

# Pulmonary Mechanics by Spectral Analysis of Forced Random Noise

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**ABSTRACT** The magnitude ( $|Z_{rs}|$ ) and phase angle ( $\theta_{rs}$ ) of the total respiratory impedance ( $Z_{rs}$ ), from 3 to 45 Hz, were rapidly obtained by a modification of the forced oscillation method, in which a random noise pressure wave is imposed on the respiratory system at the mouth and compared to the induced random flow using Fourier and spectral analysis. No significant amplitude or phase errors were introduced by the instrumentation. 10 normals, 5 smokers, and 5 patients with chronic obstructive lung disease (COPD) were studied. Measurements of  $Z_{rs}$  were corrected for the parallel shunt impedance of the mouth, which was independently measured during a Valsalva maneuver, and from which the mechanical properties of the mouth were derived. There were small differences in  $Z_{rs}$  between normals and smokers but both behaved approximately like a second-order system with  $\theta_{rs} = 0^\circ$  in the range of 5–9 Hz, and  $\theta_{rs}$  in the range of  $+40^\circ$  at 20 Hz and  $+60^\circ$  at 40 Hz. In COPD,  $\theta_{rs}$  remained more negative (compared to normals and smokers) at all frequencies and crossed 0 between 15 and 29 Hz. Changes in  $Z_{rs}$ , similar to those in COPD, were also observed at low lung volumes in normals. These changes, the effects of a bronchodilator in COPD, and deviations of  $Z_{rs}$  from second-order behavior in normals, can best be explained by a two-compartment parallel model, in which time-constant discrepancies between the lung parenchyma and compliant airways keep compliant greater than inertial reactance, resulting in a more negative phase angle as frequency is increased.

## INTRODUCTION

The description of the respiratory system in terms of electrical analogs (1) by Otis et al. (2) and others (3–15),

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has facilitated solutions to many problems involving the dynamic behavior of the lungs and chest. Most authors, as a first approximation, have considered the resistive, inertial, and elastic properties of the respiratory system analogous to a simple series resistance-inductance-capacitance (RLC)<sup>1</sup> electrical network or to a resistance-mass-spring mechanical system (3, 4, 9, 10, 13).

There are numerous schemes for studying the properties of physical systems (17), although few have been applied to biological systems. DuBois et al. (3) first employed forced sinusoidal pressure oscillations at the mouth or around the thorax and measured the induced flow at the subject's mouth. By comparing the induced pressure and flow oscillations for magnitude and phase, he could determine the magnitude ( $|Z_{rs}|$ ) and phase angle ( $\theta_{rs}$ ) of the impedance<sup>2</sup> for the total respiratory system at different frequencies (3–10 Hz) and confirm that it behaved approximately like a second-order system. At low frequencies,  $|Z_{rs}|$  was high and  $\theta_{rs}$  was negative (pressure-lagged flow) due to the elasticity or compliance of the system. As the frequency of induced oscillations increased,  $|Z_{rs}|$  decreased and reached a minimum at about 6 Hz, the resonant frequency ( $f_n$ ), at which  $\theta_{rs}$  was 0 and  $|Z_{rs}|$  was entirely resistive. As frequency was further increased,  $|Z_{rs}|$  increased and  $\theta_{rs}$  became positive (pressure-led flow) due to the inertial properties of the system. Many investigators have employed DuBois' technique or a modification to study respiratory mechanics in man and animals (4, 5, 7–10, 13, 18–25). With few exceptions (7, 8, 13), most observations are over a limited frequency range (3–10 Hz) and, in general, similar to those of DuBois et al. (3).

<sup>1</sup> The abbreviations used in this manuscript to describe the analogous properties of electrical, mechanical, and physiological systems will be as in reference 16 unless otherwise specified.

<sup>2</sup> The complex quantity impedance ( $Z$ ) which has both real (resistive) and imaginary (reactive) parts can alternately be expressed in polar coordinates in terms of magnitude ( $|Z|$ ) and phase ( $\theta$ ).

There have been few observations of respiratory impedance in man at frequencies greater than 10 Hz (7, 8, 13) and little data exist for  $\theta_{rs}$  at frequencies other than resonance (3, 13). Virtually no information is available on  $|Z_{rs}|$  and  $\theta_{rs}$  at different frequencies in patients with lung disease, although respiratory resistance has been measured at multiple frequencies (10).

Our purpose was to develop a technique with which  $|Z_{rs}|$  and  $\theta_{rs}$  can be quickly and accurately obtained over an expanded frequency range with a frequency resolution impractical by conventional techniques. We have employed the technique in normal subjects and patients with obstructive pulmonary disease and interpreted the results in terms of electrical models of the lung. The hypothesis of Mead (11), that uneven time constants between the airways and parenchyma may be an important source of frequency-dependent compliance, has been evaluated and compared to other parallel two-compartment models.

The technique is a modification of the DuBois' method (3, 9, 25) except that a random noise pressure wave, containing all frequencies of interest, is imposed on the respiratory system and a random flow signal is induced. Until recently, analysis of wave forms other than sinusoidal has been a complex problem. However, with the development of various algorithms for efficient digital implementation of the fast Fourier transform (FFT) (26-28), it is now relatively easy to employ spectral analysis techniques (29-34) to determine the impedance of an unknown system. The Fourier transform (26-28) is a mathematical tool which can resolve any wave form into its individual frequency components. Thus, if a random pressure wave is imposed on the respiratory system, it can be resolved into a series of terms containing both magnitude and phase information which can be correlated with the resulting flow to obtain  $|Z|$  and  $\theta$  of the respiratory system at each frequency present in the input wave form. Similar techniques have been used by Taylor (35) to study aortic and femoral arterial impedance during random electrical pacing of the heart. Some advantages of spectral analysis techniques are speed of measurement and simultaneous determination of  $|Z_{rs}|$  and  $\theta_{rs}$  at each frequency of interest, reducing variability with frequency which may actually be due to time-dependent changes in the system.

## METHODS

*Principles of spectral analysis.* With recent widespread use of computers, and the introduction of the FFT (26-28), digital solutions to cumbersome but powerful mathematical techniques for frequency analysis are now practical. The essential aspects of these techniques as they apply to this study will now be reviewed. For a more detailed consideration the interested reader is referred to references 26-34.

Fourier analysis is a mathematical tool for determining the frequency content of a time-varying signal. The Fourier

transform ( $S_x$ ) is the weighted integral of the time-varying function  $x(t)$ :

$$S_x = \int_{-\infty}^{\infty} x(t)e^{-j2\pi ft} dt = A_x + jB_x, \quad (1)$$

where  $f$  = frequency at which the integral is evaluated,  $t$  = time in seconds, and  $j = \sqrt{-1}$ .  $A_x$  and  $B_x$  are the real and imaginary components of  $S_x$  at frequency  $f$ , and contain magnitude and phase information of this frequency component of  $x(t)$ .

For a simple system with input  $x(t)$  and output  $y(t)$ , the transfer function ( $H$ ) can be obtained as follows:

$$H = \frac{S_y}{S_x} = \frac{\text{Fourier transform of output}}{\text{Fourier transform of input}}. \quad (2)$$

If  $x(t)$  is random noise,  $H$  can be found at all frequencies in  $x(t)$ . If  $x(t)$  is random pressure and  $y(t)$  flow, then impedance is simply the reciprocal of  $H$ . Because of synchronization problems and statistical considerations related to the randomness of the input signal, the computation of  $H$  and  $Z$  by this method is not practical (32-34). Therefore, the concept of power spectra will be introduced. For the variables in the above system,  $S_x$  and  $S_y$  can be used to compute three power spectra. The input power spectrum is,

$$G_{xx} = S_x S_x^* = (A_x + jB_x)(A_x - jB_x) = A_x^2 + B_x^2, \quad (3)$$

where  $S_x^*$  is the complex conjugate of  $S_x$ . This product ( $A_x^2 + B_x^2$ ) no longer contains phase information. Similarly, the output power spectrum is,

$$G_{yy} = S_y S_y^* = A_y^2 + B_y^2. \quad (4)$$

The cross-power spectrum, defined as

$$G_{yx} = S_y S_x^* = (A_y A_x + B_y B_x) + j(B_y A_x - B_x A_y), \quad (5)$$

preserves the phase relationship between input and output signals and can be used to compute impedance, magnitude as follows:

$$|Z| = \frac{G_{xx}}{|G_{yx}|}. \quad (6)$$

The phase angle ( $\theta$ ) is contained in  $G_{yx}$  and is given by

$$\theta = -\tan^{-1} \frac{(B_y A_x - B_x A_y)}{(A_y A_x + B_y B_x)}. \quad (7)$$

The advantage of computing a transfer function or impedance in this way is the rapidity with which both phase and magnitude can be obtained over a wide range of frequencies. Further, the computation of  $Z$  does not depend on the character of  $x(t)$ , since  $Z$  is obtained as a ratio of the input and cross-power spectra. In other words, it is not required that  $x(t)$  be gaussian white noise (33).

The principles outlined above apply to one input/one output, linear systems not contaminated by extraneous "noise." To apply spectral analysis in biological systems where these ideal conditions are unlikely, a method of

evaluating differences between input and output, which may be caused by factors other than the transfer characteristics of the system, is necessary. The coherence function ( $\gamma^2$ ) provides this need.

$$\gamma^2 = \frac{|G_{yx}|^2}{G_{xx}G_{yy}} \quad 0 \leq \gamma^2 \leq 1. \quad (8)$$

$\gamma^2$  is a number between 0 and 1 similar to a correlation coefficient (33) and provides an index of causality between the input and output of a linear system. The value of  $\gamma^2$  is less than 1 if the output is the result of more than one input, if the system is nonlinear, or if the system is contaminated by extraneous noise (e.g., electrical noise). Using  $\gamma^2$ , confidence limits for spectral estimates may be obtained (31, 33).

**Data processing.** To implement the Fourier transform (Eq. 1) on a digital computer, it is necessary to convert the continuous wave form into discrete samples. Because of this the frequency range over which reliable magnitude and phase information can be obtained is limited by the sample interval ( $\Delta t$ ). Shannon's sampling theorem states that to define a sinusoid, slightly more than two equally spaced samples per period are required. This means that a time-varying wave form must be sampled at least twice the highest frequency of interest ( $F_{\max}$ ), that is

$$F_{\max} < \frac{1}{2\Delta t}. \quad (9)$$

Once  $F_{\max}$  or  $\Delta t$  are chosen, the basic frequency resolution or elementary bandwidth ( $\Delta f$ ) and total record length or time of sample ( $T$ ) are dictated by the size of the data array ( $N$ ) available in the computer as follows:

$$T = N \times \Delta t \quad (10)$$

$$F_{\max} = \frac{N}{2} \times \Delta f. \quad (11)$$

Actually,  $T$  or  $\Delta f$  could be chosen which would determine  $F_{\max}$  and  $\Delta t$ . Limiting the value of  $T$  results in a finite number of data points and a truncated Fourier transform, the Discrete Finite transform (DFT) which can be digitally computed:

$$\text{DFT} = S_x' = \Delta t \sum_{n=0}^{N-1} x(n\Delta t) e^{-j2\pi(m\Delta f) \cdot n\Delta t}, \quad (12)$$

where  $0 \leq m \leq N/2$ , indicating that  $N/2$  frequency components are produced by  $N$  samples of data.

In this study  $F_{\max} = 50$  Hz, hence pressure and flow were sampled at 100 Hz ( $\Delta t = 0.01$  s). The data array size ( $N$ ) was 64; therefore  $T = 0.64$  s and  $\Delta f = 1.5625$  Hz. A fully described point in the frequency domain must have both magnitude and phase represented by the real and imaginary parts of the DFT. Thus, when 0.64 s of data are sampled every 0.01 s resulting in 64 time points ( $N$ ), a spectrum with  $N/2 = 32$  frequency points, is computed; each point has two independent bits of information, magnitude and phase, at frequency intervals ( $\Delta f$ ) of 1.5625 Hz. The power in  $\Delta f$  can be obtained from Eq. 3 and the resulting elementary spectral estimate is said to have 2 degrees of freedom, corresponding to a chi-square value of  $x_2^2 = x_1^2 + x_2^2$  where  $x_1^2$  and  $x_2^2$  are analogous to  $A_x^2$  and  $B_x^2$  (Eq. 3). By averaging several ( $M$ ) power spectra, confidence limits

can be computed for the final spectral estimate about a chi-square distribution with  $k = 2M$  degrees of freedom (31).

