Some Effects of Respiratory Frequency on Pulmonary Mechanics *

CHARLES D. ALBRIGHT AND STUART BONDURANT †

(From the Department of Medicine, Indiana University Medical Center, Indianapolis, Ind.)

In 1956 Otis and co-workers (1) compared the behavior of a single pulmonary pathway to an electrical circuit consisting of a capacitor and resistor in series with a sinusoidally varying voltage source. In a pulmonary pathway driven by a sinusoidally varying pressure, the resultant flow curve is also a sine wave and leads the pressure curve by an amount θ , which is determined by the relationship,

$$\theta = \tan^{-1} (1/2\pi fRC), \quad [1]$$

where θ is the phase angle in degrees between the pressure and flow curves, f is the frequency in cycles per second, R is resistance in centimeters of water per liter per second, and C is compliance in liters per centimeter of water. The product RC is the time constant and at any given frequency determines the phase angle of the system. A sinusoidally driven system of multiple parallel pathways can be considered as a single pathway only if the time constants of the individual pathways are the same. With different time constants, the effective resistance and compliance of the system will decrease with increasing frequency.

Otis and co-workers observed a constant pulmonary compliance (C_L) at frequencies of 10 to 120 respirations per minute in three normal subjects. Two of these subjects breathed a histamine aerosol and at 120 respirations per minute had a decrease in C_L to 30 to 50% of control values before histamine. An asthmatic was shown to have a higher and more constant but nevertheless still

decreasing C_L following epinephrine as compared with values before epinephrine. One patient with emphysema showed marked fall of C_L over the range of 20 to 55 respirations per minute. Defares and Donleben (2) reported a small percentage of normal subjects with frequency dependent pulmonary compliance. Frank, Mead, and Ferris (3) studied nine healthy elderly adults at increasing frequencies and consistently found small decreases in C_L . Others (1, 4, 5) have demonstrated constant C_L in normal subjects with increasing frequency.

Although the chest wall and lungs moving together determine the characteristics of the total respiratory system, the effect of respiratory frequency on total thoracic and chest wall mechanics has not been extensively studied. This study was undertaken to evaluate total thoracic, pulmonary, and chest wall compliance, resistance, and impedance as a function of frequency in normal subjects.

Methods

The subjects sat in a body plethysmograph with the head protruding through a rubber neckpiece. The plethysmograph was constructed of 1-inch plywood and measured $20 \times 26 \times 34$ inches on the inside. Sinusoidally varying plethysmograph pressures were produced by a 16-inch diameter piston driven by an electric motor at a frequency of 10 to 130 cycles per minute. The piston stroke was adjusted to produce peak to peak plethysmograph pressures of 20 to 40 cm H_2O . The plethysmograph pressure was measured by a Statham PM5TC strain gauge. The esophageal pressure was measured by a 15-cm long thin wall balloon attached to a 50-cm long polyethylene tube with internal diameter of 0.070 inch. The tube was passed through the nares for a distance of 35 cm and inflated with 1 ml of air. The balloon was attached to one side of a Statham PM5TC differential strain gauge while the other side was connected to a mouth pressure tap. Air flow was measured by a warmed 400-mesh wire screen flowmeter connected to a Statham PM97TC differential strain gauge. The flowmeter was linear over the range of flow rates measured. Volume was determined by electrical integration of the flow sig-

* Submitted for publication December 28, 1964; accepted April 28, 1965.

This work was supported in part by grants HE 04080 and HE 06308 from the U. S. Public Health Service, by a grant from the American Heart Association, and by U. S. Air Force contract 33(616)8378.

Abstracted in *Circulation* 1964 (suppl. 3), 30.

† Address requests for reprints to Dr. Stuart Bondurant, Department of Medicine, Indiana University Medical Center, 1100 West Michigan Street, Indianapolis, Ind. 46207.

nal. The output of the strain gauges was recorded on a recorder¹ at paper speeds of 25 to 100 mm per second.

