.g., obstructive lung disease) the shunt capacitance of the upper airway may become increasingly important as a determinant of thoracic impedance. Therefore, in subjects with lung disease, the effective total respiratory resistance is theoretically a complex function of resistance and reactance.

**Technique of total respiratory resistance measurement.** Oscillating airflows were produced at the mouth with a variable frequency valveless pump<sup>1</sup> that delivered a sine

<sup>1</sup> The pump used in this study was made with a flexible metallic bellows in the machine shop of the Moore School of Electrical Engineering of the University of Pennsylvania. A pump with similar frequency and volume characteristics might be obtained on special order from Harvard Apparatus Co., Inc., Dover, Mass., but we have not tried one of these. Alternatively, a loudspeaker driven by a special low frequency sine wave generator and low frequency power amplifier may be used (5). However, the use of a loudspeaker which has low mechanical impedance may result in variability of the volume of air delivered in the presence of a variable airway resistance.

wave of fixed stroke volume (approximately 30–40 ml). A portion of the pump stroke was vented to the atmosphere through a side tube of variable resistance; the latter also served as an opening for spontaneous respiration by the subject. By varying the size of the vent opening, it was possible to adjust the amount of air going to and from the subject and the amplitude of the flow rate of the induced oscillations. The oscillations, then, were superimposed upon the normal respiratory pattern of the subject. Airflow, measured with a Lilly pneumotachygraph interposed between the pump and the mouth of the subject, and driving pressure, determined at the mouth with a capacitance manometer, were displayed on the X and Y axes of an oscilloscope; pressure-flow changes associated with respiration and those associated with the forced oscillations could be easily differentiated because of the approximate 30-fold difference in frequency. Measurements were made at functional residual capacity which was recognized as the phase of the respiratory cycle when the superimposed pressure-flow waves oscillated symmetrically about the zero point. The subject was instructed to relax the muscles of the chest wall and upper airways at the end of expiration and to prolong the pause between breaths. Closure of the glottis could be recognized by an abrupt and large increase in the slope of the oscillations approaching an infinite resistance. The size of the vent opening was adjusted to give a flow rate that oscillated between plus 0.5 and minus 0.5 liter/sec measured at the mouth (peak to peak flow 1 liter/sec). The pump frequency was adjusted until the loop formed on the oscilloscope screen during each oscillation was either narrowed into a line or made minimal in size. The slope of this line was read from the oscilloscope face with the direct reading attachment described by Comroe, Botelho, and DuBois (8) and multiplied by the ratio of pressure to flow calibrations (generally 4 cm H<sub>2</sub>O pressure per inch deflection on the vertical axis and 1 liter/sec flow per inch deflection on the horizontal axis of the oscilloscope). The resistance of the flowmeter was subtracted to yield total respiratory resistance. The apparatus was calibrated daily. The flowmeter was calibrated with a commercial rotameter which had been previously calibrated by airflow into a recording Tissot spirometer. The mouth pressure gauge was calibrated with a water manometer.

**Experimental procedures.** Cigarette smokers were requested not to smoke for at least 1/2 hr before the tests. All measurements were performed with the subjects seated, wearing a nose clip, and breathing through a rubber mouthpiece. The functional residual capacity (FRC) and the airway resistance ( $R_A$ ) and simultaneous thoracic gas volume (TGV)<sup>2</sup> of each subject were determined using a body plethysmograph (1). Shortly thereafter, total respiratory resistance ( $R_T$ ) was measured

<sup>2</sup> FRC represents the thoracic gas volume at the end-expiratory resting level, TGV represents the thoracic gas volume during the measurement of airway resistance performed panting, and V represents the thoracic gas volume under the conditions specified in the text.

by forced oscillations while the subject pressed his palms firmly against his cheeks to prevent facial motion. All  $R_T$  results represent the mean of at least eight individual measurements. Vital capacity (VC) and expiratory flow rates were measured with a 13.5 liter Collins spirometer. The spirometry was performed in the clinical pulmonary function laboratory as long as 3 wk before or after the other tests; therefore, in most cases the results of spirometry and resistance measurements are not strictly comparable. Static lung volumes were converted to body temperature, saturated with water vapor (BTPS).

We used the values of Needham, Rogan, and McDonald for predicted lung volumes of normal subjects (9) and Goldman and Becklake for predicted lung volumes of patients (10). The upper limit of normal airway resistance was taken from the data of Briscoe and DuBois to be 7.7 cm H<sub>2</sub>O/liter per sec per liter of lung volume (11). Statistical significance of results was assessed by the *t* test and the level of significance was taken as  $P < 0.05$  (12).

**Studies of the effect of lung volume.** Because of the known effect of lung volume upon airway resistance (11), total respiratory resistance was measured in nine subjects at various stages of lung inflation. For these determinations, mouth pressure, airflow, and integrated airflow (which equals volume) were displayed simultaneously as a function of time on an Electronics for Medicine eight channel oscilloscope and recorded with a "rapid writing" photographic attachment. The lung volume was determined by adding the volume change obtained from the integrated airflow signal to the FRC measured in the body plethysmograph. The subject varied the inspiratory tidal volume and the depth of expiration below FRC. The total thoracic resistance was calculated at FRC and at the height or depth of the various sized breaths and related to the calculated lung volume.

## RESULTS

**Normal subjects.** The mean and range of the results of tests made in normal subjects are presented in Table I. Compared with predicted values, vital capacity was 79–124% (mean 101%) and FRC varied from 68 to 140% (mean 102%):

The mean airway resistance ( $R_A$ ) was 1.3 cm H<sub>2</sub>O/liter per sec and was within the predicted limits of normal for each subject. The mean total respiratory resistance ( $R_T$ ) was 2.3, SD 0.5, cm H<sub>2</sub>O/liter per sec and the range was 1.3–3.3 cm H<sub>2</sub>O/liter per sec. The variation of each  $R_T$  result (representing the mean of eight or more individual determinations) was calculated for 10 randomly selected subjects; the standard deviation ranged from 1.7 to 5.6% (mean 3.5%) of the reported value.