Ensemble averages of 25 spectra ( $k = 50$ ) were computed requiring  $25 \times 0.64 = 16$  s of pressure and flow data. Thus, at each frequency, the power spectra used to compute  $|Z|$ ,  $\theta$ , and  $\gamma^2$  (Eqs. 3-8) represent an ensemble average of 25 frequency points. The relationships between  $\gamma^2$ ,  $k$ , and the confidence intervals for magnitude and phase are given by the following equations (31). For the 100 ( $1 - \alpha$ ) percent confidence intervals:

$$|\bar{Z}| \left\{ 1 \pm \sqrt{\frac{2}{k-2} f_{2,k-2}(1-\alpha) \left( \frac{1-\gamma^2}{\gamma^2} \right)} \right\} \quad (13)$$

$$\bar{\theta} \pm \sin^{-1} \sqrt{\frac{2}{k-2} f_{2,k-2}(1-\alpha) \left( \frac{1-\gamma^2}{\gamma^2} \right)}, \quad (14)$$

where  $|\bar{Z}|$  = ensemble average for  $|Z|$ ,  $\bar{\theta}$  = ensemble average for  $\theta$ ,  $k$  = equivalent number of degrees of freedom, and  $f_{2,k-2}(1-\alpha) = F$  distribution value corresponding to 2 and  $k-2$  degrees of freedom and cumulative probability ( $1-\alpha$ ).

Two other factors are necessary to obtain reliable spectral estimates. The first is a phenomenon known as "aliasing" (29-34), wherein energy originating above  $F_{\max}$  is "folded" back into the frequency range from 0 to  $F_{\max}$ . This problem is remedied by sampling at a frequency slightly  $> 2F_{\max}$  and by matched low-pass filtering of the input and output wave forms (see Hardware and Calibration), at a frequency slightly less than  $F_{\max}$ , before sampling. The second factor, known as "leakage" (29-34), is a type of sampling error associated with the DFT. Leakage results from unsynchronized combinations of sampling rate ( $\Delta t$ ) and length of data ( $T$ ). This produces discontinuities at the beginning and end of the data sample ( $T$ ) which can result in errors in the DFT. These leakage effects can be reduced by multiplying the sampled time data, before taking the DFT, by  $|\frac{1}{2} - \frac{1}{2} \cos(2\pi t/T)|$ , a bell-shaped function known as the Hanning window (29-34).<sup>3</sup>

The data reported in this study were processed on a Hewlett-Packard model 5451A Fourier analyzer (Hewlett-Packard Co., Palo Alto, Calif.) using a FFT subroutine based on the Cooley-Tukey algorithm (27) for implementing the DFT. The spectral analysis was written in assembly language and the statistical subroutines were written in FORTRAN. The results of a given measurement were immediately available on the oscilloscope screen of the Fourier analyzer and were stored on paper tape and printed on a teletype. Later, the results were plotted on a Hewlett-Packard model 7034A X-Y recorder. The results could be interchangeably displayed in polar coordinates as impedance magnitude and phase, or in rectangular coordinates as the real (resistance) and imaginary (reactance) parts of the impedance. The electrical impedance of a series RLC network determined both by sinusoidal and spectral analysis was virtually the same as the calculated values, providing an empirical check on the reliability of the analog hardware, the sampling techniques, and the computer program.

**Hardware and calibrations.** The apparatus is similar to that used in previous studies (10, 21, 23, 24) and is shown schematically in Fig. 1. Pressure fluctuations are induced

<sup>3</sup> In practice, this smoothing procedure may be implemented by convolving the Fourier transform of the time window with the Fourier transform of the input (pressure) and output (flow).

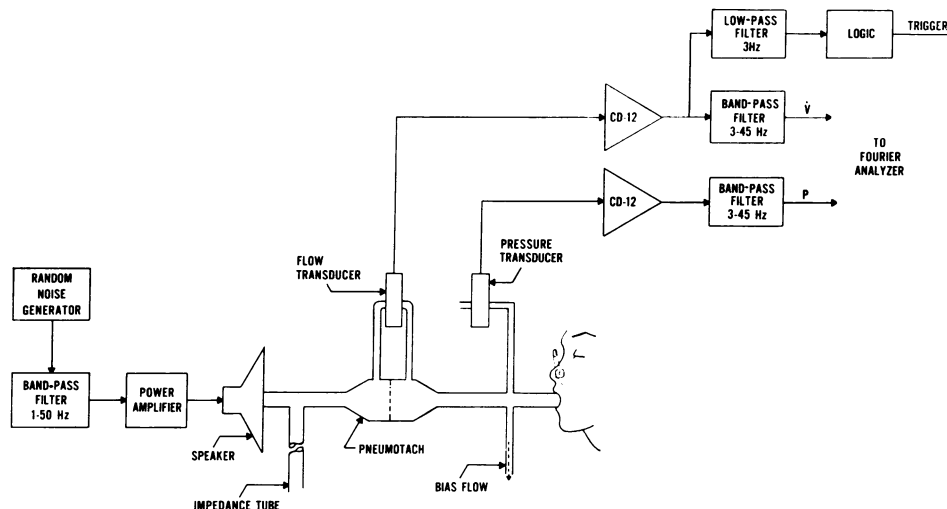


FIGURE 1 Schematic representation of the apparatus. Not shown are the subject's hands supporting his cheeks.

at the subject's mouth by a 12-inch loudspeaker (Acoustic Research, Inc., Cambridge, Mass.) and measured with a Validyne model DP45 ( $\pm 2.5$  cm H<sub>2</sub>O) variable reluctance differential pressure transducer (Validyne Engineering Corp., Northridge, Calif.). The resulting flow was measured as the pressure drop, sensed with a matched Validyne DP45 transducer, across a Silverman (screen type) pneumotachograph ( $R = 0.2$  cm H<sub>2</sub>O/liter per s). The amplified pressure and flow signals (Validyne model CD-12 carrier demodulators) were band-pass filtered between 3 and 45 Hz (Krohn-Hite model 3343R, Krohn-Hite Corp., Cambridge, Mass.), thus eliminating both respiratory and high-frequency (to minimize aliasing) variations from the induced pressure and flow fluctuations. The pressure and flow signals were processed as already discussed. The flow signal was also low-pass filtered (3 Hz), and used to identify various parts of the respiratory cycle. A long, large bore tube (Fig. 1) provides a low impedance to the subject's low frequency respiration but, as an acoustical inductor, impedes the higher frequencies which are then induced at the subject's mouth. A continuous 0.5-liters/s bias flow eliminates CO<sub>2</sub> buildup.

The loudspeaker was driven with a random noise signal via a transistorized power amplifier (Hewlett-Packard model

6823A). The noise signal was produced with a Burr-Brown model 4006/25 noise generator function module (Burr-Brown Research Corp., Tucson, Ariz.). When a periodic clocking signal (square wave) is applied, this module generates random binary noise which, after low-pass or band-pass linear filtering, will produce a gaussian white, analog noise signal over a bandwidth which is small ( $1/4$ ) compared to the clocking frequency. A 200-Hz square-wave clocking signal was used in this study and the binary output was band-pass filtered (1-50 Hz), resulting in analog random noise with a gaussian amplitude distribution. An example of the random pressure and flow signals that were used in this study is shown in Fig. 2.

The frequency response of the two pressure transducers, their associated Tygon tubing (0.476 cm ID  $\times$  10 cm long) (U. S. Stoneware Co., Akron, Ohio) and amplifiers was checked by response to a step input (36) and to a sinusoidal input, the latter by comparison to a catheter tip transducer (Millar model PC 350, Millar Instruments Inc., Houston, Tex.), shown (impulse response) to be flat  $\pm 1\%$  to 5 kHz. Both DP45 transducers were flat  $\pm 1\%$  to 25 Hz and 1 dB up at 50 Hz. With both DP45 transducers measuring a common pressure (the opposite port of each referenced to

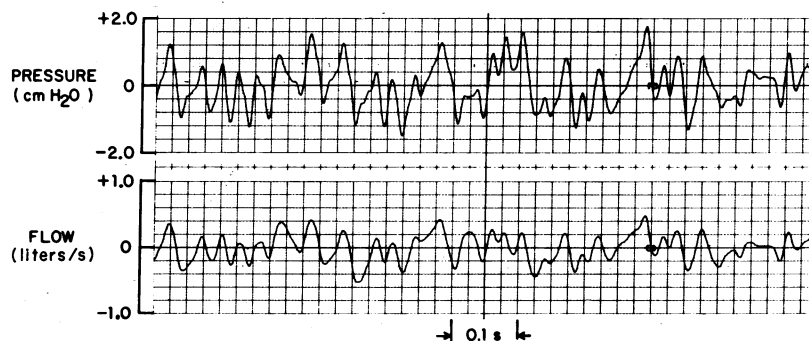


FIGURE 2 Example of induced random oscillations of pressure and flow.

atmosphere), there was less than  $1^\circ$  phase shift between, and less than 1% difference in, the amplitude ratio of the two transducers (and their respective amplifiers and filters) from 3 to 50 Hz.

The pneumotachograph was calibrated *in situ* with continuous flow from a rotameter. Although the pressure and flow transducers are matched for both amplitude and phase over the frequency range of interest, it is necessary to test the dynamic properties of the pneumotachograph to determine if any phase shift is introduced by the pneumotachograph itself. In this regard, the screen-type pneumotachograph should be better than the Fleisch, since the amount of gas that needs to be accelerated (and thus the inertance) is very small in the former, as confirmed by Finucane et al. (37) and Peslin et al. (38). The dynamic relationship between the pressure and flow measuring systems was tested by determination of the impedance and phase of a purely elastic system, the adiabatic compression of a mass of gas (38). This was accomplished by replacing the subject, on the apparatus shown in Fig. 1, with a large, wide-mouth bottle and comparing the induced random pressure and flow signals using spectral analysis. The phase angle between pressure and flow was  $-90^\circ \pm <1^\circ$  from 3 to 40 Hz, and  $<\pm 3^\circ$  at 45 Hz, indicating that the pneumotachograph (and associated electronics) provides reliable information as to the phase of flow over this frequency range.

Lung volumes and flow rates were measured with a water-filled spirometer. Functional residual capacity (FRC) and airway resistance ( $R_{aw}$ ) were determined by body plethysmography (39).

**Procedure.** 10 normal subjects, 5 smokers, and 5 patients with chronic obstructive pulmonary disease (COPD) were studied in the sitting position while breathing quietly into the apparatus (Fig. 1) via a rubber mouthpiece. A noseclip was worn and the cheeks compressed with the palms. After 30 s of breathing, the subject performed an inspiratory vital capacity to standardize the volume history of the lung. After another 30–60 s of quiet breathing, 16 s of pressure and flow data were simultaneously sampled during continuous respiration, and processed on line as outlined above under Data Processing. For a given subject, the time required to obtain a phase or impedance plot on the oscilloscope screen of the Fourier analyzer was approximately 20 s. Additionally, by use of appropriate logic circuits, the low-pass (3 Hz) filtered flow signal was used to trigger the Fourier analyzer so that the induced pressure and flow signals were sampled and analyzed only at FRC, or during early inspiration when respiratory flow was between 0.25 and 0.50 liters/s. Although the data thus obtained represent different time samples of the respiratory system, it can be used for an approximate comparison of phase and impedance data between various portions of the respiratory cycle. One of the subjects with COPD (R. C.) was studied before and after inhalation of isoproterenol. In one normal subject (E. M.), impedance was measured during slow panting (1–1.5 Hz) at FRC and at different volumes, from 2 liters below to 2.5 liters above FRC. Also, in the same subject, impedance was measured, during quiet breathing, while simulated upper airway obstruction was produced by mild external tracheal compression.

The relationship between resistance and flow in the respiratory system is determined, in part, by turbulence related to the geometry of the airways. Thus, potential variation in the impedance could occur due to different flow rates. The magnitude of the induced oscillations was such that the effective magnitude of the induced random flow signal was equivalent to a sinusoidal flow of  $\pm 0.32$  liters/s  $\pm <10\%$

for the normal subjects and  $\pm 0.28$  liters/s  $\pm <20\%$  for the obstructed groups.<sup>4</sup>

In each subject, the impedance ( $Z_M'$ ) of the mouth (including oral cavity cheeks, pharynx, and larynx) and mouthpiece was determined by spectral analysis of the induced pressure and flow during a Valsalva maneuver<sup>5</sup> (cheeks compressed with palms). Since  $Z_M'$  is acoustically in parallel with the remainder of the respiratory system ( $Z_{rs}$ ), this measurement can be used to correct the impedance measurements obtained during quiet breathing ( $Z_{rs}'$ ) for the characteristics of the mouth, to obtain the true  $Z_{rs}$  (peripheral to the glottis) as follows:

$$Z_{rs} = \frac{Z_M' \times Z_{rs}'}{Z_M' - Z_{rs}'} \quad (15)$$

This computation was performed as a subroutine to the spectral analysis program. The measurement of  $Z_M'$  includes and corrects for the characteristics of the mouthpiece and the compressibility of gas in the flowmeter-mouthpiece assembly. Additionally, an impedance measurement was made with the mouthpiece occluded and a correction, similar to Eq. 15, was applied to obtain the true impedance of the mouth ( $Z_M$ ). In two subjects (E. M. and E. G.),  $Z_M$  was obtained with the cheeks unsupported and relaxed.