The frequency response of the strain gauges and amplifier was measured by cycling pressure in the plethysmograph. The response of the Statham gauges was compared to that of a Sanborn 270 differential transducer² known to be linear over the pertinent frequency range. There was no difference in amplitude or phase response of the gauges over the experimental frequencies. However, at frequencies of 48 to 130 cycles per minute with the esophageal balloon and flowmeter attached to the respective strain gauges, there were phase shifts of 1.4 to 7.2 degrees when compared with plethysmograph pressure. The experimental tracings were corrected at each frequency for these shifts.

Young professional subjects without pulmonary disease were trained to relax in the plethysmograph. The physical characteristics and pulmonary functions of the nine subjects are presented in Table I. The group included habitual smokers and nonsmokers. After insertion of the esophageal balloon they sat in the plethysmograph and breathed through the mouthpiece assembly and pneumotachograph. Each series of measurements was preceded by a maximal inspiration followed by an expiration back to the functional residual capacity (FRC). At this point the motor was started. The piston was so placed as to cause an initial inspiration from the FRC. The cycling lasted for approximately 60 seconds at the lower and 20 seconds at the higher frequencies. Even at the higher frequencies there were no significant changes in FRC during the cycling. The experimental frequencies were approximately 10, 18, 24, 48, 90, and 130 cycles per minute. All calculations were made from the trac-

TABLE I
Physical characteristics and pulmonary functions of subjects of study (N = 9)

Characteristic	Mean $\pm$ SD	Units
Age	24 $\pm$ 4	years
Weight	167 $\pm$ 20	pounds
Height	181 $\pm$ 5.4	cm
Surface area	1.95 $\pm$.12	m ²
Inspiratory capacity	3.4 $\pm$.36	L
Expiratory reserve volume	2.1 $\pm$.46	L
Vital capacity	5.5 $\pm$.66	L
Residual volume	1.4 $\pm$.39	L
Residual volume/total lung capacity	21 $\pm$ 5.2	%
Functional residual capacity	3.6 $\pm$.49	L
Maximal breathing capacity	144 $\pm$ 30.4	L/minute
Maximal expiratory flow rate	557 $\pm$ 61.2	L/minute

ings and represent an average of two inspirations and two expirations at each frequency; most individual measurements fell within 10% of the average. All variables were calculated from the same two inspirations and expirations. A sample of tracing is presented in Figure 1.

Total thoracic compliance (C_T) was calculated by dividing the tidal volume by the difference in plethysmograph pressures at points of zero air flow. Pulmonary compliance (C_L) was calculated similarly from the transpulmonary pressure. With the compliances assumed to act in series, the chest wall compliance (C_W) was calculated from the equation,

$$1/C_W = 1/C_T - 1/C_L. \quad [2]$$

The total thoracic resistance (R_T) was calculated from the box pressure curve by subtracting away that pressure required to overcome elastic recoil. This method assumes that compliance is constant throughout each phase of the

FIG. 1. REPRESENTATIVE TRACING ILLUSTRATING THE SINUSOIDAL WAVE FORMS.

¹ Electronics for Medicine, White Plains, N. Y.

² Sanborn Co., Waltham, Mass.

FIG. 2. RELATIONSHIP BETWEEN TOTAL THORACIC, PULMONARY, AND CHEST WALL COMPLIANCES AND RESPIRATORY FREQUENCY. Circled numbers indicate data of individual subjects.

respiratory cycle. The remaining area was integrated mechanically, as was the flow curve, and R_T was calculated by dividing the pressure area by the flow area. The pulmonary resistance (R_L), including both airway and tissue resistance, was calculated in a similar manner, from the esophageal pressure curve. This is a modification of the method of Attinger, Monroe, and Segal (4).

Again with the elements assumed to act in series, chest wall resistance (R_w) was calculated as the difference between R_T and R_L . R_T and R_L include the resistance of the mouthpiece and pneumotachograph, approximately 0.160 cm H₂O per L per second. The phase angle between the sine waves of plethysmograph pressure and air flow was determined from the mid-points of the respective