Repeat measurements of  $R_A$  and  $R_T$  were made in eight subjects 2–4 wk after the original tests.

TABLE I  
Summary of Data Obtained in 42 Normal Subjects\*

	VC†		FRC		R <sub>A</sub> ‡	TGV	R <sub>T</sub>	f <sub>R</sub>
	liters	%¶	liters	%¶	cm H <sub>2</sub> O/liter per sec	liters	cm H <sub>2</sub> O/liter per sec	cycles/sec
Mean	4.3	101	3.3	102	1.3	3.5	2.3	6.6
SD					±0.3		±0.5	±0.7
Range	2.0-6.4	79-124	2.1-4.4	68-140	0.8-2.4	2.3-5.2	1.3-3.3	5.2-7.9

\* VC, vital capacity; FRC, functional residual capacity; R<sub>A</sub>, airway resistance; TGV, thoracic gas volume during panting; R<sub>T</sub>, total respiratory resistance; f<sub>R</sub>, resonant frequency of the respiratory system.

† 38 subjects only.

‡ Predicted R<sub>A</sub> can be computed from the formulae of Briscoe and BuBois (11): mean predicted R<sub>A</sub> = 4.2/TGV; range R<sub>A</sub> = 2.9/TGV to 7.7/TGV. All subjects listed in this table were within the predicted normal range.

|| 35 subjects only.

¶ Based on predicted normal values of Needham and coworkers (9).

The result of the second evaluation of both R<sub>A</sub> and R<sub>T</sub> in each of the eight subjects was within ±20% of the first test; the means of the first and second group of tests were the same (1.4 cm H<sub>2</sub>O/liter per sec for R<sub>A</sub> and 2.4 cm H<sub>2</sub>O/liter per sec for R<sub>T</sub>); the standard deviation of the mean difference using paired data for the two tests was ±0.18 cm H<sub>2</sub>O/liter per sec for both R<sub>A</sub> and R<sub>T</sub>.

The resonant frequency was between 5 and 8 cycle/sec in the 35 normal subjects in whom this parameter was recorded. In most subjects, precise tuning was not necessary because the pressure

and flow signals during the forced oscillations appeared to be in phase anywhere within the above range of frequencies.

The relationship of lung volume to both airway and total thoracic resistance was studied in five normal subjects (Fig. 1). The results are expressed as the reciprocal of resistance, i.e., conductance (G) because of the previously demonstrated linear relationship between airway conductance (G<sub>A</sub>) and lung volume (11). Similarly to G<sub>A</sub>, total respiratory conductance (G<sub>T</sub>) in each of the present subjects varied directly with lung volume.

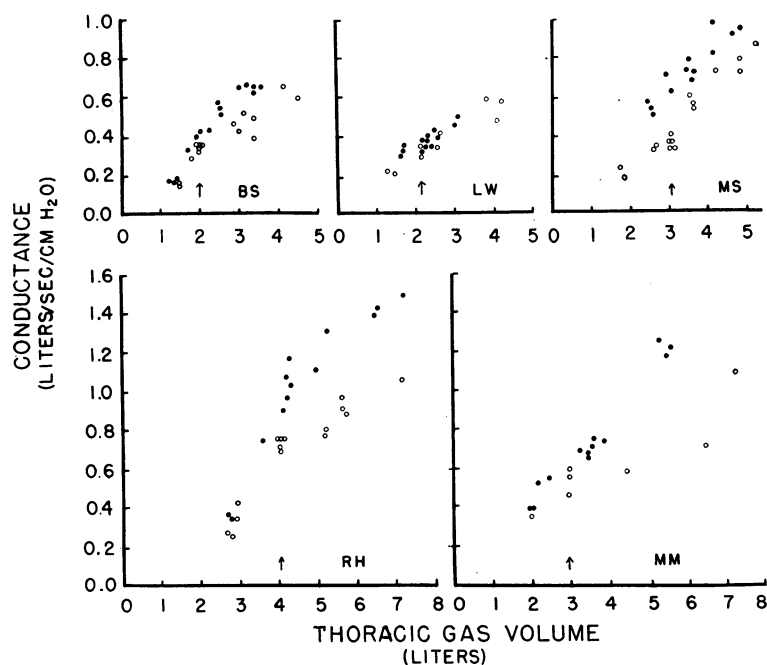


FIGURE 1 Conductance-volume diagrams for five normal subjects. ● = airway conductance and thoracic gas volume measured in the body plethysmograph; ○ = total respiratory conductance measured by forced oscillations and volume obtained by addition of integrated flow to the functional residual capacity. The functional residual capacity is indicated by an arrow.

We did not observe a significant correlation between  $R_T$  and: VC, age, height, or body weight. The correlation between  $R_T$  measured at FRC and  $R_A$  measured while panting at TGV among different normal subjects was statistically significant ( $r = 0.44$ ). The correlation between  $R_T$  and FRC was not significant over the limited FRC range of the normal subjects, but the correlation with lung volume became highly significant ( $r = -0.61$ ;  $P < 0.001$ ) when the  $R_T$  values obtained in the normal subjects at volumes above and below FRC were included. Although the linear correlation is significant, the relationship between  $R_T$  and lung volume is more precisely hyperbolic as evidenced by the high correlation ( $r = 0.84$ ) between volume and the reciprocal of  $R_T$  (Fig. 2). As mentioned above, this is similar to the relationship found previously between airway resistance and lung volume (11). The mean  $R_T$  was 0.4 cm  $H_2O$ /liter per sec greater in the female group than in the male group; this was the same as the  $R_A$  difference between these groups and could be explained by the smaller lung volume present in the females when the measurements were made. Neither the  $R_A$  nor  $R_T$  of the 13 normal cigarette smokers was significantly different from the  $R_A$  and  $R_T$  of the 29 normal nonsmokers.