## RESULTS

The spirometric data, FRC, and airway resistance are shown, along with the anthropometric data on each subject, in Table I.

The magnitude ( $|Z_M'|$ ) and the phase angle ( $\theta_M'$ ) of the mouth impedance ( $Z_M'$ ), measured during a Valsalva maneuver, is shown for all the subjects in Fig. 3.  $Z_M'$  also includes the gas compressibility and other mechanical properties of the mouthpiece assembly. The effects of  $Z_M'$  on the observed respiratory impedance ( $Z_{rs}'$ ) measured during continuous respiration, inspiration, or at FRC, were eliminated by applying Eq. 15 to obtain the true total respiratory impedance ( $Z_{rs}$ ). The measured  $Z_{rs}'$  on each subject was individually corrected with his own  $Z_M'$ .

<sup>4</sup> The effective magnitude of oscillatory flow is determined by the average deviation of the flow magnitude from 0. Effective sinusoidal flow ( $\dot{V}_e$ ) =  $2/\pi \times$  the amplitude of the sine wave or  $2\sqrt{2}/\pi \times$  its RMS (root mean square) value ( $\text{RMS}_s$ ). Effective flow with a gaussian amplitude distribution ( $\dot{V}_n$ ) =  $\sqrt{2}/\pi \times$  its RMS value ( $\text{RMS}_n$ ). Thus  $\text{RMS}_n = 2/\sqrt{\pi} \times \text{RMS}_s$ .  $\dot{V}_n$  was measured with an absolute value circuit in series with a low-pass filter and the equivalent sinusoidal flow calculated as  $\pm \pi/2 \times \dot{V}_n$ . These relationships were verified by comparing the RMS and effective values of different magnitudes of random, sinusoidal, and steady flow by measuring the resistance of a small pneumotachograph.

<sup>5</sup> To eliminate the difficulty of performing a prolonged Valsalva maneuver (expiratory effort against a closed glottis),  $Z_M'$  was measured during five separate 10-s periods, during each of which 10 ensembles were obtained and the results from the five periods averaged ( $M = 50$ ,  $k = 100$  for the  $Z_M'$  measurement). This prolonged total patient time to approximately 3 min. Equivalent sinusoidal flow during measurement of  $Z_M' = \pm 0.16$  liters/s.

TABLE I  
Anthropometric, Spirometric and Plethysmographic Data

Group	Subject*	Age	Height	Weight	Vital capacity	FEV <sub>1</sub>	FEV <sub>2</sub>	MMEFR§‡	FRC	R <sub>aw</sub>
		yr	cm	kg	liters/ BTPS‡	% vital capacity		liters/s	liters/ BTPS‡	cm H <sub>2</sub> O/ liter/s
Normal	H. E.	37	190.6	77.1	6.41	82.0	99.7	5.10	6.70	1.43
	J. R.	21	170.2	61.2	5.42	78.4	100.0	3.78	3.46	1.67
	D. H.	24	183.0	77.1	5.49	92.3	100.0	7.04	2.85	1.18
	E. G.	30	177.8	72.6	5.39	84.9	100.0	4.80	3.20	1.70
	D. E.	25	175.0	68.0	5.85	87.2	98.5	6.02	3.60	1.32
	S. S.	21	185.5	72.6	6.25	75.5	99.7	3.86	4.25	1.80
	R. O.	42	181.5	70.3	5.71	85.4	97.7	5.55	4.53	0.84
	R. D.	26	178.5	72.6	5.31	81.0	98.5	4.32	3.33	2.08
	T. G.	29	175.3	68.0	5.09	84.1	96.4	4.48	2.92	1.44
	E. M.	31	170.0	63.0	5.21	88.3	100.0	5.35	3.10	1.07
Smokers	A. M.	36	182.0	77.1	5.23	91.8	100.0	5.92	3.57	1.45
	T. C.	21	180.0	68.0	5.92	82.1	100.0	4.60	3.20	1.86
	J. J.	59	175.3	69.8	4.77	69.8	85.5	1.92	4.39	1.37
	S. H.	40	183.0	81.6	4.26	88.8	97.7	4.19	3.10	1.47
	J. N.	37	180.0	96.1	5.13	86.3	99.4	4.87	3.30	0.97
COPD	W. S.	42	177.7	86.2	3.99	64.2	83.9	1.23	3.00	2.52
	G. L.	51	175.3	68.7	2.72	41.0	67.8	0.33	5.69	6.71
	F. H.	50	178.4	68.0	4.47	52.7	79.6	1.02	5.58	2.33
	R. B.	39	188.0	72.1	4.88	52.3	77.7	1.01	5.40	2.89
	R. C.	55	177.7	70.3	3.21	49.4	78.2	0.33	5.96	3.28

\* All males.

‡ BTPS, body temperature and pressure, saturated with water vapor.

§ Measured between 25 and 75% of VC.

An example of this correction, shown in Fig. 4, illustrates the effect of  $Z_M'$  on the phase angle and magnitude of the total respiratory impedance, in a normal subject (E. M.), during quiet breathing, with and without simulated upper airway obstruction, induced by external tracheal compression.

Since  $Z_M'$  is large compared to  $Z_{rs}'$  and the variability about  $Z_M'$  is small (95% confidence intervals [CI]  $< \pm 5\%$ ), the error in  $Z_{rs}'$  introduced by correcting  $Z_{rs}'$  for  $Z_M'$  is small and is less than the variability about  $Z_{rs}'$  estimates. Also, it makes little difference if  $Z_{rs}'$  on a given subject is corrected to  $Z_{rs}$  using the mean  $Z_M'$  of all the subjects or that individuals  $Z_M'$  ( $< \pm 10\%$  for  $Z_{rs}$ ,  $< \pm 4^\circ$  for  $\theta_{rs}$ , and  $< 1$  Hz for  $f_n$ ).

It is possible to obtain the true impedance of the mouth ( $Z_M$ ) (Fig. 5) by applying a correction, similar to Eq. 15, to  $Z_M'$  using the impedance of the occluded mouthpiece assembly. Since the resonant frequency of the mouth is high (40 Hz), it is possible to estimate the value of compliance ( $C_M$ ) from the reactance ( $X_M$ ) at low frequencies (5 Hz) and inertance ( $I_M$ ) is computed assuming that  $Z_M$  is second-order (Table II). The degree to which the latter assumption is true is illustrated in Fig. 5. Also shown in Fig. 5 is  $Z_M$  measured

in two subjects with their cheeks unsupported and allowed to bulge during the forced oscillations. Compared to the supported cheeks,  $|Z_M|$  is less at the lower frequencies, probably due to increased  $C_M$  (estimated as above to be 0.0028 liters/cm H<sub>2</sub>O) of the unsupported cheeks and the shape of  $Z_M$  and  $\theta_M$  vs. frequency is

TABLE II  
Mechanical Properties of the Mouth\*

	$C_M$	$I_M$	$f_n$
	liters/cm H <sub>2</sub> O $\times 10^{-4}$	cm H <sub>2</sub> O/liter/s <sup>2</sup>	Hz
Mean	10.09	0.0174	39.4
Min	5.79	0.0108	30.0
Max	18.72	0.0229	45.0
SD	3.09	0.0037	4.1

\* Mean, range, and SD, in 19 subjects, of  $f_n$  and estimated compliance ( $C_M$ ) and inertance ( $I_M$ ) of the mouth (cheeks supported). These parameters were obtained individually, based on each individuals  $Z_M$ . Thus, the minimum and maximum values listed for  $C_M$ ,  $I_M$ , and  $f_n$  do not coincide with a given subject, and  $f_n$  calculated from the mean estimated  $C_M$  and  $I_M$  is slightly less than the true mean  $f_n$ .

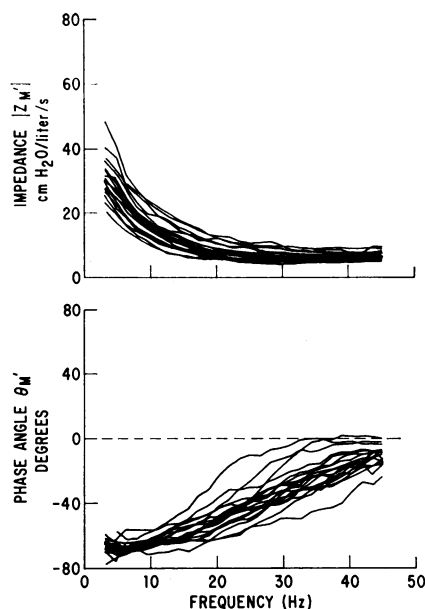


FIGURE 3 Magnitude and phase angle of the mouth impedance (including the mouthpiece assembly) for each subject. Each curve represents an average of 50 points at each of 32 frequencies, spaced 1.56 Hz.

more complex, indicating that  $Z_M$  is determined by higher order characteristics.  $R_M$  may be derived from the data in Fig. 5 as  $|Z_M| \cos \theta_M$ . The mean  $R_M$  (cheeks supported) was frequency dependent, falling from 11.4 (5.6 SD) cm H<sub>2</sub>O/liter per s at 3 Hz to 7.3 (2.2 SD) at 30 Hz, and increasing to 8.0 (2.2 SD) at 40 Hz.

The data shown in Figs. 6–10 is corrected for mouth impedance and represents the respiratory system distal to the larynx. Fig. 6 shows, in two normal subjects, the type of magnitude and phase data obtained along with coherence ( $\gamma^2$ ) and the 95% CIs (Eqs. 13 and 14). In general  $\gamma^2$  tended to be slightly less and the CIs wider at the lower frequencies and during continuous respiration compared to the measurements made during inspiration only.

$|Z_{rs}|$  and  $\theta_{rs}$ , measured during continuous respiration, are shown for nine normal subjects in Fig. 7. Each magnitude and phase curve in Figs. 4, 6, 7, 9, and 10 consists of an average of 25 complex points ( $k = 50$ ) at each of 32 frequencies, spaced at  $\Delta f = 1.56$  Hz.

The mean  $|Z_{rs}|$  and  $\theta_{rs}$  obtained during continuous respiration and during selective sampling of the respiratory cycle (FRC and inspiration), are shown in Fig. 8 for the normals, smokers, and subjects with COPD. Listed in Table III are individual values of  $|Z_{rs}|$  and

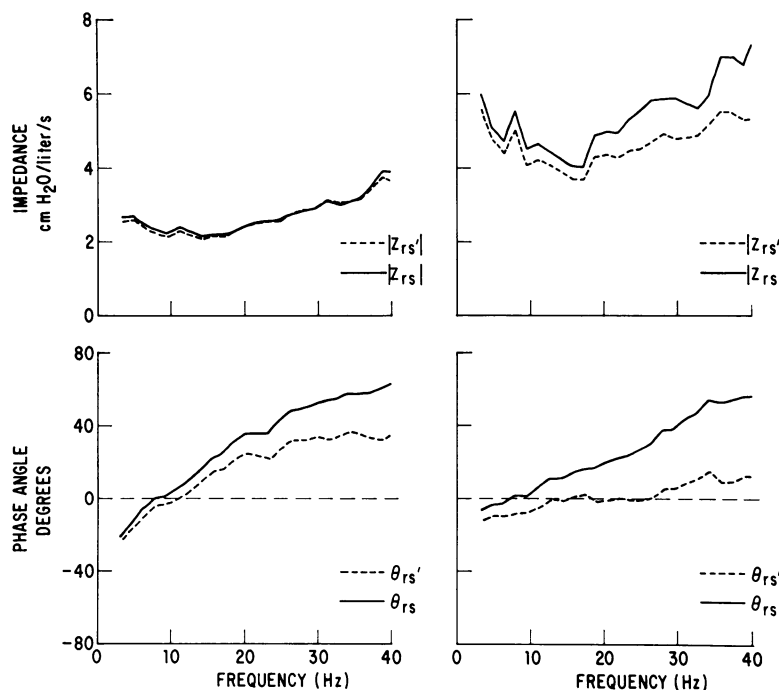


FIGURE 4 Effect of the parallel impedance of the mouth on the observed respiratory impedance (broken curves). Subject E. M. during quiet breathing without (left panels) and with (right panels) tracheal compression. The solid curves represent the corrected measurements (Eq. 15).