TABLE II
Respiratory compliances at a series of frequencies*

Frequency (f)	Total thoracic (C _T)	Pulmonary (C _L)	Chest wall (C _w)
<i>cycles/min</i>	<i>L/cm H₂O</i>	<i>L/cm H₂O</i>	<i>L/cm H₂O</i>
10.0 ± 0.0	0.084 ± 0.022	0.164 ± 0.049	0.197 ± 0.084
18.0 ± 1.7	0.080 ± 0.020	0.170 ± 0.042	0.176 ± 0.067
24.8 ± 0.4	0.073 ± 0.020	0.153 ± 0.030	0.159 ± 0.087
48.6 ± 1.4	0.060 ± 0.020	0.146 ± 0.047	0.120 ± 0.074
90.8 ± 8.2	0.046 ± 0.013	0.101 ± 0.024	0.095 ± 0.059
131.9 ± 2.0	0.041 ± 0.017	0.098 ± 0.040†	0.116 ± 0.082†

* Values at f 18 and f 24.8 do not differ significantly from those at f 10 ($p > 0.200$). At f 48.6 or greater $p < 0.025$.

† Indicates eight subjects only; other values are the mean and standard deviation for nine normal subjects.

FIG. 3. RELATIONSHIP BETWEEN TOTAL THORACIC, PULMONARY, AND CHEST WALL RESISTANCES AND RESPIRATORY FREQUENCY. Circled numbers indicate data of individual subjects.

curves and expressed in degrees. The total thoracic compliance was also calculated at each frequency from Equation 1 with the previously calculated R_T as R .

Total thoracic impedance (Z_T) was calculated by dividing peak to peak plethysmograph pressure by peak to peak air flow. Pulmonary impedance (Z_L) was calculated in a similar manner from transpulmonary pressure and flow. Since the lungs and chest wall act in series

and are in phase, chest wall impedance (Z_w) was calculated as the difference between total thoracic and pulmonary impedance. The time constant ($R_T C_{T0}$) was determined from the frequency and phase angle by Equation 1.

The values for each subject at f 10 were compared with the values at higher frequencies by the paired comparison t test (6).

TABLE III
Respiratory resistances at a series of frequencies*

Frequency (f)	Total thoracic (R_T)	Pulmonary (R_L)	Chest wall (R_w)
<i>cycles/min</i>	<i>cm H₂O/L/sec</i>	<i>cm H₂O/L/sec</i>	<i>cm H₂O/L/sec</i>
10.0 ± 0.0	11.50 ± 8.31	$7.34 \pm 6.03^\dagger$	$5.04 \pm 2.91^\dagger$
18.0 ± 1.7	7.10 ± 4.07	4.65 ± 2.80	2.47 ± 1.98
24.8 ± 0.4	6.76 ± 2.79	$4.32 \pm 1.18^\dagger$	$2.83 \pm 2.12^\dagger$
48.6 ± 1.4	5.45 ± 1.40	3.88 ± 1.24	1.57 ± 0.83
90.8 ± 8.2	4.10 ± 1.09	3.09 ± 0.74	1.00 ± 0.57
131.8 ± 2.0	4.04 ± 1.24	$2.69 \pm 1.17^\dagger$	$1.27 \pm 0.59^\dagger$

*. Values of R_T and R_w at f 18 and greater differ significantly from those at f 10 ($p < 0.025$). Values of R_L at f 90.8 and f 131.8 differ significantly from those at f 18 ($p = 0.050$).

† Indicates eight subjects only; other values are the mean and standard deviation for nine subjects.

TABLE IV
Respiratory impedances at a series of frequencies

Frequency	Total thoracic (Z_T)	Pulmonary (Z_L)	Chest wall (Z_W)
<i>cycles/min</i>	<i>cm H₂O/L/sec</i>	<i>cm H₂O/L/sec</i>	<i>cm H₂O/L/sec</i>
10.0 ± 0.0	16.7 ± 9.1	10.3 ± 4.4*	7.3 ± 5.2*
18.0 ± 1.7	9.8 ± 3.5	6.0 ± 1.7	3.9 ± 2.3
24.8 ± 0.4	9.6 ± 3.1	5.6 ± 1.5	4.0 ± 2.4
48.6 ± 1.4	7.2 ± 1.6	4.6 ± 1.3	2.6 ± 1.0
90.8 ± 8.2	5.5 ± 1.5	3.9 ± 1.2	1.7 ± 0.4
131.9 ± 2.0	5.0 ± 1.5	3.2 ± 1.4	1.7 ± 0.7

* Indicates eight subjects only; other values are the mean and standard deviation for nine subjects.