In Fig. 2, the total thoracic conductance ( $G_T$ ) of each normal subject is plotted against the volume ( $V$ ) at which  $R_T$  was measured. The mean regression line for these data calculated by the method of least squares is:

$$G_T (\text{mean}) = 0.14 V + 0.01. \quad (3)$$

The small positive intercept, 0.01, may be neglected as insignificant for the sake of simplicity. Then:

$$G_T (\text{mean}) = 0.14 V \quad (4)$$

$$R_T (\text{mean}) = 7.1/V. \quad (5)$$

The lines that include 95% of the subjects (Fig. 2) have the equations:

$$G_T = 0.086 V \text{ and } G_T = 0.25 V \quad (6)$$

$$R_T = 4.0/V \text{ and } R_T = 11.6/V. \quad (7)$$

In equations 3-7,  $V$  is in liters BTPS,  $R_T$  is in cm  $H_2O$ /liter per sec and  $G_T$  is in liters/sec per cm  $H_2O$ .

**Subjects with airway obstruction.** 17 subjects had airway obstruction on the basis of elevated

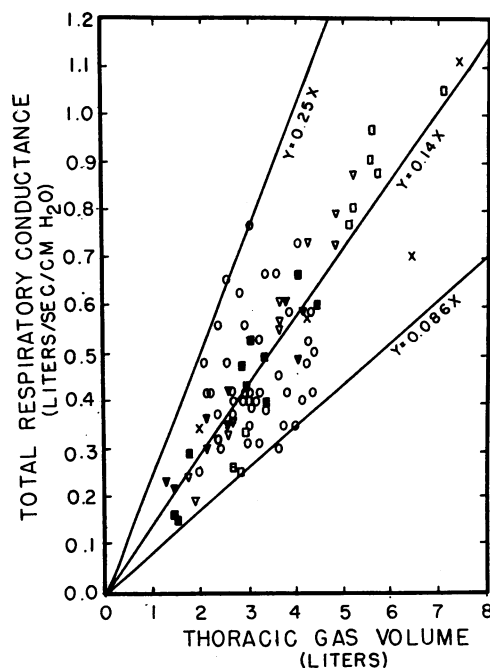


FIGURE 2 Total respiratory conductance ( $G_T$ ) vs. thoracic gas volume ( $V$ ) for 42 normal subjects. The open circles represent the mean  $G_T$  at functional residual capacity (body plethysmographic method) of each of the 42 subjects. The other points represent  $G_T$  values obtained during inspiratory or expiratory maneuvers in five subjects:  $\times$  = MM,  $\square$  = RH,  $\nabla$  = MS,  $\blacksquare$  = BS,  $\blacktriangledown$  = LW. The outer solid lines include 95% of the subjects and have the equations  $G_T = 0.25 V$  and  $G_T = 0.086 V$ . The middle line has the equation  $G_T = 0.14 V$ .

airway resistance as measured in the body plethysmograph (11). Most of the subjects in this group had decreased vital capacity and expiratory flow rates and elevated FRC (see Table II).  $R_T$  in this group ranged from 2.6 to 16.7 cm  $H_2O$ /liter per sec. The variation in  $R_T$  calculated from eight or more individual slopes was determined for all 17 subjects. The coefficient of variation of the  $R_T$  values ranged from 4.0 to 10.8% (mean 6.5%); this is approximately twice the variation observed in the normal subjects.

If the raw  $R_T$  values were uncorrected for lung volume, two subjects, both with a mild degree of airway obstruction, would have  $R_T$  values within the range observed in normal subjects: one of these (A2) was a fireman who had inhaled nitrogen dioxide fumes 1 month previously and the second (A3) had inactive tuberculosis and a five rib thoracoplasty. When lung volume was taken

TABLE II  
Subjects with Obstructive Lung Disease\*

Subjects	Clinical diagnosis	Age	Sex	VC		FRC		MMEFR	FEV% <sub>1</sub>	R <sub>A</sub> †	TGV	R <sub>T</sub>	f <sub>R</sub> ‡
				liters	%	liters	%	liter/min	%	cm H <sub>2</sub> O/liter per sec	liters	cm H <sub>2</sub> O/liter per sec	cycles/ sec
A1	Bronchitis	62	M	4.0	80	5.7	126	90	67	1.5	6.2	3.4	5.8
A2	Bronchitis (NO <sub>2</sub> )	49	M	3.0	67	5.4	138	45	51	1.8	5.7	2.8	5.5
A3	TB, thoracoplasty	57	M	2.8	65	5.0	139	39	48	1.9	5.6	2.6	5.9
A4	Emphysema	60	M	3.0	66	5.8	142	20	26	2.0	6.6	6.7	4.4
A5	Bronchitis	50	M	4.2	94	3.7	96	39	50	2.1	4.3	4.2	4.7
A6	Emphysema	42	F	1.7	45	4.2	135	20	44	2.2	5.0	11.3	
A7	Emphysema	68	F	1.4	47	4.7	170	13	42	2.3	5.0	8.1	4.8
A8	Carcinoma of lung	58	M	2.8	70	4.9	140	26	37	2.6	6.0	5.8	3.7
A9	Emphysema	62	M	2.3	62	5.8	165	35	43	2.9	6.3	9.9	7.0
A10	Emphysema	57	M	1.8	43	4.8	133	20	47	3.4	5.0	4.6	5.2
A11	Emphysema	60	M	2.5	52	5.2	133	59	42	3.4	5.7	4.8	5.5
A12	Emphysema	51	M	2.1	46	7.5	192	20	41	4.6	8.0	6.2	4.1
A13	Emphysema	49	F	1.3	37	5.8	200	13	41	5.3	6.2	12.8	4.2
A14	Carcinoma of lung	57	M	4.0	87	4.0	100	65	59	5.4	4.6	8.1	6.0
A15	Emphysema	40	M	1.6	29	7.8	178	25	25	6.7	8.6	16.7	5.1
A16	Emphysema	60	M	2.2	66	7.2	232	19	34	6.8	9.0	14.3	4.1
A17	Emphysema	65	M	2.6	61	7.8	195	13	23	7.3	7.7	14.8	
Mean		56		2.6	60	5.6	154	33	42	3.7	6.2	8.1	5.1