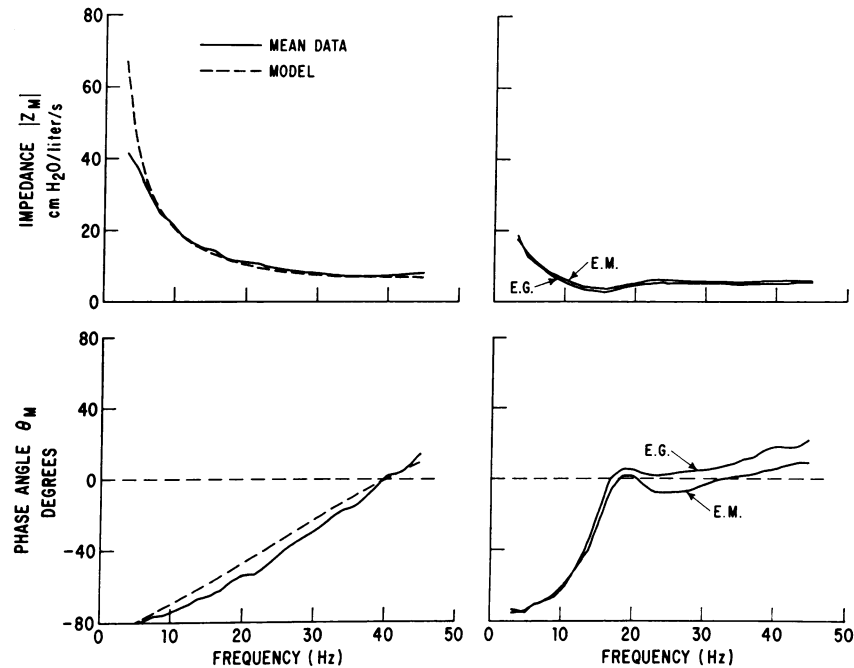


FIGURE 5 The solid curves in the left panels show the mean  $|Z_M|$  and  $\theta_M$  (corrected for mouth-piece assembly) for the 20 subjects with cheeks supported. The broken curves represent a second-order model, the coefficients of which were derived from the mean data. The right panels show  $|Z_M|$  and  $\theta_M$  in two subjects with the cheeks unsupported and allowed to bulge during the forced oscillations.

$\theta_{rs}$  at selected frequencies, illustrating the variability among normal subjects and those with varying degrees of obstruction, as well as differences between phases of the respiratory cycle.

The minimum value for  $|Z_{rs}|$  occurred at a frequency somewhat higher than the resonant frequency ( $f_n$ ), depending on the subject group and the phase of the respiratory cycle. For the data obtained at FRC the mean and range (in parenthesis) of the difference, between the frequency where  $|Z_{rs}|$  was minimum and  $f_n$ , for the three groups of subjects are as follows: normals, 2.17 Hz (−0.20–9.50); smokers, 2.70 Hz (1.30–5.40); COPD, 5.60 Hz (1.80–8.00). The minimum values for  $|Z_{rs}|$  were only slightly less than  $|Z_{rs}|$  at  $f_n$ . For the data obtained at FRC, the mean and range of these differences (centimeters of  $H_2O$  per liter per second) are as follows: normals, 0.12 (0.00–0.30); smokers, 0.22 (0.00–0.72); COPD, 0.48 (0.18–0.80). Frequency and magnitude differences, similar to the above, were also observed in the data obtained continuously and during inspiration.

For one subject (R. C.) with COPD, the respiratory impedance before and after inhalation of isoproterenol is shown (Fig. 9) both in polar coordinates ( $|Z_{rs}|$  and  $\theta_{rs}$ ) and in rectangular coordinates as the real or resistive ( $R_{rs}$ ) and imaginary or reactive ( $X_{rs}$ ) parts of  $Z_{rs}$ .

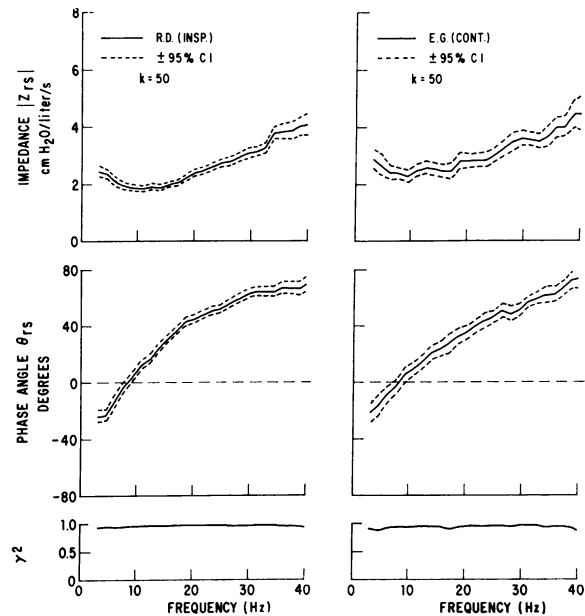


FIGURE 6 Magnitude and phase angle of  $Z_{rs}$  along with the coherence function ( $\gamma^2$ ) and the calculated (Eqs. 13 and 14)  $\pm 95\%$  confidence intervals (CI). For subject E. G., measurement was obtained during continuous respiration and for subject R. D., during the inspiratory part of the respiratory cycle.



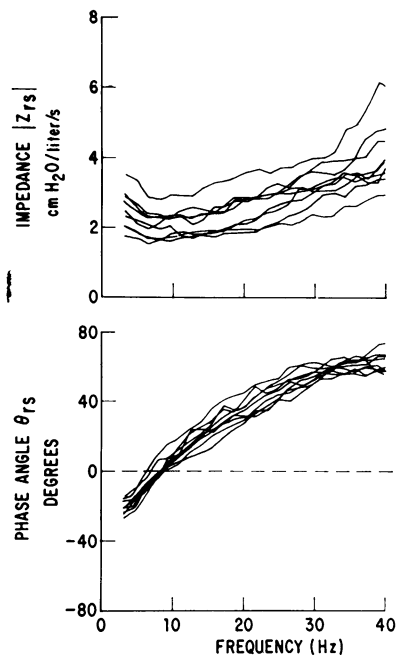


FIGURE 7  $|Z_{rs}|$  and  $\theta_{rs}$  measured continuously during quiet breathing in nine normal subjects.

Fig. 10 shows  $|Z_{rs}|$  and  $\theta_{rs}$  obtained in a normal subject (E. M.), during slow panting (1–1.5 Hz) at FRC and at different volumes from 2.0 liters below to 2.5

liters above FRC.  $Z_{rs}$  is also displayed in rectangular coordinates as  $R_{rs}$  and  $X_{rs}$ .

## DISCUSSION

*General comments and variability of spectral estimates.* The magnitude and phase angle of the respiratory impedance in the normal subjects (Figs. 4, 6, 7, 10) appear to be determined by approximately second-order characteristics. However, the curves are not as smooth as might be expected in a simple, linear, second-order, resistance-inertance-compliance (RIC) system. These observations can be explained, in part, both by physiological and statistical considerations. It has been emphasized by Shephard (6) that local resonances in branches of a complex series-parallel circuit may produce dips and peaks in the overall impedance curve. A difference in the frequency at which the impedance magnitude is minimum and at which the phase angle is zero, is consistent with circuits containing parallel elements, and is in keeping with various electrical models of the respiratory system (2, 6–8, 11–13), and the observations of DuBois et al. (3).

The behavior of complex circuits, such as the lung-chest system, may not be adequately described by a single, linear differential equation. Nonlinearities could introduce statistical variability into the spectral estimates which would be reflected by reduced values for coherence. A similar effect could be seen if any parameter in the system were changing nonlinearly with respect

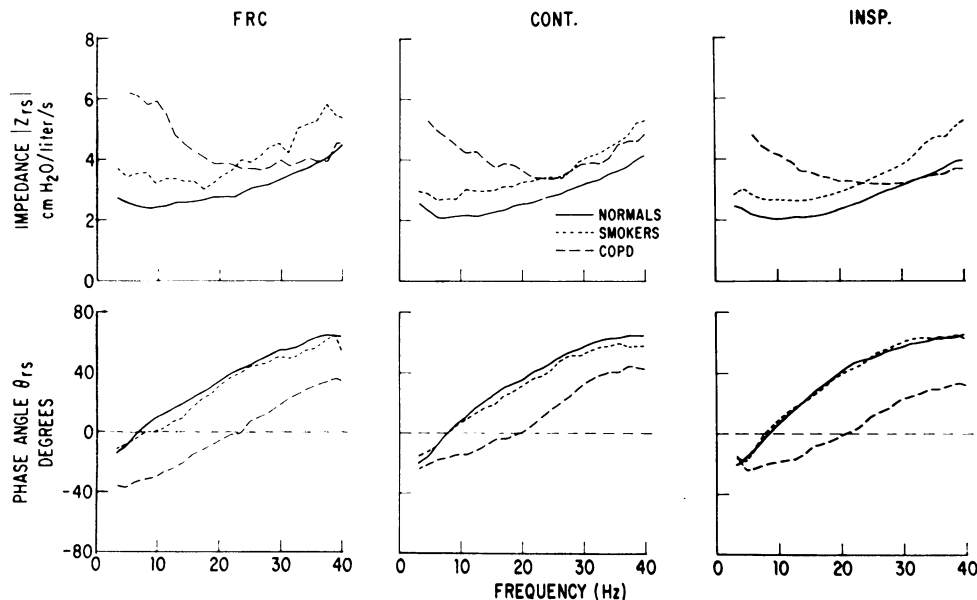


FIGURE 8 Mean  $|Z_{rs}|$  or  $\theta_{rs}$  for the three groups of subjects, measured continuously during quiet breathing (cont.), and during the inspiratory (insp.) and FRC portions of the respiratory cycle.

TABLE III  
Impedance Magnitude ( $|Z_{rs}|$ ), Phase ( $\theta_{rs}$ ), and Resonant Frequency ( $f_n$ )\*

Group	Subject	$f_n$			$ Z_{rs} $ at $f_n$			$\theta_{rs}$ at 12 Hz			$ Z_{rs} $ at 40 Hz			$\theta_{rs}$ at 40 Hz		
		FRC	Cont.	Insp.	FRC	Cont.	Insp.	FRC	Cont.	Insp.	FRC	Cont.	Insp.	FRC	Cont.	Insp.
		Hz			cm H <sub>2</sub> O/liter/s			degrees			cm H <sub>2</sub> O/liter/s			degrees		
Normal	H. E.	5.9	6.9	6.7	1.85	2.00	2.13	+26.0	+19.5	+17.5	4.40	3.80	4.10	+66.0	+66.0	+66.0
	J. R.	8.0	8.5	9.5	2.68	2.83	3.00	+9.0	+7.0	+5.5	3.81	6.00	5.00	+58.0	+60.0	+54.0
	D. H.	7.0	8.9	9.1	2.13	1.62	1.63	+12.0	+13.0	+10.0	4.18	3.41	3.00	+53.0	+58.0	+63.0
	E. G.	6.4	8.3	9.0	1.82	2.36	1.92	+22.0	+13.0	+14.4	4.60	4.45	3.98	+74.0	+85.0	+83.0
	D. E.	6.7	6.1	7.7	1.66	1.58	1.69	+22.0	+23.5	+20.5	3.80	3.80	3.80	+64.0	+67.0	+62.0
	S. S.	6.2	8.6	8.1	3.16	2.28	2.10	+20.0	+20.0	+20.0	5.40	4.85	4.60	+46.0	+54.0	+54.0
	R. O.	5.6	7.8	8.6	2.48	1.70	1.90	+18.0	+19.0	+14.5	5.75	3.92	3.90	+73.0	+73.0	+73.0
	R. D.	6.8	8.3	8.0	3.18	2.32	1.94	+12.0	+13.0	+16.4	5.80	3.90	4.10	+61.0	+57.0	+70.0
	T. G.	8.5	9.0	8.7	3.10	2.06	2.30	+5.0	+9.0	+10.0	4.00	3.00	3.75	+57.0	+64.0	+65.0
	E. M.	‡	8.5	‡	‡	2.30	‡	‡	+8.1	‡	‡	3.91	‡	‡	+63.0	‡
	Mean§	6.79	8.04	8.38	2.45	2.08	2.07	+16.2	+15.2	+14.3	4.63	4.12	4.03	+61.3	+64.9	+65.6
	SD	0.95	0.96	0.85	0.61	0.41	0.41	7.0	5.5	5.0	0.81	0.88	0.56	9.1	9.5	9.1
	SE	0.32	0.32	0.28	0.20	0.14	0.14	2.3	1.8	1.7	0.27	0.30	0.19	3.0	3.2	3.0
Smokers	A. M.	14.4	8.0	8.3	5.60	2.61	1.79	-4.0	+10.5	+18.6	7.80	5.70	3.80	+63.0	+61.0	+73.0
	T. C.	5.4	5.9	6.5	3.15	3.19	5.18	+21.8	+21.0	+20.4	6.40	8.00	9.40	+56.0	+59.0	+63.0
	J. J.	15.9	8.2	9.6	1.95	2.80	1.39	-13.0	+11.0	+15.9	2.75	4.80	3.60	+50.0	+57.0	+70.0
	S. H.	6.9	8.5	7.6	2.60	2.26	2.21	+18.0	+12.0	+16.0	7.40	4.25	4.45	+62.0	+60.0	+60.0
	J. N.	7.4	9.2	9.9	2.41	2.38	2.60	+11.2	+5.5	+2.5	3.80	3.43	3.43	+55.0	+47.0	+44.0
COPD	W. S.	‡	21.3	‡	‡	5.21	‡	‡	-8.0	‡	‡	7.30	‡	‡	+32.0	‡
	G. L.	28.5	21.6	30.3	4.05	3.20	3.39	-24.0	-18.5	-31.0	3.59	4.07	3.90	+22.0	+26.0	+8.0
	F. H.	16.2	8.9	14.5	‡	3.50	2.60	-22.0	-7.0	-4.0	‡	6.55	4.12	+32.0	+59.0	+52.0
	R. B.	15.0	18.0	16.3	4.10	4.60	3.65	-4.2	-11.5	-7.5	5.30	5.60	4.30	+35.0	+31.0	+31.0
	R. C.	24.8	25.8	24.5	3.90	3.00	2.90	-43.0	-25.0	-21.0	5.00	3.65	2.92	+38.0	+39.0	+34.0

\* Data from different portions of the respiratory cycle, abstracted from computer drawn curves similar to those shown in Figs. 4, 6-8. Measurements were made (see Methods) continuously during quiet breathing (Cont.), during inspiration (Insp.) and at FRC.