Results

The total thoracic, pulmonary, and chest wall compliances are plotted against frequency in Figure 2. In general the compliances decrease as frequency increases. The mean values for the group at each frequency are summarized in Table II. The compliances at f 18.0 and f 24.8 were not significantly different from those at f 10 ($p > 0.200$). At f 48.6 and greater, the mean compliances differ significantly from those at f 10 ($p > 0.025$).

The total thoracic, pulmonary, and chest wall resistances are plotted against frequency in Figure 3. In general the resistances decrease with increasing frequency. The mean values at each frequency are presented in Table III. Values of R_T and R_W at f 18 and greater differ significantly from those at f 10 ($p < 0.025$). Values of R_L at f 90.8 and f 131.9 differ significantly from those at f 18 ($p = 0.050$). The mean values of total thoracic (Z_T), pulmonary (Z_L), and chest wall (Z_W) impedance are presented in Table IV.

The mean and standard deviation of the phase angle (θ) between pressure and flow, total thoracic

time constant ($R_T C_T$), and the total thoracic compliance ($C_{T\theta}$ calculated from Equation 1) are presented in Table V. All vary inversely with frequency. $C_{T\theta}$ and C_T differ significantly ($p < 0.05$) at f 10, f 18.4, and f 24.8. The values are not different at the higher frequencies ($p > 0.5$) (Tables II and V).

Discussion

The method of measuring total thoracic compliance by cycling pressure around the thorax depends upon the ability of the subject to relax for 10 to 20 seconds and be passively ventilated. Each interval of pressure cycling started as an inspiration from the resting FRC. Since the piston reached its desired speed almost instantaneously, data could be obtained after the first few seconds while the subject was still relaxed from the previous passive expiration. When a subject failed to relax, it was evident from nonsinusoidal irregular flow patterns, changing phase angles, or transpulmonary pressures that exceeded the driving pressure. Of 13 subjects studied four were discarded for these reasons. Records of the remaining nine

TABLE V
Respiratory phase angle, total thoracic compliance, and time constants at a series of frequencies*

Frequency	Phase angle (θ)	Total thoracic compliance ($C_{T\theta}$)	Time constant† ($R_T C_{T\theta}$)	Time constant‡ ($R_T C_T$)
<i>cycles/min</i>	<i>degrees</i>	<i>L/cm H₂O</i>	<i>seconds</i>	<i>seconds</i>
10.0 ± 0.0	46.4 ± 14.2	0.094 ± 0.024	1.04 ± 0.66	0.95 ± 0.59
18.0 ± 1.7	42.5 ± 10.1	0.093 ± 0.023	0.64 ± 0.29	0.55 ± 0.30
24.8 ± 0.4	38.5 ± 9.5	0.082 ± 0.024	0.54 ± 0.18	0.47 ± 0.19
48.6 ± 1.4	32.8 ± 6.4	0.061 ± 0.020	0.32 ± 0.08	0.31 ± 0.09
90.8 ± 8.2	29.8 ± 4.8	0.049 ± 0.015	0.18 ± 0.08	0.17 ± 0.04
131.9 ± 2.0	28.1 ± 7.2	0.040 ± 0.025	0.15 ± 0.04	0.16 ± 0.06

* Values are the mean and standard deviation for nine subjects.

† Time constant calculated directly from the phase angle using Equation 1.

‡ Time constant calculated from the product of the separately calculated resistance and compliance.

subjects revealed no evidence of voluntary respiratory activity, although the possibility that the observed changes in C_T are in part due to failure to relax cannot be excluded.

In so far as intraesophageal pressure changes differ from intrapleural pressure changes, the division of total thoracic resistance, compliance, and impedance into that due to lung and that due to chest wall will be in error (7). Daly and Bonduant (8) have shown that phase shifts between intraesophageal and intrapleural pressure are small. This suggests that modification of phase or amplitude of intrapleural pressure by the esophagus is not a source of large error in the division of total thoracic compliance, resistance, and impedance into its components.