MMEFR, maximal mid-expiratory flow rate; FEV%<sub>1</sub>, per cent of vital capacity forcibly exhaled in one second; see Table I for other abbreviations.

\* Subjects listed in order of increasing airway resistance values.

† All R<sub>A</sub> values listed in this table are above the predicted upper limit of normal (11).

‡ The actual f<sub>R</sub> in most of these subjects could not be measured; the value recorded represents the frequency at which the phase angle between mouth pressure and rate of air flow was minimal (see text).

|| Based on predicted normal values of Goldman and Becklake (10).

into account (equation 7), the R<sub>T</sub> of both of these subjects was elevated. The presumptive diagnosis of the remaining 15 patients in this group was emphysema in 11, chronic bronchitis in 2, and obstructing carcinoma in 2; R<sub>T</sub> in all 15 patients was > 3.3 cm H<sub>2</sub>O/liter per sec which is above the range observed in normal subjects and is also elevated in relation to lung volume (see Fig. 3).

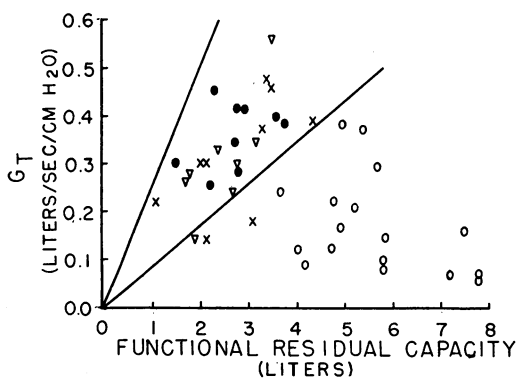


FIGURE 3 Total respiratory conductance vs. functional residual capacity for subjects with various thoracic diseases. The solid lines indicate the limits of normal obtained from Fig. 2. ○ = obstructive lung disease; ● = diffuse nonobstructive lung disease, ▽ = obesity and thoracic wall abnormalities; × = miscellaneous subjects.

The conductance-volume curves of three subjects with emphysema was measured; all showed changes compared to normal of displacement to the right and two showed a decrease in slope (subjects A11 and A12) (Fig. 4). The slope of the curves is similar for both airway and total thoracic conductance.

In many of the subjects in this group, the phase

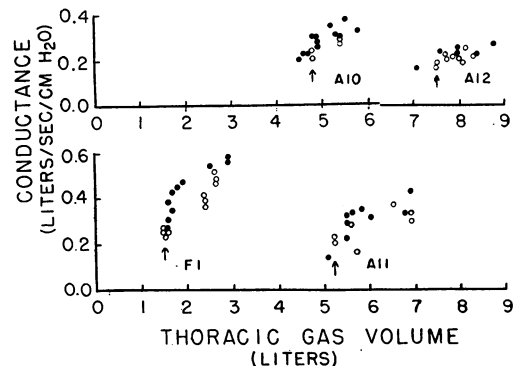


FIGURE 4 Conductance-volume diagrams for three subjects with obstructive lung disease (A10, A11, and A12) and one obese subject (F1). ● = airway conductance and ○ = total respiratory conductance, both measured as in Fig. 1. Note the increased slope of the airway conductance-volume curve in subjects F1 and A11 as functional residual capacity (shown by arrow) is approached.

TABLE III  
*Subjects with Diffuse Pulmonary Disease without Airway Obstruction*

Subject	Clinical diagnosis	Age	Sex	VC	FRC	MMEFR	FEV% <sub>1</sub>	R <sub>A</sub> *	TGV	R <sub>T</sub>	f <sub>R</sub>
		yr		liters %	liters %†	liters/ min	% H <sub>2</sub> O/liter per sec	cm H <sub>2</sub> O/liter per sec	liters H <sub>2</sub> O/liter per sec	cm H <sub>2</sub> O/liter per sec	cycles/ sec
R1	Idiopathic fibrosis	46	M	3.5 87	1.5 47	123	76	0.8	1.8	3.3	4.0
R2	Idiopathic fibrosis	60	F	1.6 60	2.3 90	103	89	1.2	2.4	2.2	8.7
R3	Idiopathic fibrosis	47	F	1.7 55	2.8 98	83	75	1.5	3.1	3.5	8.2
R4	Sarcoidosis	26	M	3.7 70	2.8 75	208	84	0.8	3.4	2.4	
R5	Sarcoidosis	36	M	3.0 59	3.6 90	175	84	0.8	4.0	2.5	7.5
R6	Sarcoidosis	39	F	3.1 88	2.2 79	76	66	2.3	2.3	3.9	4.0
R7	Alveolar proteinosis	62	M	3.4 97	2.8 85	168	81	1.3	3.7	2.9	5.5
R8	Silicosis	62	M	2.9 78	3.8 108	39	51	1.5	4.3	2.6	8.2
R9	Pulmonary carcinomatosis	65	F	3.0 93	3.0 100	85	67	1.7	3.3	2.4	5.8
	Mean	49		2.9 76	2.8 86	118	75	1.3	3.1	2.9	6.6

See Tables I and II for abbreviations.