‡ Data not obtained (subjects E. M. and W. S.) or lost (subject F. H.).

§ Mean does not include Cont. values for subject E. M.

to time or the frequency of the random input; for example, variability in upper airway resistance or chest wall compliance during the respiratory cycle. Another factor which could result in variability of spectral estimates is the contamination of the output, of the system in question, by an extraneous "noise" source that is uncorrelated with the random input. The cardiogenic oscillations were found to be a source of uncorrelated noise in the flow signal but their effects on the spectral estimates of respiratory impedance were minimized by increasing the amplitude of the forced oscillations.

**Characteristics of the mouth.** The few available measurements of the mechanical properties of the mouth, either are unpublished or do not specify if the characteristics of the mouthpiece assembly were taken into account. Clements et al. (40) studied two normal subjects (checks relaxed), with the interrupter technique, by conducting air into one nostril at 0.5 or 1.0 liter/s and measuring mouth pressure, with the other nostril and glottis closed. From this they calculated that the resistance ( $R_M$ ) and compliance ( $C_M$ ) were 5 cm H<sub>2</sub>O/liter per s and 0.001 liters/cm H<sub>2</sub>O, respectively. From the frequency of oscillation after closure of the interrupter, they concluded that inertance ( $I_M$ ) was negligible. Shephard (41) reports, from unpublished

data, a range of 0.0004-0.0048 liters/cm H<sub>2</sub>O for  $C_M$ . Mead<sup>6</sup> has measured  $C_M$  in one subject and found it to be 0.0008 liters/cm H<sub>2</sub>O with the cheeks relaxed and 0.0004 liters/cm H<sub>2</sub>O if the cheeks were supported. The random noise method provides the opportunity to obtain  $Z_M$  over a wide range of frequencies (Fig. 5, Table II).

**Analysis of respiratory impedance in normal subjects.** Fig. 11 shows the extent to which the mean impedance of the normal subjects can be described by a second-order system. The coefficients for the model of  $Z_{rs}$  were derived from the mean normal  $Z_{rs}$  (average of data in Fig. 7, see also Table III), assuming that, at 40 Hz, the measured net reactance ( $X_{rs} = |Z_{rs}| \sin \theta_{rs}$ ) was essentially equal to inertial reactance and that compliant reactance was negligible. Respiratory inertance ( $I_{rs}$ ) was estimated as  $I_{rs} = X_{rs}/\omega$ , where  $\omega = 2\pi f$  and  $f = 40$  Hz.  $C_{rs}$  was then computed assuming second-order RIC behavior, as  $C_{rs} = (4\pi^2 f_n^2 I_{rs})^{-1}$  where  $f_n$  is the resonant frequency. The error in the estimation of  $I_{rs}$  in this way would be less than 3% for reasonable physiological values of  $C_{rs} \cdot R_{rs}$  for the model was obtained simply as  $|Z_{rs}|$  at  $\theta_{rs} = 0$ . The mean values,

<sup>6</sup> Dr. Jere Mead. Personal communication.

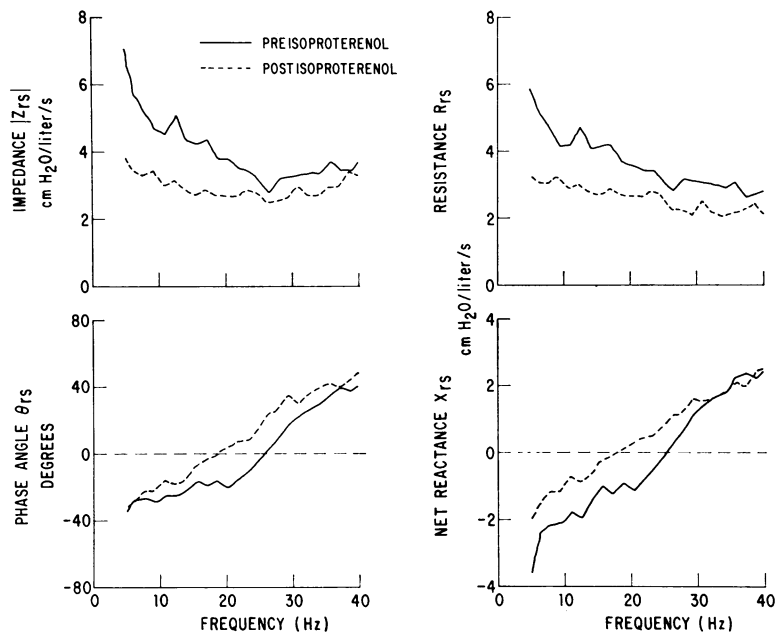


FIGURE 9 Components of the respiratory impedance obtained during quiet breathing in subject R. C. (COPD) before and after inhalation of isoproterenol.  $Z_{rs}$  is displayed in polar (left panels) and rectangular (right panels) coordinates.

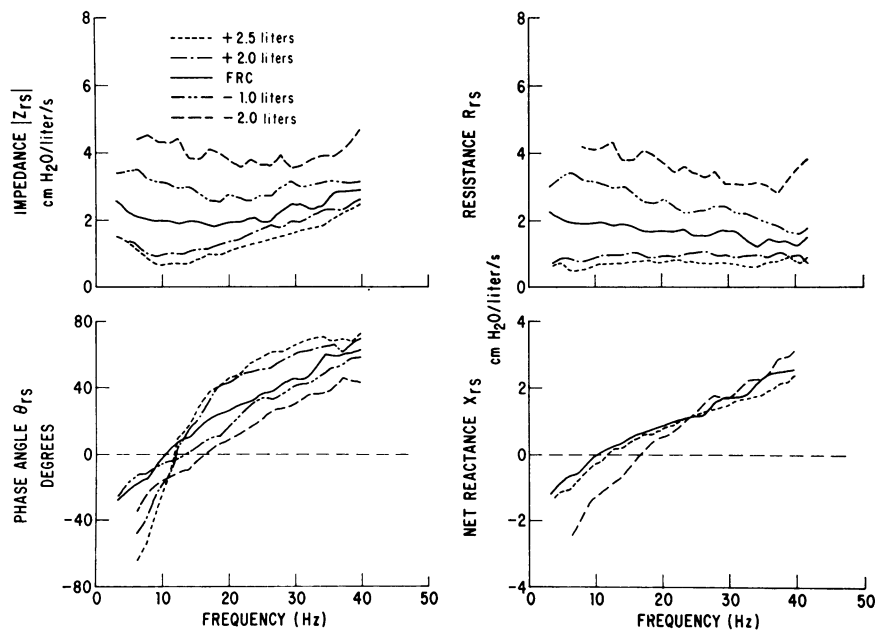


FIGURE 10 Polar (left) and rectangular (right) displays of  $Z_{rs}$  at different lung volumes in a normal subject (E. M.). The data obtained at 2.0 liters above and 1.0 liters below FRC have been omitted from the lower right-hand panel for clarity, since the curves were almost superimposed on those obtained at FRC and +2.5 liters.

range, and SD, for  $I_{rs}$  and  $C_{rs}$  estimated in this way for nine normal subjects are given in Table IV.

The respiratory impedance ( $Z_{rs}'$ ), uncorrected for the effects of the mouth and mouthpiece assembly ( $Z_M'$ ), is also modeled in Fig. 11.  $Z_M'$  is assumed to be an RC system in parallel with  $Z_{rs}$ . The R and C values for  $Z_M'$  were obtained from the average measured  $Z_M'$  (Fig. 3). The relationship between  $Z_{rs}$ ,  $Z_{rs}'$ , and  $Z_M'$  in the model is given by Eq. 15 and comparison with the mean data (Fig. 11) illustrates that  $Z_{rs}$  deviates only slightly from second-order behavior, primarily at frequencies less than 6 and greater than 25 Hz. The model also shows that correction of respiratory impedance assuming that  $Z_M'$  is a parallel RC pathway, is reasonable.

The values for  $R_{rs}(|Z_{rs}| \text{ at } \theta_{rs} = 0)$ , obtained by the spectral analysis technique in normal subjects (Table III), are similar to previously reported values for resistance measured by the forced oscillation technique (9, 24, 42). For the measurements made at FRC, the fre-

TABLE IV  
Respiratory Inertance ( $I_{rs}$ ) and Compliance ( $C_{rs}$ )  
in Normal Subjects\*

	$I_{rs}^\dagger$			$C_{rs}^\S$		
	FRC	Cont.	Insp.	FRC	Cont.	Insp.
	cm H <sub>2</sub> O/liter/s <sup>2</sup>			liters/cm H <sub>2</sub> O		
Mean	0.0150	0.0146	0.0143	0.0361	0.0293	0.0262
Min	0.0129	0.0107	0.0106	0.0263	0.0170	0.0174
Max	0.0219	0.0207	0.0161	0.0455	0.0489	0.0378
SD	0.0025	0.0028	0.0017	0.0068	0.0102	0.0062

\* Mean values, range, and SD of  $I_{rs}$  and  $C_{rs}$  derived from  $Z_{rs}$ , measured in nine normal subjects (Table II) continuously (Cont.), at FRC, or during inspiration (Insp.).

†  $I_{rs}$  estimated from net reactance ( $X_{rs}$ ) at 40 Hz as described in the text.  
§  $C_{rs}$  computed as described in text, from individual values of  $I_{rs}$  and  $f_n$  (Table II).

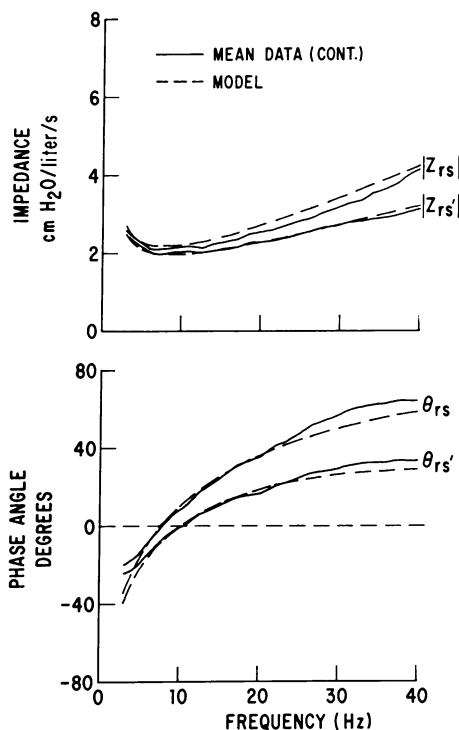


FIGURE 11 Components of total respiratory impedance with ( $Z_{rs}$ ) and without ( $Z_{rs}'$ ) correction for the impedance of the mouth and mouthpiece assembly ( $Z_M'$ ). The solid curves represent the mean values for the normal subjects (Fig. 7). The broken curves represent the impedance of a series circuit with coefficients derived from the mean data as described in the text. The relationships between  $Z_{rs}$ ,  $Z_{rs}'$ , and  $Z_M'$  are given by Eq. 15.

quency at which  $\theta_{rs} = 0$  (Table III) is in the range of 5.6–8.5 Hz, shown by some investigators (3, 9) to be the  $f_n$  of the respiratory system, but somewhat higher than reported by others (13, 20, 25). This could be due to differences in method or among subjects. Few measurements of the phase angle between pressure and flow, during forced oscillations, have been made at small frequency intervals over a wide range of frequencies. Most studies (3, 9, 18, 20) have been confined to observation of the phase relationship on an oscilloscope screen, and report, in some subjects, a single value for “in phase” resonance. Actually, several authors (3, 9, 21) have not been able to demonstrate a phase angle of 0 in some normal subjects, over a frequency range of 3–10 Hz. This could be explained by resonance occurring outside the frequency range studied—perhaps due to failure to take into account the parallel impedance of the mouth.