Milic-Emili, Mead, Turner, and Glauser (9) have shown that balloon volume is a determinant of apparent esophageal pressure measured at the extremes of the vital capacity. In the present study inspiration was started from the FRC, which in these subjects represented approximately 38% of vital capacity, and tidal volumes were such that a level of 60% of vital capacity was seldom reached. The balloon contained 1.0 ml of air. The data of Milic-Emili and associates indicate that within this range of lung volume change, the observed pressure changes in the balloon are reliable measurements of intrapleural pressure changes. The 15-cm balloon used in the present study was placed with the balloon tip 35 cm from the nares. This avoided the lower one-third of the esophagus and its pressure artifacts. However, the top of the balloon extended into the upper third of the esophagus, in which tracheal artifacts are present upon movement of the head and neck, tracheal compression, or change in body position (10). These artifacts should not be significant in the present study, since the subjects were held in a fixed position during the experiment by the neckpiece and mouthpiece.

Determinations of dynamic compliance are based upon the assumption that accelerative pressures are negligible and hence the pressures at instants of zero air flow relate solely to the elastic recoil of the lungs and thorax. As Sharp and co-workers have pointed out, in normal subjects breathing quietly, accelerations of 2 to 10 L per second squared are encountered; these accelerations would require pressures of only 0.02 to 0.10 cm H₂O,

calculated from the observed value of total thoracic inertance of 0.0098 cm H₂O per L per second squared (11). Thus at low frequencies, inertance should have little influence on the determination of dynamic compliance. At higher frequencies larger accelerations are found. In the present study at frequencies of 130 cycles per minute accelerations of about 40 to 50 L per second squared were present. If inertance is constant as frequency increases, these accelerations would require pressures of 0.4 to 0.5 cm H₂O. Pressures of this magnitude would affect the current results slightly. One subject whose acceleration was 50 L per second squared at 130 cycles per minute had a calculated C_T of 0.030 L per cm H₂O. If corrected for inertance, the C_T would be 0.029 L per cm H₂O. Jaeger and Otis (12) have pointed out that an observed shift of dynamic compliance with frequency may be considered as the result of two opposing factors, i.e., the effect of unequal ventilation causing decreased compliance and the effect of inertance making dynamic compliance appear larger.

In the present study resonant frequencies were not reached, even at the highest frequency of 2.2 cps. Sharp and co-workers (11) determined the mean resonant frequency of eight normal subjects to be 5.0 cps.

The compliance values C_T , C_L , and C_W reported here at a frequency of 10 cycles per minute are similar to values previously reported in studies in which all three were measured (Table VI). C_L has not been measured over a wide range of frequencies by the pressure cycling method. C_L has been reported by several observers (1, 4, 5, 21) to remain constant in normal subjects during spontaneous breathing at increasing frequencies. All of the nine healthy elderly subjects reported by Frank and co-workers (3) showed small decreases in pulmonary compliance from a mean of 0.120 L per cm H₂O at an average of 15.3 respirations per minute to 0.101 L per cm H₂O at 49.2 respirations per minute. Peslin, Saunier, LaCoste, and Sadoul (22), in nine normal young adults, found mean elastance of 4.2, 5.31, 7.1, and 11 cm H₂O per L at 0 to 10, 10 to 20, 20 to 30, and 30 respirations per minute, respectively. In a study of 100 normal subjects Defares and Donleben (2) found a "small number" in whom C_L fell with increasing frequency. In the four with the most marked change

TABLE VI
Total thoracic (C_T), pulmonary (C_L), and chest wall (C_W) compliance in normal human subjects

Author	Reference	Subjects	Method	C_T	C_L	C_W
				<i>L/cm H₂O</i>	<i>L/cm H₂O</i>	<i>L/cm H₂O</i>
Butler and Smith	(13)	33	Relaxation	0.086	0.159*	0.213
Knowles, Hong, and Rahn	(14)	4	Relaxation	0.086*	0.221*	0.170*
McIlroy, Tierney, and Nadel	(15)	12	Time constant	0.080	0.212	0.176
Heaf and Prime	(16)	9	Pressure breathing	0.093	0.191	0.189
Naimark and Cherniak	(17)	24	Pressure breathing	0.119	0.283	0.224
Cherniak and Hodson	(18)	9	Pressure breathing	0.110	0.282	0.221
Ferris, Mead, Wittenberger, and Saxton	(19)	2	Pressure cycling†	0.098	0.260	0.186
Bergofsky, Turino, and Fishman	(20)	2	Pressure cycling†	0.112	0.194	0.289
Sharp and associates	(11)	8	Pressure breathing	0.104	0.214	0.211
Present work		9	Pressure cycling†	0.084	0.164	0.197

* Calculated from author's data from 0- to 1.0-L volume.