\* All R<sub>A</sub> values listed in this Table are within the predicted limits of normal (11).

† Based on predicted normal values of Goldman and Becklake (10).

angle ( $\phi$ ) between mouth pressure and airflow was not zero at any frequency tested in the range 2–10 cycle/sec. Under this circumstance, measurements were made at the frequency at which the loop was narrowest; the slope was taken as the longest axis of the loop.<sup>3</sup> The minimum phase angle in all cases appeared to be less than 10°. The frequency used to measure R<sub>T</sub> in these subjects ranged from 3.7 to 7.0 cycle/sec; the mean, 5.1 cycle/sec, was significantly lower than the mean f<sub>R</sub> (6.6 cycle/sec) of the normal subjects.

*Diffuse pulmonary disease without airway obstruction.* Nine subjects had diffuse lung disease by chest roentgenogram and no evidence of airway obstruction on the basis of the airway resistance measurements (see Table III). The diagnosis was confirmed by tissue examination in seven subjects: idiopathic fibrosis was present in three, sarcoidosis in three, and alveolar proteinosis in one. One of the remaining two subjects had silicosis and the other had diffuse carcinomatosis. Vital capacity, FRC, and expiratory flow rates were normal or slightly reduced. The single breath diffusing capacity for carbon monoxide, measured in six subjects of this group, was 15–61% of predicted values (13).

In these subjects with diffuse pulmonary diseases, the range of R<sub>T</sub> was 2.2–3.9 (mean 2.9)

<sup>3</sup> Measurement of the mean slope rather than the slope at maximum flow was done for the sake of simplicity and ease of reproducibility; this will cause an underestimate of the impedance by about 1% in the presence of a 10° phase angle.

cm H<sub>2</sub>O/liter per sec and f<sub>R</sub> was 4.8–8.7 (mean 6.6) cycle/sec. Neither of these mean values is significantly different from those obtained in the normal subjects. Although three subjects had total respiratory resistance greater than 3.3 cm H<sub>2</sub>O/liter per sec, when lung volume was taken into account R<sub>T</sub> was normal in all subjects of this group (solid circles in Fig. 3).

*Subjects with obesity and thoracic wall abnormalities.* The body weight of the five obese subjects (Table IV) was 160–245 lb. or 145–255% of ideal weight.<sup>4</sup> Vital capacity, FRC, and expiratory flow rates were normal or slightly low. Although subject F3 had a history of asthma and subject F4 had been treated for pulmonary embolism, neither had evidence of lung disease at the time the tests were performed. R<sub>A</sub> measured at a panting lung volume slightly greater than FRC was within the predicted normal range. R<sub>T</sub> values of 3.6, 3.8, and 7.0 cm H<sub>2</sub>O/liter per sec were obtained in three of the five obese subjects; however, only the 7.0 cm H<sub>2</sub>O/liter per sec value is abnormal when the prediction formula based on lung volume is used (see Fig. 3). The conductance-volume curve of one of the obese subjects (F1) is shown in Fig. 4.

The remaining three subjects listed in Table IV had abnormalities of the thoracic skeleton. One of these (F8) had severe kyphosis with a 0.6 liter vital capacity and an R<sub>T</sub> of 4.3 cm H<sub>2</sub>O/liter per sec while subject F7 had rheumatoid spon-

<sup>4</sup> Ideal weight from tables of the Metropolitan Life Insurance Company Statistical Bureau, 1959.

TABLE IV  
Subjects with Obesity or Other Thoracic Wall Abnormalities

Subject	Height	Weight		Age	Sex	VC		FRC		MMEFR	FEV% <sub>1</sub>	R <sub>A</sub> *	TGV	R <sub>T</sub>	f <sub>R</sub>
	in.	lb.	%†	yr		liters	%‡	liters	%§	liters/min	%	cm H <sub>2</sub> O/ liter per sec	liters	cm H <sub>2</sub> O/ liter per sec	cycles/ sec
F1	60	160	145	32	F	2.9	94	1.7	76			2.0	2.1	3.8	6.1
F2	65	245	160	47	M	2.4	63	2.4	100	51	74	1.8	2.8	3.6	6.0
F3	62	232	186	18	F			1.8	71			1.8	2.2	3.0	
F4	63	265	192	26	F	3.1	86	3.2	89	155	82	1.2	3.5	2.9	5.6
F5	62	345	255	41	F	2.8	90	1.9	75	156	79	1.6	3.1	7.0	5.1
Mean	62	249	188	33		2.8	83	2.2	82	121	78	1.7	2.7	4.1	5.7
Clinical diagnosis															
F6	Rheumatoid spondylitis			49	M	3.6	86	3.5	97			0.8	4.0	1.8	5.0
F7	Rheumatoid spondylitis			49	M	2.0	49	2.8	80	90	80			3.5	6.3
F8	Severe kyphosis			77	F	0.6	28	2.7	123	33	90			4.3	7.2

See Tables I and II for abbreviations.

\* All R<sub>A</sub> values listed in this table are within the predicted limits of normal (11).

† Based on ideal weight from tables of the Metropolitan Life Insurance Co. Statistical Bureau, 1959.

§ Based on predicted normal values of Goldman and Becklake (10).

|| Estimated from radiographic determination of total lung capacity by the method of Barnhard et al., adapted by Loyd, String, and DuBois (14); the inspiratory capacity was assumed to represent two-thirds of the vital capacity.

dylitis with evidence of thoracic wall restriction (decreased vital capacity) and an R<sub>T</sub> of 3.5 cm H<sub>2</sub>O/liter per sec. Body plethysmographic studies could not be done in these two patients but airway obstruction was judged not to be present on the basis of spirometry and physical examination; the FRC was estimated by subtracting two-thirds of the vital capacity from the radiographic total lung capacity measured by the method of Barnhard et al., adapted by Loyd, String, and DuBois (14). Total respiratory resistance related to this calculated FRC was within predicted normal limits (Fig. 3). Subject F6 also had rheumatoid spon-

dylitis but had a normal vital capacity and normal R<sub>T</sub> of 1.8 cm H<sub>2</sub>O/liter per sec.