*Comparison to data of Peslin et al. (13).* Fig. 12 shows the mean  $|Z_{rs}|$  and  $\theta_{rs}$  measured, during quiet breathing and at FRC, in the normal subjects by the random noise technique, compared to the average data of Peslin et al. (13). Using a body plethysmograph with an airtight neck seal, they measured total respiratory impedance at FRC in five normal subjects over a frequency range of 3–70 Hz by comparing, for magnitude and phase, sinusoidal perithoracic pressure oscillations with flow measured at the mouth. The  $f_n$  measured at FRC is similar in both studies. However,  $|Z_{rs}|$  measured by Peslin et al. is higher and  $\theta_{rs}$  is more positive at frequencies above  $f_n$ , compared to the random noise data, suggesting that the behavior of the respiratory system is determined by fourth-order characteristics. Factors which could possibly account for the differences between our data and those of Peslin et al. (13) will now be considered. Both real and theoretical differences in respiratory impedance, depending

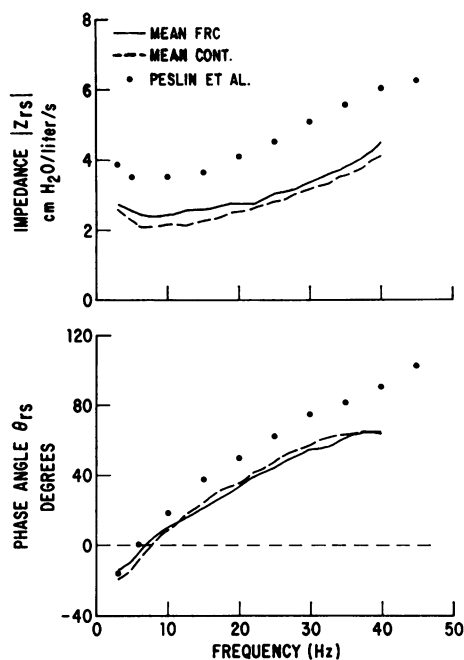


FIGURE 12 Comparison of mean normal data, measured continuously or at FRC during quiet breathing, to average data from five subjects studied by Peslin et al. (13).

on the site of application of the forced oscillations have been discussed by others (3, 6, 25). It can be shown that the impedance of a system, obtained when the input and the output (i.e., pressure and flow) are measured at the same point, is not necessarily the same as when the input is measured at one point and the output at a different point in the system. If the forced oscillations are applied at the mouth and both pressure and flow are measured at the mouth, the input impedance of the system is determined. On the other hand, if the oscillations are applied and pressure is measured around the chest and the resulting flow measured at the mouth, the so-called transfer impedance of the system is obtained. This impedance will be the same as the input impedance only if no parallel impedance is interposed between the sites of pressure and flow measurement. Thus, if the oscillations are applied around the chest, the flow measured at the mouth will be less than the total flow into the system depending on the distribution of and the extent to which compliance of gas or airways behave as a parallel elastic shunt. This could explain the larger impedance magnitude and more positive phase angle reported by Peslin et al. (13) compared to the present study (Fig. 12). The use of a neck seal could also contribute to the higher  $|Z_{rs}|$  measured by Peslin et al.

*Analysis of impedance in obstructed subjects.* Although the individual variability of  $|Z_{rs}|$  and  $\theta_{rs}$  is

greater among the obstructed subjects, as compared with the normal ones (Table III), several general conclusions may be drawn from observation of the mean data (Fig. 8). Regardless of the portion of the respiratory cycle sampled, the characteristics of normal subjects and the smokers approximate those of a second-order system, although the mean value of the minimum  $|Z_{rs}|$  in the smokers is slightly greater.  $|Z_{rs}|$  in the subjects with COPD is quite high at low frequencies and decreases to a minimum at a much higher frequency compared to the normals and smokers.

In both the normal and obstructed subjects  $\theta_{rs}$  is negative at low frequencies. As frequency is increased,  $\theta_{rs}$  in the normals and smokers crosses 0 and is in the range of  $40^\circ$  at 20 Hz and  $60^\circ$  at 40 Hz, although between 8 and 15 Hz  $\theta_{rs}$ , measured at FRC, is less positive in the smokers. In the subjects with COPD,  $\theta_{rs}$  does not cross 0 until approximately 20 Hz and remains less positive than in the normals and smokers. Since both resistance and inertance are inversely proportional to the radius of a tube, it might be expected that the obstructed subjects would have a higher inertance (and possibly a higher lung compliance) and hence a lower  $f_n$  when, in fact, the opposite appears to be the case. Thus, other factors must account for the observed differences between normal and obstructed subjects.

*Consideration of data in terms of models of frequency-dependent mechanics.* Otis et al. (2) using a two-compartment, parallel pathway analog of the lung, predicted that patients with obstructive lung disease should exhibit a fall in both compliance and resistance with increasing frequency due to an unequal distribution of time constants throughout the lung. Frequency dependence of compliance has been observed in patients with COPD (43) and has been used to determine the presence of early peripheral airways obstruction when the elastic properties of the lung are normal and airways resistance is still in the normal range (44, 45). Grimby et al. (10) and Hyatt et al. (24), using modifications of the forced oscillation technique demonstrated, in obstructed subjects, a fall in respiratory resistance with increasing frequency. This decrease in resistance can account in part for the decrease in impedance observed in our COPD subjects as frequency increases. The negative phase angle from 3 to 20 Hz and the high  $f_n$  in our subjects with COPD might be explained by a fall in compliance with frequency, keeping compliant reactance greater than inertial reactance. The negative phase angles we observed are consistent with the observations of others who have used the forced oscillation technique to study patients with obstructive lung disease. Grimby et al. (10) noted that often resonance could not be demonstrated at frequencies up to 10 Hz in patients with COPD. They suggested that reductions in dynamic compliance with increasing frequency, in

these patients, caused the  $f_n$  to remain above the applied frequency. Fisher et al. (9) showed that the phase angle between pressure and flow, in many subjects with emphysema, was not 0 at any frequency in the range of 2–10 Hz. These authors commented that the failure to detect resonance could be due to a change in effective compliance with frequency, keeping capacitive reactance greater than inductive reactance at all frequencies, and suggested that resonance might be found outside the frequency range studied. Sobel (21) was unable to find an  $f_n$  between 3 and 10 Hz in many normal subjects; and in all subjects with obstructive lung disease and he suggested that the airways, as a compliant element in parallel with the lung and chest, could account for phase shifts in lungs with increased resistance. Also, preliminary reports by others using electrical models (46) or high-frequency forced oscillations (47) have suggested that negative phase angles over a wide range of frequencies would be expected in patients with obstructive lung disease.

*Three models of frequency dependence.* Several two-compartment, parallel RC models have been proposed to explain the frequency dependence of compliance and resistance observed in obstructive lung disease. In the model of Otis et al. (2) time constants are unevenly distributed throughout the lung parenchyma. Another model, proposed by Hogg et al. (48) considers the resistance of channels for collateral ventilation to be too high to result in frequency-dependent behavior in normal lungs. But flow through these channels can become important with obstruction of the peripheral airways, causing time-constant discrepancies, between collaterally and normally ventilated areas of lung, accounting for frequency-dependent compliance in emphysematous lungs. Mead (11) considered the airways to be expanding structures in parallel with the air spaces, and using a two-compartment parallel model, showed that time-constant differences between the airways and the parenchyma caused frequency dependence of compliance and resistance. The fall in resistance and compliance predicted for normal subjects by Mead's model is too small to be apparent in measurements made at practical breathing frequencies, although there have been several reports of frequency-dependent compliance occurring in normal subjects (49–51). As peripheral airway resistance is increased, the time-constant differences between the airways and parenchyma become more prominent, and can account for most of the frequency-dependent behavior observed in diseased lungs without having to invoke a generalized distribution of peripheral time-constant discrepancies.

*Analysis of data in terms of an electrical model of the total respiratory impedance.* To determine to what extent frequency-dependent changes in the mechanical properties of the lung can account for our observations

we have employed an electrical model of the respiratory system. The three different anatomical models described in the previous section, have all been interpreted within the framework of a single electrical analog model shown in Fig. 15 (Appendix). The two-compartment parallel section of the model ( $Z_{pp}$  in Fig. 15) has a different anatomical counterpart in each of the three models. Since all three of these anatomical models can be represented by a single electrical analog, each might explain the results, if the anatomical counterparts of the components in the electrical analogy are given appropriate characteristics. The conclusion, that any particular model is superior to another in terms of explaining the impedance data, may be drawn since the physical characteristics which must be applied to the rejected models are ridiculously unlikely.

The effective values for resistance and net reactance, arising from time-constant discrepancies in a parallel, two-compartment RIC pathway ( $Z_{pp}$  in Fig. 15), were incorporated in series with a circuit containing resistive, capacitive, and inductive components, representing respectively the lumped tissue, large and upper airway resistance, the chest wall resistance and compliance, and the total respiratory inertance, all three of which are shared by the parallel two-compartment portion of the model. It is then possible to determine the effect of parallel time-constant discrepancies on  $|Z_{rs}|$  and  $\theta_{rs}$  in the context of the mechanical properties shared by the two compartments. The equations describing the behavior of the model are shown in the Appendix.

Since  $X_{rs}$  is determined both by compliance and inertance, and our measurements of  $Z_{rs}$  were made at relatively high frequencies, the inertial component of the impedance cannot be neglected in the model. There is evidence (52–54) that the effect of inertance on the measurement of dynamic lung compliance is important at low frequencies. The assumption that inertance in an RIC system is negligible, implies that compliant reactance ( $X_C = -1/\omega C$ ,  $\omega = 2\pi f$ ) equals net reactance ( $X_T$ ) when, actually,  $X_T = X_I - X_C$ , ( $X_I = \omega I$ ). To the extent that  $X_C$  does not equal  $X_T$ , the dynamic compliance will increase with frequency. For reasonable values of lung or total inertance (0.010–0.015 cm H<sub>2</sub>O/liter per s<sup>2</sup>) dynamic compliance will begin to increase between 1 and 2 Hz and tend toward infinity as the  $f_n$  of the system is approached, above which the values for dynamic compliance would become negative. The effect of neglecting inertance on dynamic compliance would be greater for the lung alone than for the total respiratory system, which has a lower compliance due to the series chest wall component. Although the frequency-dependent properties in our model have been expressed in terms of total reactance ( $X_{rs}$ ) and resistance ( $R_{rs}$ ), it is still reasonable to think in terms of an effective value of compliance or inertance at a

given frequency if it is remembered that their effects cannot be separated by measurement.

Since inertance varies as the square and resistance as the fourth power of the radius, peripheral airway inertance must be a very small fraction of total inertance. The equations of Otis et al. (2), have been modified (Appendix) to include inertance terms. Uneven distribution of peripheral inertance had no effect on the total impedance ( $Z_{rs}$ ) of the model because peripheral, compared to total, inertance is so small. Thus, peripheral inertance has been neglected and the frequency-dependent portion of the model may be considered in terms of the more familiar parallel RC network (2). The shared inertance however, greatly influences the effective reactance of the model.

The graphical solutions to Eqs. 1A-11A (Appendix), showing the effects of frequency on  $Z_{rs}$  that would be expected for time-constant discrepancies between the dead space (compliant airways) and parenchyma (11), produced by varying the peripheral airway resistance (models A-C) and compliance as in COPD (model D), are shown in Fig. 13. The values of compliance and resistance in the two parallel compartments are similar to those used by Mead (11). The curves shown in Fig. 13 are similar to those observed in our subjects (Figs. 8-10), suggesting that observation of  $f_n$  or of  $\theta_{rs}$  in the range

of 10-20 Hz provides an estimate of time-constant unevenness. The frequency dependence of effective compliance, which keeps compliant reactance greater than inertial as frequency is increased, results in negative values of net reactance. Hence  $\theta_{rs}$  remains negative to higher frequencies as small airway obstruction increases.

Since it is not practical to show the graphical solutions for all of the models discussed, the coefficients used in these solutions, along with the resulting  $f_n$ ,  $\theta_{rs}$  at 12 Hz and the effects on peripheral and total resistance, are listed in Table V of the Appendix. It is important to realize that these coefficients (Table V), representing different discrete anatomical models, are used in a single electrical analogy (Fig. 15) where an infinite number of solutions are possible but which will explain the data only when  $R_2$  is made to approach 0 and  $C_2$  made very low. It will be seen that  $R_2$  and  $C_2$  refer to relatively normal lung in the models of Otis et al. (2) and Hogg et al. (48). Values  $R_2$  and  $C_2$  on the other hand, required to explain the data, seem ridiculously low for application to the normal lung, but quite appropriate for the centrally located airways in Mead's (11) model.