† Measured during relaxation as transthoracic pressure was mechanically cycled.

C_L fell from a mean of 0.21 at zero to 0.06 L per cm H₂O at 60 cycles per minute, but all four had linear semilog nitrogen washout curves. Defares concluded on mathematical and experimental grounds that frequency dependent pulmonary compliance does not invariably indicate unequal ventilation.

In the present study a significant decrease ($p < 0.025$) in C_L was observed at frequencies of 48 cycles per minute and greater. It is unlikely that this decrease was due to alveolar closure because the cycling runs were very brief at the rapid frequencies, and the subjects performed a maximal inspiration before each trial. Furthermore, each run started as an inspiration from the normal and expiratory level, and as recorded by the volume tracing, there were no significant shifts in FRC during the cycling. The tidal volume decreased as frequency increased; this alone should not have caused the marked falls in compliance, as the experiments were run on the relatively linear part of the pressure volume curves of the lungs and thorax. Total thoracic and chest wall compliance were also found to vary inversely with frequency. If the present analog is appropriate for the chest wall, these observations suggest that the chest wall of normal subjects is composed of elements that have different time constants, a concept consistent with its structure and geometry.

Calculation of the C_T from the phase angle between pressure and flow has not been previously reported although Miller and Simmons (23) have used the theory to determine C_L . If the wave forms are purely sinusoidal and if the resistance,

frequency, and phase angle are accurately determined, C_T calculated from pressure and volume measurements will be equal to $C_{T\theta}$ calculated from phase angle measurements. Although in this study the results (Table II and Table V) are similar, there are significant differences at the lower frequencies. This may be due to the fact that flow departed somewhat from a sine wave at low frequencies, whereas at high frequencies it followed a sine wave quite closely.

Attinger and co-workers (4) estimated R_L during a respiratory cycle by subtracting the elastic component of transpulmonary pressure from total transpulmonary pressure at 0.04- to 0.10-second intervals and dividing by the instantaneous flow. In the present study, the respective pressures and flows are integrated and then divided to give a resistance for the whole cycle. Since resistance varies appreciably during the respiratory cycle, the latter value is more appropriate to use in calculations depending upon equations drawn from sinusoidal electrical circuits. In the present study R_T , R_L , and R_W all decreased with increasing frequency. The average flow rate was not constant; however, Mead and Wittenberger (24) have shown that, except at near maximal expiratory efforts, pulmonary resistance is not appreciably altered by changing flow rates. In seven normal subjects they found a mean pulmonary resistance of approximately 2.1 cm H₂O per L per second at a flow rate of 1 L per second and 2.3 cm H₂O per L per second at a flow rate of 2 L per second.

The lungs and the chest wall may each be considered as multiple parallel pathways, each path-

way containing a compliance and resistance element connected in series. Otis and co-workers (1) have shown that in sinusoidally driven ventilatory systems, if the time constants of the parallel pathways are equal, the effective compliance and resistance will be independent of frequency. If the time constants are unequal, the effective compliance and resistance will decrease with increasing frequency. The pulmonary and chest wall compliances and resistances presented here follow the prediction of Otis and co-workers for a multipathway system of unequal time constants, i.e., the effective resistance and compliance decreased with increasing frequency. Since the chest wall and lungs act in series, a decrease in pulmonary and chest wall compliance and resistance will be accompanied by a decrease in total thoracic compliance and resistance.