The f<sub>R</sub> of all eight subjects in this group (5.0–7.3 cycle/sec) was within the range observed in normal subjects.

*Nine miscellaneous subjects.* R<sub>T</sub> was elevated in relation to lung volume in one subject (M4) with quiescent asthma and a second patient (M9) with chronic congestive heart failure due to rheumatic involvement of aortic and mitral valves (Table V). The 4.5 cm H<sub>2</sub>O/liter per sec R<sub>T</sub> value obtained in a subject (M1) with pleural fibrosis and atelectasis of one lung due to carci-

TABLE V  
Subjects with Miscellaneous Disease

Subject	Clinical diagnosis	Age	Sex	VC		FRC		MMEFR	FEV% <sub>1</sub>	R <sub>A</sub> *	TGV	R <sub>T</sub>	f <sub>R</sub>
		yr		liters	%†	liters	%	liters/min	%	cm H <sub>2</sub> O per liter per sec	liters	cm H <sub>2</sub> O/liter per sec	cycles/ sec
M1	Carcinoma, atelectasis, pleural fibrosis	53	F	1.0	35	1.1	46	45	81	2.4	1.2	4.5	
M2	Bronchiectasis both lower lobes	29	F	3.4	81	3.4	110	32	51	1.0	3.8	2.1	8.2
M3	Small cysts right upper lobe	30	F	3.4	90	4.4	147	165	85	0.9	5.0	2.6	4.1
M4	Asthma in remission	46	F	2.3	70	3.1	111	32	52	1.7	4.0	5.5	4.6
M5	Asthma in remission	47	F			2.0	83			1.1	2.4	3.3	4.8
M6	Asthma in remission	50	M	5.3	106	3.5	82	130	71	1.0	4.2	2.2	4.4
M7	Upper respiratory infection	34	F		69	2.1	78			2.6	2.3	3.3	
M8	Polycythemia vera	73	M	2.7	69	3.3	87	71	68	1.7	3.8	2.7	
M9	Congestive heart failure	68	F	2.0	65	2.1	75	150	90	2.2	2.4	7.2	4.7

See Tables I and II for abbreviations.

\* All R<sub>A</sub> values listed in this table are within the predicted limits of normal (11).

† Based on predicted normal values of Goldman and Becklake (10).



noma was within the range predicted for the low lung volume (see Fig. 3).

## DISCUSSION

*Prediction of normal  $R_T$ .* When the prediction formulae relating total respiratory resistance and lung volume (equation 7) were applied to the abnormal subjects, high  $R_T$  values were found in all subjects with obstructive disease while a normal  $R_T$  was demonstrated in each subject with nonobstructive diffuse lung disease; slightly elevated  $R_T$  despite a normal airway resistance was found in one obese subject (F5), a subject with quiescent asthma (M4), and a subject with congestive heart failure (M9) (possible explanations for discrepancies between airway and total respiratory resistance are discussed below). If the effects of lung volume were ignored and the normal range of  $R_T$  was defined as the mean  $\pm 2$  SD of the normal subjects, i.e. 1.3–3.3 cm H<sub>2</sub>O/liter per sec), the ability to differentiate obstructive and non-obstructive lung disease on the basis of this test would be greatly impaired. Thus, 12% of the subjects with elevated airway resistance would have been falsely labeled as having a normal  $R_T$  while elevated  $R_T$  would have been found in 33% of patients with diffuse nonobstructive pulmonary disease, 62% of the subjects with obesity and thoracic wall abnormalities, and 33% of the subjects with miscellaneous diseases.

*Comparison with previous measurements of total thoracic resistance.* In the initial report which utilized the forced oscillation technique to evaluate total respiratory resistance at the resonant frequency in humans, Dubois, Brody, Lewis, and Burgess obtained a mean  $R_T$  value of 4.6 cm H<sub>2</sub>O/liter per sec in seven normal supine subjects (3). Lower values would be expected in seated subjects since several investigators have demonstrated that  $R_T$  increases approximately 15% when normal persons change from a sitting to a supine position (15, 16); this positional effect on resistance can be accounted for by the effect of position on lung volume (17). The four seated subjects studied by Ferris, Mead, and Opie had a mean  $R_T$  of 2.0 cm H<sub>2</sub>O/liter per sec if their data are calculated for a flow rate of 1 liter/sec (5). Schwaber, Khan, Tanabe, and Stein obtained a mean  $R_T$  of 2.4 cm H<sub>2</sub>O/liter per sec in 19 seated subjects (18). Sharp and associates applied the

oscillations to the body surface of the subject seated in a plethysmograph and found a mean  $R_T$  of 1.9 cm H<sub>2</sub>O/liter per sec for eight normal persons (16). The mean  $R_T$  of the 31 seated subjects included in the above reports is 2.2 cm H<sub>2</sub>O/liter per sec as compared to the 2.3 cm H<sub>2</sub>O/liter per sec value that was obtained in the 42 normal seated subjects of the present study. Brody and coworkers applied the oscillations at the mouth of the subject at a fixed frequency of 10 cycle/sec which may be expected to yield slightly higher results than the tuning method. Indeed, these latter investigators obtained a mean  $R_T$  of 2.9 cm H<sub>2</sub>O/liter per sec in eight normal seated subjects (15); subsequent evaluation of a larger group by the same method yielded the higher mean  $R_T$  of 3.5 (SD  $\pm 1.6$ ) mm Hg/liter per sec (6).