In the models of Otis et al. (2) and Hogg et al. (48), the fall in effective compliance is complete at 2-3 Hz and tends to approach some value of parenchymal com-

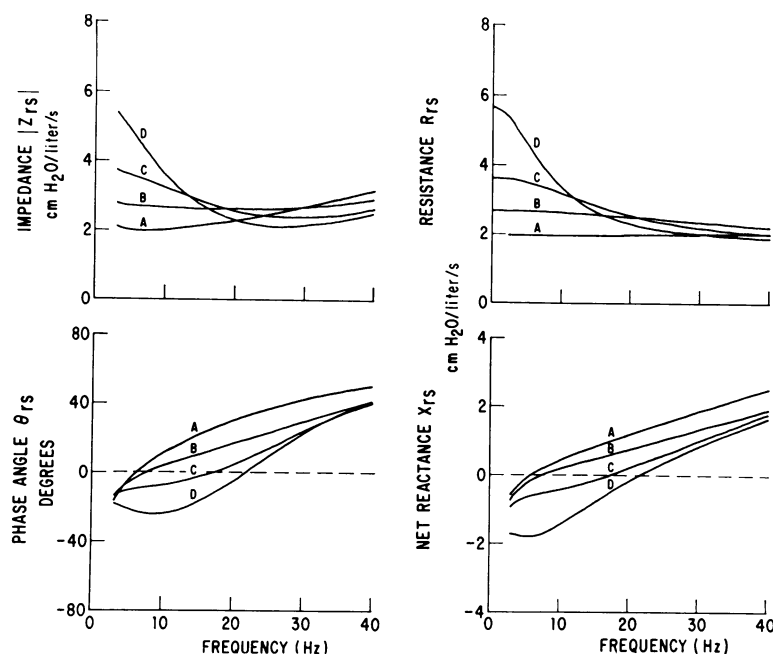


FIGURE 13 Polar (left) and rectangular (right) presentations of the solutions to Eqs. 1A-11A. Model A represents the normal respiratory system. Models B-D show the effect of increasing peripheral resistance and time-constant discrepancies between the airways and parenchyma (11). Lung compliance is increased (as might be expected in COPD) in model D. Note the similarities of this family of curves to the data (Figs. 8-10). The coefficients used in these and other models are given in Table V in the Appendix.

TABLE V  
Characteristics of Various Lung Models

Model	Type*	$R_1$ ‡	$R_2$	$C_1$	$C_2$	$V_1$ §	$V_2$ §	$T_1$	$T_2$	$f_n$	$\theta_{rs}$ at 12 Hz	$R_{pp}$ ¶	$R_{rs}$
		cm H <sub>2</sub> O/liter/s		liters/cm H <sub>2</sub> O				s		Hz	degrees	cm H <sub>2</sub> O/liter/s	
A	D	0.25	0.00	0.200	0.005			0.05	0.00	6.0	+15.9	0.24	1.99
B	D	1.00	0.00	0.200	0.005			0.20	0.00	8.0	+6.4	0.95	2.70
C	D	2.00	0.00	0.200	0.005			0.40	0.00	17.5	-6.2	1.90	3.65
D	D	4.00	0.00	0.400	0.005			1.60	0.00	22.0	-22.0	3.90	5.65
E	P	0.50	0.50	0.100	0.100	0.50	0.50	0.05	0.05	6.0	+16.5	0.25	2.00
F	P	2.00	0.50	0.100	0.100	0.50	0.50	0.20	0.05	6.3	+14.8	0.63	2.38
G	P	4.00	0.50	0.300	0.100	0.50	0.50	1.20	0.05	6.3	+15.7	2.28	4.03
H	P	0.36	0.83	0.140	0.060	0.70	0.30	0.05	0.05	6.0	+16.5	0.25	2.00
I	P	2.86	0.83	0.140	0.060	0.70	0.30	0.40	0.05	7.0	+12.8	1.47	3.22
J	P	2.86	0.83	0.340	0.060	0.70	0.30	0.97	0.05	7.0	+12.8	2.08	3.83
K	P	0.28	2.50	0.180	0.020	0.90	0.10	0.05	0.05	6.0	+16.5	0.25	2.00
L	P	2.22	2.50	0.180	0.020	0.90	0.10	0.40	0.05	7.0	+10.2	1.83	3.57
M	P	1.01	25.0	0.198	0.002	0.99	0.01	0.20	0.05	6.0	+12.9	0.99	2.74
N	C	0.50	0.00	0.100	0.100	0.50	0.50	0.05	0.00	6.5	+14.5	0.13	2.13
O	C	5.00	0.00	0.100	0.100	0.50	0.50	0.50	0.00	7.0	+14.1	1.25	3.25
P	C	15.00	0.00	0.100	0.100	0.50	0.50	1.50	0.00	7.0	+14.1	3.75	5.75
Q	C	5.00	0.00	0.400	0.100	0.50	0.50	2.00	0.00	7.0	+14.1	3.20	5.20
R	C	0.50	0.00	0.140	0.060	0.70	0.30	0.07	0.00	7.0	+13.1	0.25	2.25
S	C	5.00	0.00	0.140	0.060	0.70	0.30	0.70	0.00	8.0	+12.3	2.45	4.45
T	C	5.00	0.00	0.180	0.020	0.90	0.10	0.90	0.00	12.0	+0.2	4.05	6.05
U	C	5.00	0.00	0.380	0.020	0.90	0.10	1.90	0.00	12.0	+0.2	4.51	6.51
V	C	5.00	0.00	0.198	0.002	0.99	0.01	0.99	0.00	31.0	-18.8	4.90	6.90

\* Type of time-constant unevenness between the compartments of  $Z_{pp}$ . P, peripheral, as described by Otis et al. (2); C, collateral, as described by Hogg et al. (48); D, dead space vs. peripheral lung, as described by Mead (11).  $C_1$  represents collaterally ventilated lung in type C and the parenchyma and peripheral airways in type D.

§  $V_1$  and  $V_2$  are the fractional volumes of the two compartments in  $pp$ . For all of the models (except E, H, and K in which  $T_1 = T_2$ )  $V_2$  is the fast and  $V_1$  the slow compartment.

‡ All values of  $R$  are rounded off to the second decimal.

|| Not applicable since it is assumed that  $C_1 \neq C_2$  because of intrinsic differences in tissue elasticity.

¶  $R_{pp}$  is computed as  $(R_1C_1^2 + R_2C_2^2)/(C_1 + C_2)^2$  which is  $\lim_{\omega \rightarrow 0}$  Eq. 2A.

pliance which, if anything, might be increased in obstructive disease. Table V shows that  $Z_{rs}$  in these models is not affected. In Mead's model (11), effective compliance continues to decrease over most of the frequency range, approaching the very low value of the airways.

Thus far, the volumes of the two parallel compartments in the models of Otis et al. (2) and Hogg et al. (48) have been considered equal. If the volume of the fast compartment (shorter time constant) is small, its compliance could be quite low. In the model of Otis et al. (2) for example, if total lung compliance is 0.2 liters/cm H<sub>2</sub>O and the volumes of the slow and fast compartments ( $V_1$  and  $V_2$ , respectively) are distributed such that  $V_1:V_2 = 0.7:0.3$ , then  $C_1$  and  $C_2$  would be 0.14 and 0.06 liters/cm H<sub>2</sub>O, respectively. If initially the resistances are assigned to make  $R_1C_1 = R_2C_2$  and then  $R_1$  is increased to produce a 4- to 20-fold difference in time constants, most of the fall in effective lung

compliance, to about half of the static value, occurs at 3 Hz but  $\theta_{rs}$  and  $f_n$  are only minimally affected. Even if  $V_1:V_2$  were distributed 0.9:0.1 or 0.99:0.01, with  $C_2 = 0.02$  or 0.002 liters/cm H<sub>2</sub>O, the change in  $f_n$  and  $\theta_{rs}$  is small (Table V).

Similar to Mead's model (11), the value of  $R_2$  (and hence the time constant) of the normally ventilated (fast) compartment in the collateral model (48) is effectively 0. If the compartmental volumes in the collateral model are equal, the fall in effective compliance is limited and  $\theta_{rs}$  is only slightly affected, even if the resistance is as high as 15 cm H<sub>2</sub>O/liter per s or the time constant as long as 2.0 s for the collaterally ventilated pathway (Table V). If the volume of the fast, compared to the collateral, compartment is small, the model is similar to Mead's (11) in that the compliance of the fast compartment can be quite low. However, for the collateral model to produce changes in effective compliance that result in increased  $f_n$  and negative



values for  $\theta_{rs}$  at higher frequencies, requires that the distribution of  $V_1:V_2$  (collateral:normal) be 0.90:0.10 or 0.99:0.01 and the increases in peripheral resistance are even greater than in Mead's model (Table V).

It is possible that gas compressibility might cause parallel elastic shunt effects similar to those due to compliant airways. We have considered this in our model (assuming a gas compliance of 0.0035 liters/cm H<sub>2</sub>O) and concluded that gas compressibility has no significant effect on the input impedance of the model. Gas compliance depends on volume, the majority of which is contained in the alveoli. The small volume of gas in the conducting airways accounts for a negligible portion of the total gas compressibility and the parallel elastic shunt due to gas compliance is between the small airways and the pleura. On the other hand, none of the airway compliance is located in the alveoli and the parallel shunt is between the airways and the alveoli. We have modeled several distributions of airway compliance and our data can best be explained by a distribution localizing most of the airway compliance in the small airways.

Thus, although the frequency dependence of effective compliance in obstructive lung disease, over the range of practically achievable breathing frequencies, can be explained by any of the three parallel two-compartment models (and more than one of these models may be simultaneously contributing to the behavior of the lung), our measurements of  $|Z_{rs}|$  and  $\theta_{rs}$  can best be accounted for by time-constant discrepancies between the airways and the air spaces, as described by Mead (11).

Administration of a bronchodilator in a subject with COPD (Fig. 9) resulted in a fall of  $f_n$  from 25.8 to 18.6 Hz, a less negative  $X_{rs}$  over most of the frequency range (less frequency dependence of compliance), and  $R_{rs}$  was less frequency dependent. The similarity between Fig. 9 and the model (Fig. 13), is consistent with a fall in peripheral resistance after the bronchodilator.

*Differences dependent on the phase of the respiratory cycle.* Most previous measurements employing the forced oscillation technique have been made at FRC. There are differences in  $|Z_{rs}|$  and  $\theta_{rs}$  depending on the portion of the respiratory cycle sampled for analysis (Table III, Fig. 8). Although the data obtained continuously during quiet breathing represent a different time sample of the respiratory system and cannot be directly compared to that sampled during inspiration (between 0.25 and 0.5 liters/s) or at FRC, several conclusions may be drawn from the observed differences.

Using the forced oscillation technique, Peslin et al. (55) measured total respiratory resistance during the respiratory cycle in normal subjects. They found that the resistance followed variations in respiratory flow, although the degree of change in resistance for a given

flow was variable between subjects. In the present study,  $R_{rs}(|Z_{rs}| \text{ at } f_n)$  measured during early inspiration (corresponding approximately to inspiratory fraction 2 of Peslin et al. [55]), compared to FRC, was slightly higher (2–15%) in four and moderately lower (20–64%) in five of our normal subjects. This variability could be due to different respiratory flows at the time of measurement or variability of upper airway area.

$f_n$  in the normal subjects was uniformly higher ( $P < 0.001$ ) during inspiration compared to FRC (Table III). This can be explained in part by a fall in airway inertance during inspiration. The subjects exhibiting the largest falls in  $R_{rs}$  during inspiration also had greater increases in  $f_n$ . Since resistance depends both on the magnitude of respiratory flow and on cross-sectional area, it is not possible to estimate the change in  $I_{rs}$  from the observed change in  $R_{rs}$ . If  $R_{rs}$  was minimally dependent on flow, as in one of the subjects reported by Peslin et al. (55),  $I_{rs}$  estimated from the observed differences in  $R_{rs}$  at FRC and during inspiration (Table III) would not be sufficient to account for the observed increase in  $f_n$ . Thus, an inspiratory fall in  $R_{rs}$ , due to an increase in airway diameter, must be masked by a flow related increase in  $R_{rs}$ , or other factors (such as a fall in lung or chest wall compliance) may account for the higher  $f_n$  observed during inspiration.

In the obstructed patients (Table III, Fig. 8) additional factors such as dynamic compression of large airways during respiration, or small airway closure at FRC could partially account for the greater differences in  $Z_{rs}$  between different parts of the respiratory cycle. The latter might reduce lung compliance or produce a greater frequency dependence of effective compliance and an increase of  $f_n$ .