In a resistive-elastic system driven by a sinusoidal pressure, the magnitude of the air flow is determined by the impedance, Z , and the maximal pressure change, ΔP . Thus:

$$\dot{V}_m = \Delta P / Z, \quad [3]$$

where $\dot{V}_m$ equals maximal flow rate. Impedance may further be expressed by the equation:

$$Z = \sqrt{R^2 + (1/2\pi fc)^2}. \quad [4]$$

From the latter equation it is apparent that as the frequency increases, the term $(1/2\pi fc)^2$ approaches zero and the impedance approaches the flow resistance. In the present study Z_T approaches R_T as frequency increases (Tables III and IV). Mead (25) modified the method of DuBois, Brody, Lewis, and Burgess (26) and estimated the total respiratory resistance by applying sinusoidally varying pressures at 3 to 7 cycles per second and measuring the flow rate. By Equation 3 Z_T is obtained which at this frequency approaches the resistance (R_T). Mead obtained a mean Z_T of 5.5 cm H₂O per L per second, DuBois and co-workers obtained a mean Z_T of 4.6 at 5.8 cycles per second, and Brody and co-workers (27) obtained a Z_T of approximately 3.0 at 10 cycles per second. These values compare with a Z_T of 5.0 cm H₂O per L per second at 2.2 cycles per second found in the present study.

As frequency increases, pulmonary and chest wall impedances decrease and approach their respective resistances (Tables III and IV). These

impedances could be used as an estimate of pulmonary and chest wall resistance as Z_T is used to approximate R_T at high frequencies.

The phase angle between pressure and flow observed in the present study (Table V) is similar to those reported by DuBois and co-workers (26). The phase angle at any given frequency is a function of the effective time constant of the system at that frequency. Total thoracic time constants ($R_T C_T$) have been reported by McIlroy, Tierney, and Nadel (15), who calculated $R_T C_T$ directly from plots of volume change against flow during a relaxed expiration. It is not possible to state exactly what frequency this represents. The $R_T C_T$ reported here were calculated at each frequency directly from the phase angle θ by Equation 1. At each frequency in this study the results are similar to time constants calculated from the product of the separately determined R_T and C_T (Table V). The $R_T C_T$ reported here are the effective time constants of the whole system. The fact that the effective time constants decrease with increasing frequency implies that the separate pathways have different time constants.

The respiratory system is composed of many elements of different composition arranged in a complex heterogeneous network. It appears unlikely that even in normal subjects the different pathways of such a system could have the same time constant, although the differences are not apparent when a narrow range of frequencies is examined.

Frequency dependent compliance and resistance are important determining factors in the selection of natural breathing frequency, work of breathing, and distribution of pulmonary ventilation. In the diseases in which time constants of the separate pathways are widely variant, frequency dependence is more marked and is probably of even greater significance.

Summary

The effect of respiratory frequency on pulmonary mechanics was studied systematically in nine healthy subjects who sat in a body plethysmograph with the head protruding while respiration was driven by sinusoidal plethysmograph pressures at a series of frequencies from 10 to 132 cycles per minute.

The total thoracic, pulmonary, and chest wall

compliances and resistances varied inversely with frequency of respiration. The variations are not significant over a narrow range of frequencies. The total thoracic, pulmonary, and chest wall impedances varied inversely with frequency and approached their respective resistances as frequency increased. The phase angle between pressure and flow and the time constant also varied inversely with frequency. The absolute values are generally consistent with previous limited observation at isolated frequencies or observations over a smaller range of frequencies.

The data presented here support the concept that compliance and resistance are frequency dependent even in normal subjects.