Reports of measurements of  $R_T$  by forced oscillations in subjects with thoracic disease are scant. Sharp and associates reported elevated mean  $R_T$  in a group of obese patients (16). However, the difference of mean  $R_T$  between their normal and obese subjects is small if the difference in lung volume is taken into account; if our criteria (equation 7) are applied to their subjects, only 1 of the 12 obese subjects studied by forced oscillations had elevated  $R_T$ . Elevated  $R_T$  has also been observed in a patient with alveolar proteinosis (19) and in several of a group of subjects with paralysis agitans (20). Since body plethysmography was not performed in these subjects, the anatomic basis for the increased resistance is not apparent.

*Partition of total respiratory resistance.* The total respiratory resistance can be divided into its component parts of airway and tissue resistances. In the present study,  $R_A$  measured with the body plethysmograph represents 57%, i.e., 1.3/2.3, of  $R_T$  measured by forced oscillations. However, compared with the plethysmographic measurements,  $R_T$  was measured under the different conditions of a smaller lung volume, higher flow rate, and without the panting maneuver. The expected net result of these three factors would be to increase the airway resistance component during the time that  $R_T$  was being measured. Therefore, in the present normal subjects, airway resistance would probably represent somewhat more than 57% of the total respiratory resistance. Indeed,

this is in keeping with the value of 65% found by Ferris, Mead, and Opie in four human subjects (5). Also, Brody and DuBois found in four cats that the airways accounted for a mean of 69% of the total respiratory resistance (21).

**Thoracic wall resistance.** Since the airways account for approximately two-thirds of the total respiratory resistance in normal subjects (see above), the tissue resistances must account for about one-third. Most of the latter is due to the combined resistances of the lung tissue, the thoracic wall, and the liver (22). The subjects listed in Table IV were studied in an effort to determine whether thoracic wall disease results in a significant increase of the resistance to breathing. In some of these subjects, gross obesity or severe degrees of thoracic restriction (e.g., F7 with spondylitis and F8 with kyphosis) resulted in at most only a slight elevation of  $R_T$ . The conductance-volume diagrams of the emphysematous subjects (Fig. 4) show a close correspondence between airway and total respiratory conductance which indicates that the tissue component of  $R_T$  was not elevated. It appears, therefore, that thoracic wall abnormality per se does not greatly affect the over-all resistance to breathing except through a secondary effect upon lung volume.

However some subjects, e.g., F5 with obesity or A6 with obstructive lung disease, had a large difference between  $R_T$  measured at FRC and  $R_A$  measured during panting (see Tables II and IV). Possible reasons for the relatively high  $R_T$  compared with  $R_A$  are: (a) failure of some subjects to maintain a fully patent glottis during the application of the oscillations; (b) the lower lung volume at which  $R_T$  measurements were made; (c) closure of airways at low lung volumes; and (d) overestimate of the true resistive component of impedance due to inclusion of in phase reactance in the measurements (see Methods, *Theoretical aspects*). Partial closure of the glottis was unlikely to have been of major significance since maintaining an open glottis would tend to diminish any uncomfortable sensations in the upper airway produced by the rapidly oscillating airflows. The effects of low lung volume are illustrated by the conductance-volume diagrams of Fig. 4 which suggest airway closure in an obese (F1) and an emphysematous (A11) subject as FRC is approached. The similarity of airway and total

respiratory conductance-volume curves in subjects with emphysema (Fig. 4) suggests that unequal time constants have little effect on the difference between  $G_A$  and  $G_T$ , probably because the frequencies used are so high.

**Significance of resonant frequency.** At the resonant frequency ( $f_R$ ), the inertial and capacitive reactances of the simple series circuit are of equal magnitude.<sup>5</sup> Therefore, from equation 2:

$$|2\pi f_R M_T| = |1/(2f_R C_T)| \quad (8)$$

Rearranging and simplifying:

$$f_R = |1/(2\pi\sqrt{M_T C_T})| \quad (9)$$

where  $M_T$  is the total respiratory inertance and  $C_T$  is the total respiratory compliance. Equation 9 indicates that the magnitude of the resonant frequency is inversely proportional to the square root of the magnitude of both total respiratory inertance and total respiratory compliance. Therefore, mass loading of the thorax (increased inertance) should result in a decreased  $f_R$  provided that total compliance does not decrease in proportion. Such an effect of lowered  $f_R$  was demonstrated by DuBois and associates when a lead weight was placed upon the anterior chest wall of a normal subject (3). Although the  $f_R$  values of the present obese subjects were all within normal limits, a progressive decrease of  $f_R$  with increasing body weight was observed. A similar lowering of  $f_R$  might be expected from the increased lung compliance that frequently accompanies emphysema. However, we were unable to test this hypothesis in the present subjects with obstructive lung disease because an accurate assessment of the resonant frequency could not be made.

The failure to find a resonant frequency in some subjects with obstructive lung disease deserves comment. It is possible that resonance would have been found at a frequency outside of the range (2–10 cycle/sec) that was tested but this seems unlikely since we did observe a minimum phase angle. Shephard (23), using an electrical analogue of the respiratory system, noted that a 10-fold increase of "airway resistance" resulted in a situation where resonance could not be obtained; the phase angle in this circumstance was determined largely by the shunt capacitance representing the

<sup>5</sup> This is only approximately true for complex circuits such as the lungs.

cheek compliance. We confirmed the importance of cheek compliance in subjects with obstructive lung disease since increased stiffening of the cheeks resulted in a smaller phase angle. Another possible reason for the failure to find resonance in subjects with elevated resistance is that the reactive component was not linearly related to frequency. This might occur in the lung composed of pathways with unequal mechanical properties where the change of effective compliance with frequency, such as found in patients with emphysema (24), could keep the capacitive reactance greater than the inductive reactance at all frequencies.