*Effects of lung volume.* The effects of lung volume on the components of the total respiratory impedance are shown in Fig. 10. As lung volume increases,  $R_{rs}$  falls and the system appears less damped. The family of  $|Z_{rs}|$  and  $\theta_{rs}$  curves is very similar to that of a second-order system with various degrees of damping (4). At 2.0 and 2.5 liters above FRC,  $f_n$  is slightly higher than at FRC, presumably due to lower inertance or increased stiffness of the system. Below FRC, where  $R_{rs}$  and  $I_{rs}$  are greater and  $f_n$  might be expected to fall,  $f_n$  increases. The increase of  $f_n$  at low lung volumes could be accounted for by a fall in effective compliance with frequency in part due to an increase of small airway resistance and increasing time-constant discrepancies between larger airways and alveoli as lung volume is reduced (i.e., by Mead's model as discussed earlier). The frequency dependence of  $R_{rs}$  at low lung volumes (Fig. 10) is also consistent with this explanation. A fall in chest wall compliance or a fall in lung compliance,

as the lung volume at which airway closure occurs is approached, might contribute to the increase of  $f_n$  at lower lung volumes.

**Effects of the parallel shunt impedance of the mouth.** The correction of the measured respiratory impedance for the parallel shunt impedance of the mouth (Eq. 15, Fig. 4) is greater as  $Z_{rs}$  is increased, since relatively more of the induced flow is shunted via the mouth. This means that  $|Z_{rs}'|$  will underestimate differences, among subjects with varying degrees of airway obstruction, compared to  $|Z_{rs}|$ . On the other hand, if the observed phase angle ( $\theta_{rs}'$ ) is not corrected for the mouth pathway,  $\theta_{rs}'$  will be more negative than  $\theta_{rs}$  at all frequencies. This is consistent with reports (3, 9, 21) that in some normal subjects resonance has not been detected. Also, the uncorrected  $f_n$  ( $f_n'$ ) is higher for a given increase in  $R_{rs}$  and there is a greater difference in  $f_n'$  among subjects with varying degrees of obstruction. These relationships are illustrated in Fig. 14.

**Further considerations of data in normal subjects.** The deviation of  $Z_{rs}$  in the normal subjects (Fig. 11), from second-order behavior is further illustrated by calculation of  $R_{rs}(|Z_{rs}| \cos \theta_{rs})$ , which shows that  $R_{rs}$  is frequency dependent, falling approximately 20% between 5 and 40 Hz. This fall in  $R_{rs}$  can account for the observa-

tion that the minimum value for  $|Z_{rs}|$  occurs at frequencies slightly higher than  $f_n$ . Models B-D, L, N, and R-V (Table V) show differences between  $f_n$  and the frequency at which  $|Z_{rs}|$  is minimum, similar to the observed (Results section) values.

The estimates of respiratory inertance (Table IV) show little variability and are in the range of previously reported measurements (3, 20, 52-53, 56-57). The calculated values of  $C_{rs}$ , on the other hand, are more variable and, assuming a static lung compliance of 0.2 liters/cm H<sub>2</sub>O, would require that the average chest wall compliance ( $C_W$ ) be about 0.031 liters/cm H<sub>2</sub>O, somewhat lower than most previously reported static measurements (16, 50). A similar discrepancy was noted by DuBois et al. (3) who attributed it to the failure of the lungs and chest wall to behave as a single, lumped system. More specifically, perhaps, the variability and low value for  $C_{rs}$  could be due to a low  $C_W$  during continuous breathing, dependence of the calculated  $C_{rs}$  on both the  $f_n$  and estimated inertance, or a fall in effective lung compliance at the higher frequencies. The observed fall in  $R_{rs}$  suggests that the latter possibility is reasonable. The values of  $C_{rs}$  in Table IV are also consistent with previously reported changes of  $C_{rs}$  with frequency (50).

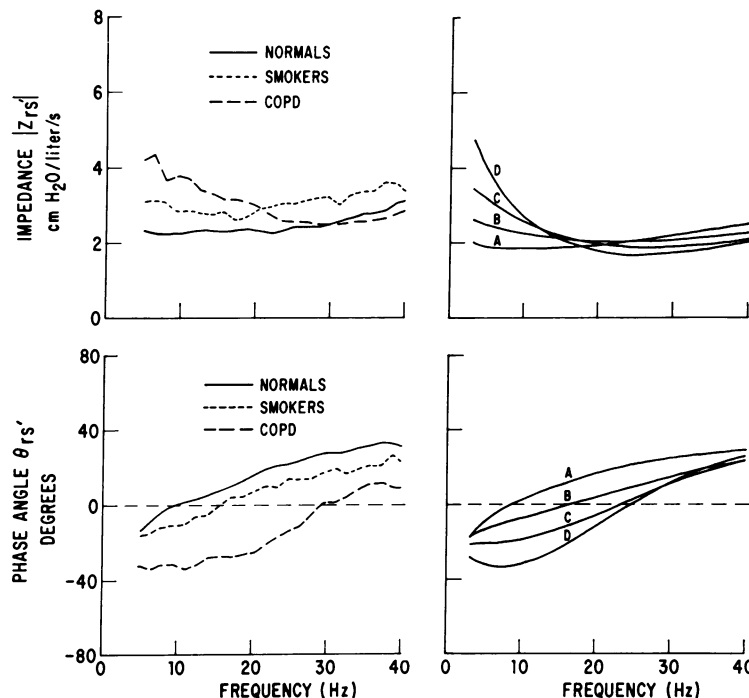


FIGURE 14 Components of the respiratory impedance, uncorrected for the parallel shunt impedance of the mouth. Left panels represent the mean data obtained during quiet breathing, in the three groups of subjects. Right panels show the graphical solutions to the same models illustrated in Fig. 13, except that the shunt impedance of the mouth (Fig. 5) is included.

It is of interest that, in several subjects,  $R_{rs}$  tended to increase between 30 and 45 Hz. At these higher frequencies, an uneven distribution of  $R/I$  time constants would be expected to result in an increase in effective resistance and inductance, similar to the fall in effective compliance and resistance described by Otis et al. (2), due to  $RC$  time-constant unevenness. This type of behavior may also account for some of the previously described characteristics of the mouth.

*Some final comments.* Although the random noise method may appear complicated at first, once the computer program and response characteristics of the instrumentation are worked out, the rapid measurement of the magnitude and phase of the respiratory impedance over a large range of frequencies by this method is relatively simple. In addition to improving our understanding of the dynamic mechanical properties of the respiratory system, interpretation of the data obtained in this study, in terms of an electrical model, suggests that frequency dependence of respiratory resistance or reactance, as well as the phase angle between pressure and flow at certain frequencies provides a "noninvasive" means of assessing the uneven distribution of lung time constants in disease.

## APPENDIX

Fig. 15 shows an electrical analog of the respiratory system in which a two-compartment parallel pathway ( $pp$ ) is incorporated into a model representing the components of the respiratory impedance shared by  $pp$ . By computing the impedance ( $Z_{pp}$ ) of this pathway, it is possible to determine the effect of uneven time constants in  $pp$  on the total respiratory impedance. This allows interpretation of our data in terms of the apparent frequency dependence of mechanical properties which may arise from time-constant discrepancies in  $pp$ . By selection of appropriate coefficients, the two compartments of  $pp$  may represent two peripheral areas (2), col-

lateral and normally ventilated lung (48), or the properties of the large airways and peripheral units (11). The impedance of  $pp$  is given by

$$Z_{pp} = R_{pp} + jX_{pp}, \quad (1A)$$

where  $R_{pp}$  is the real or resistive part, and  $X_{pp}$  the imaginary or reactive part of  $Z_{pp}$ ,  $j = \sqrt{-1}$ .

The equations of Otis et al. (2) have been modified to include the effects of inductance in each compartment of  $pp$ :

$$R_{pp} = \frac{\omega^4(GD - BF) + \omega^2(AF - DH - EG) + (EH - CF)}{\omega^4G^2 + \omega^2(F^2 - 2GH) + H^2}, \quad (2A)$$

$$X_{pp} = \frac{\omega^6BG + \omega^4(FD - AG - BH) + \omega^2(AH + GC - FE) - HC}{\omega^5G^2 + \omega^3(F^2 - 2GH) + \omega H^2}, \quad (3A)$$

where

$$A = R_1R_2 + \frac{I_1}{C_2} + \frac{I_2}{C_1}, \quad B = I_1I_2, \quad C = \frac{1}{C_1C_2},$$

$$D = R_1I_2 + R_2I_1, \quad E = \frac{R_1}{C_2} + \frac{R_2}{C_1}, \quad F = R_1 + R_2,$$

$$G = I_1 + I_2, \quad H = \frac{1}{C_1} + \frac{1}{C_2}, \quad \text{and} \quad \omega = 2\pi f.$$

By incorporating the shared resistance ( $R_{uaw}$ ) and inductance ( $I_{uaw}$ ) of the large and upper airways (for simplicity, tissue inductance is neglected and all of the shared inductance is assumed to be airway), the pulmonary impedance ( $Z_L$ ) may be computed as follows:

$$Z_L = R_L + jX_L, \quad (4A)$$

where

$$R_L = R_{pp} + R_{uaw}, \quad (5A)$$

and

$$X_L = X_{pp} + \omega I_{uaw}. \quad (6A)$$

The total respiratory impedance ( $Z_{rs}$ ) may be obtained by including ( $C_W$ ) the series chest wall compliance (for simplicity, small tissue and chest wall resistance are incorporated into  $R_{uaw}$ ):

$$Z_{rs} = R_{rs} + jX_{rs} \quad (7A)$$

$$R_{rs} = R_L \quad (8A)$$

$$X_{rs} = X_L - \frac{1}{\omega C_W}. \quad (9A)$$

$Z_{rs}$  may alternately be expressed in terms of magnitude ( $|Z_{rs}|$ ) and phase angle ( $\theta_{rs}$ ):

$$|Z_{rs}| = \sqrt{R_{rs}^2 + X_{rs}^2}, \quad (10A)$$

$$\theta_{rs} = \tan^{-1} \frac{X_{rs}}{R_{rs}}. \quad (11A)$$

The measurement of respiratory impedance with forced oscillations applied at the mouth, includes the parallel shunt

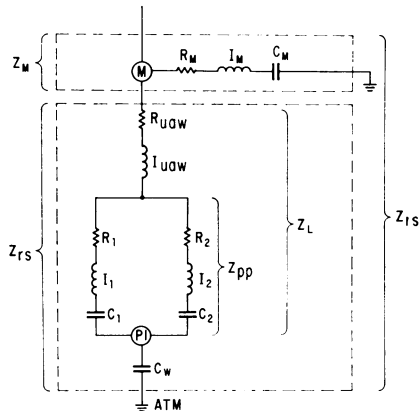


FIGURE 15 Electrical analog of respiratory system used in interpretation of data. The abbreviations are defined in the Appendix. ATM represents atmosphere (electrical ground); M, mouth; Pl, plural space.

impedance of the mouth ( $Z_M$ ); the relationship of the measured respiratory impedance ( $Z_{rs}'$ ) to  $Z_{rs}$  and  $Z_M'$  is given by Eq. 15 in the Methods section. For the purposes of the electrical model:

$$Z_M = R_M + jX_M \quad (12A)$$

$$X_M = \omega I_M - \frac{1}{\omega C_M}. \quad (13A)$$

The coefficients  $R_M$ ,  $C_M$ , and  $I_M$  may be derived from the mean  $Z_M$  data either including (Fig. 3) or excluding (Fig. 5) the characteristics of the mouthpiece assembly.

Using the above equations, it is possible to compute the magnitude and phase angle of the total respiratory impedance that would be expected for various combinations of  $R$ ,  $I$ , and  $C$  in the model. Table V lists the coefficients used for models A-D (plotted in Fig. 13), as well as those used in several other models that are discussed but not plotted because of space availability. For the models listed in Table V, only  $R_1$ ,  $R_2$ ,  $C_1$ , and  $C_2$  are varied to determine the effects on  $Z_{rs}$  of time-constant discrepancies in  $pp$ , produced by the various pathophysiologic situations described in the text. Also given in Table V are the fractional volumes and time constants of the two compartments; the expected  $f_n$  and  $\theta_{rs}$  at 12 Hz; and the resulting peripheral ( $R_{pp}$ ) and total ( $R_{rs}$ ) respiratory resistance.

For the models listed in Table V,  $R_{uav} = 1.75$  (types P and D) or 2.0 (type C), and  $C_W = 0.1$ .  $I_{uav} = 0.010$ – $0.011$ , depending on the increase in peripheral inertance associated with the increase in  $R_{pp}$ . Actually this range of  $I_{uav}$  had negligible effect on  $Z_{rs}$ . As mentioned in the Discussion section, the partitioning of inertance had no effect on  $Z_{rs}$  since  $I_1$  and  $I_2$  were so small relative to  $I_{uav}$  and may be considered zero for the models listed in Table V.

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