References

- Otis, A. B., C. B. McKerrow, R. A. Bartlett, J. Mead, M. B. McLroy, N. J. Silverstone, and E. P. Radford. Mechanical factors in distribution of pulmonary ventilation. *J. appl. Physiol.* 1956, **8**, 427.
- Defares, J. G., and P. G. Donleben. Relationship between frequency-dependent compliance and unequal ventilation. *J. appl. Physiol.* 1960, **15**, 166.
- Frank, N. R., J. Mead, and B. G. Ferris, Jr. The mechanical behavior of the lungs in healthy elderly persons. *J. clin. Invest.* 1957, **36**, 1680.
- Attinger, E. O., R. G. Monroe, and M. S. Segal. The mechanics of breathing in different body positions. I. In normal subjects. *J. clin. Invest.* 1956, **35**, 904.
- Cherniack, R. M. The physical properties of the lung in chronic obstructive pulmonary emphysema. *J. clin. Invest.* 1956, **35**, 394.
- Mainland, D. *Elementary Medical Statistics*, 2nd ed. Philadelphia, W. B. Saunders, 1963, p. 48.
- Clements, J. A., J. T. Sharp, R. P. Johnson, and J. O. Elam. Estimation of pulmonary resistance by repetitive interruption of airflow. *J. clin. Invest.* 1959, **38**, 1262.
- Daly, W. J., and S. Bondurant. Direct measurement of respiratory pleural pressure changes in normal man. *J. appl. Physiol.* 1963, **18**, 513.
- Milic-Emili, J., J. Mead, J. M. Turner, and E. M. Glauser. Improved technique for estimating pleural pressure from esophageal balloons. *J. appl. Physiol.* 1964, **19**, 207.
- Milic-Emili, J., J. Mead, and J. M. Turner. Topography of esophageal pressure as a function of posture in man. *J. appl. Physiol.* 1964, **19**, 212.
- Sharp, J. T., J. P. Henry, S. K. Sweany, W. R. Meadows, and R. J. Pietras. The total work of breathing in normal and obese men. *J. clin. Invest.* 1964, **43**, 728.
- Jaeger, M. J., and A. B. Otis. Measurement of airway resistance with a volume displacement body plethysmograph. *J. appl. Physiol.* 1964, **19**, 813.
- Butler, J., and B. H. Smith. Pressure-volume relationships of the chest in the completely relaxed anesthetized patient. *Clin. Sci.* 1957, **16**, 125.
- Knowles, J. H., S. K. Hong, and H. Rahn. Possible errors using esophageal balloon in determination of pressure-volume characteristics of the lung and thoracic cage. *J. appl. Physiol.* 1959, **14**, 525.
- McLroy, M. B., D. F. Tierney, and J. A. Nadel. A new method for measurement of compliance and resistance of lungs and thorax. *J. appl. Physiol.* 1963, **18**, 424.
- Heaf, P. J. D., and F. J. Prime. The compliance of the thorax in normal human subjects. *Clin. Sci.* 1956, **15**, 319.
- Naimark, A., and R. M. Cherniack. Compliance of the respiratory system and its components in health and obesity. *J. appl. Physiol.* 1960, **15**, 377.
- Cherniack, R. M., and A. Hodson. Compliance of the chest wall in chronic bronchitis and emphysema. *J. appl. Physiol.* 1963, **18**, 707.
- Ferris, B. G., Jr., J. Mead, J. L. Wittenberger, and G. A. Saxton, Jr. Pulmonary function in convalescent poliomyelitis patients. III. Compliance of the lungs and thorax. *New Engl. J. Med.* 1952, **247**, 390.
- Bergofsky, E. H., G. M. Turino, and A. P. Fishman. Cardiorespiratory failure in kyphoscoliosis. *Medicine (Baltimore)* 1959, **38**, 263.
- Otis, A. B., W. O. Fenn, and H. Rahn. Mechanics of breathing. *J. appl. Physiol.* 1952, **2**, 592.
- Peslin, R., C. Saunier, J. LaCoste, and P. Sadoul. Variations of pulmonary elasticity in the function of respiratory frequency in normal man. *C. R. Soc. Biol. (Paris)* 1961, **155**, 1106.
- Miller, J. H., and D. H. Simmons. Rapid determination of dynamic pulmonary compliance and resistance. *J. appl. Physiol.* 1960, **15**, 967.
- Mead, J., and J. L. Wittenberger. Physical properties of human lungs measured during spontaneous respiration. *J. appl. Physiol.* 1953, **5**, 779.
- Mead, J. Control of respiratory frequency. *J. appl. Physiol.* 1960, **15**, 325.
- DuBois, A. B., A. W. Brody, D. H. Lewis, and B. F. Burgess, Jr. Oscillation mechanics of lungs and chest in man. *J. appl. Physiol.* 1956, **8**, 587.
- Brody, A. W., P. S. O'Halloran, H. J. Wander, J. J. Connolly, Jr., E. E. Roley, and E. Kobold. Ventilatory mechanics and strength: long-term re-examinations and position change. *J. appl. Physiol.* 1960, **15**, 561.