*Comparison of spirometry and measurements of resistance.* Comparison of the results from spirometry with the results from either the plethysmograph or the forced oscillations reveals seven instances where discrepant diagnoses might be reached. Subjects R6, M2, and M4 had normal  $R_A$  but forced spirograms suggesting airway obstruction. It was subsequently demonstrated that the disease process in these subjects had a large reversible component; since intensive treatment with bronchodilators was instituted during the 2–3 days between the abnormal spirogram and the normal resistance measurements, this presumably explains the discrepancy in these three subjects. Analysis of the reasons for the discrepancy between the results of spirometry and resistance measurements in subjects F2, M8, R8, and R9 illustrates some of the pitfalls in the interpretation of forced spirograms. These four subjects had slowing of forced expiration which suggested airway obstruction but had normal airway resistance measurements; none of these four had evidence for obstructive lung disease on the basis of roentgenography of the lungs or measurements of functional residual capacity, helium mixing efficiency, and arterial  $P_{CO_2}$ . F4 was an obese subject referred to the laboratory because of somnolence; the maximal voluntary ventilation (MVV) was reduced; normal results were obtained for physical examination of the lungs,  $DL_{CO}$ , and the ventilatory response to exogenous carbon dioxide. It was concluded that this subject failed to exert maximal effort during the spirometry and MVV measurements. Subject M8 was referred for evaluation of polycythemia; low maximal inspiratory and expiratory pressures measured at the mouth indicated the presence of muscle weakness as a factor

in the genesis of the abnormal spirogram; the polycythemia was found to be a primary hematologic abnormality and subsequently acute leukemia developed. Subject R8 had silicosis with bilateral conglomerate nodules; a normal maximal mid-inspiratory flow rate (246 liters/sec) and the fluoroscopic demonstration of air trapping in the right lung during forced expiration combined with the normal resistance measurements suggest that bronchial compression by the nodules rather than the presence of obstructive lung disease accounted for the abnormal forced expiratory spirogram. Subject R9 had diffuse alveolar cell carcinoma; the MVV (84 liters/min) was normal. Analysis of the expiratory spirogram in this patient revealed that the abnormality was confined to the latter half of the expiratory effort; this information combined with the normal resistance measurements suggests that areas of regional obstruction rather than diffuse obstructive lung disease was present. The four cases considered above demonstrate that reliance upon spirometry alone may lead to erroneous conclusions in regard to the presence of obstructive lung disease and indicate a need for the direct measurement of the resistance to breathing.

*Clinical use of the forced oscillation technique.* In assessing the applicability of the forced oscillation method for routine clinical use, a comparison with the body plethysmographic technique is helpful. Both methods have requirements of a similar order of magnitude with regards to the practical aspects of cost and the technical skills and time required for resistance measurements. Both techniques are accepted by most subjects although the plethysmograph may elicit claustrophobia in some and the rapid oscillations may cause dyspnea in patients with advanced lung disease. To achieve diagnostic specificity, both methods require a determination of the lung volume at which resistance was measured. This determination is routinely made in the case of the plethysmograph but requires an independent technique in the case of the forced oscillation method. The need to measure lung volume independently appears to be a major disadvantage of the oscillation method with respect to use in the routine clinical laboratory. A second disadvantage of the forced oscillation technique is that the result is less specific than that of the plethysmographic method since tissue re-

sistances are included in the  $R_T$  value and the panting maneuver is not used to minimize upper airway resistance. On the other hand, the forced oscillation method does not require subject cooperation and the apparatus can be made portable and brought to the bedside; therefore, this technique may be of value in the study of the acutely ill, anesthetized, or otherwise unresponsive patients. The forced oscillation method also provides information about the resonant frequency of the respiratory system but at present this information has no clinical value. In summary, plethysmography appears to be the preferable method for clinical use except in the special circumstances outlined above or in those cases when it is desired to evaluate the tissue resistances.

The proper use of the forced oscillation technique requires attention to several practical details. First, because of the nonlinear relationship between pressure and flow, it is important to specify the flow rate of both the forced oscillation and the spontaneous respiration of the subject (we measured  $R_T$  during the pause in spontaneous respiration, but  $R_T$  could be measured at various phases of the respiratory cycle). Second, the subject must be encouraged to relax the upper airway during the test; the variability of this factor may be decreased if measurements are made during inspiration (J. Mead, personal communication) but then the test conditions of inspiratory flow rate and lung volume become more difficult to reproduce. Third, it is necessary to compress the cheeks to minimize flow into this "shunt" pathway so that resonance can be achieved. Finally, a measure of lung volume is necessary; if inert gas techniques are used for this purpose, a sufficiently long wash-out period must be used to ensure complete equilibration (25-27) and without such precautions the "true" lung volume may be underestimated in some subjects with obstructive lung disease. It is obvious from the above that it is mandatory to carefully supervise the performance of the forced oscillation test if reproducible results are to be obtained.

#### ACKNOWLEDGMENTS

The authors wish to thank the many persons who volunteered as normal subjects, Drs. Robert Mayock and Robert Rogers from whose practice the majority of patients were obtained, and Mrs. Joan Mount for making the lung volume measurements from roentgenograms.

This paper was supported in part by a contract DAAA-15-67-C-1054 with the Medical Laboratories, Army Chemical Center, Edgewood, Md. Dr. Fisher carried out this investigation in part during the tenure of a Pennsylvania Thoracic Society Fellowship (1965-66), and was a recipient of a National Institutes of Health postdoctoral training grant 2T1-GM-957-05 (1966-68). Dr. DuBois is a recipient of a Research Career Award of the National Institutes of Health.

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