STUDIES OF RESPIRATORY PHYSIOLOGY IN THE NEWBORN INFANT. III. MEASUREMENTS OF MECHANICS OF RESPIRATION¹

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Considerable attention has recently been focused on the mechanical factors in respiration of normal adults and of those with respiratory abnormalities. This report presents observations on the mechanics of respiration in 23 normal newborn infants and 2 infants critically ill with neonatal respiratory distress. The data are derived from simultaneous measurements of tidal volume and intraesophageal pressure changes.

MATERIAL AND METHODS

The infants, all of whom were born at the Boston Lying-in Hospital, weighed from 2.4 to 3.8 Kg. at birth and were from 1 hour to 7 days old at the time of study. History, physical examination and, in most cases, chest x-rays were used to determine presence or absence of respiratory distress. On the basis of observation and previously established criteria (1), 18 of the normal infants were considered to have been studied during periods of quiet, resting respiration. In all, 47 studies were made on 28⁵ newborn infants ranging from the 18 infants breathing quietly to those who were sick or disturbed by the procedure. The respiratory rates varied from 24 to 136 per minute.

The two infants studied when critically ill and during recovery were diagnosed as having the neonatal respiratory distress syndrome. This syndrome, which is also called the hyaline membrane syndrome or resorption atelectasis, is characterized by a history of premature birth, cesarean section, fetal distress, or maternal diabetes and the clinical picture of increasing respiratory difficulty, cyanosis, and frequently typical x-ray findings (2).

The infants were placed in a 65-liter body plethysmograph (Figure 1) with their faces emerging through a pneumatic cuff. Pressure changes within the plethysmograph for an average respiration were approximately 0.3 cm. H₂O and were measured by an electrical manometer (3). With a calibrated syringe and pump, breathing was simulated and the pressure changes were calibrated in terms of volume. Although this calibration was performed after the infant was removed, the resulting error was less than 5 per cent and was therefore not taken into consideration in the calculation. Intraesophageal pressure changes as indices of intrapleural pressure changes were measured with a small water-filled polyethylene catheter (internal diameter 1.0 mm.) passed 10 to 11 cm. through the nose or mouth into the esophagus and connected to a second manometer 6 calibrated in cm. H₂O. When inserted to this distance, the open catheter tip was shown by x-ray of two infants to be at the junction of the middle and upper thirds of the esophagus. Volume and pressure were recorded simultaneously on a direct-writing oscillograph.6

Pulmonary compliance was expressed as the ratio of tidal volume to the change in intraesophageal pressure measured between points of no flow, *i.e.*, at the extremes of tidal volume (Figure 2). Respiratory resistance was measured as the ratio of the total pressure change to the corresponding total flow change between points of equal volume approximately midway in inspiration and expiration (Figure 3). This calculation of resistance has provided a satisfactory approximation of the average flow-resistance of the lungs and air passages during the respiratory cycle in adults (4). The average compliances of the individual infants were calculated from 10 to 20 representative respirations and average resistances from 5 to 10 respirations (Table I).

From the simultaneous recordings of pressure and volume, pressure-volume loops for the respiratory cycle were plotted and from 3 to 6 representative breaths a graphic solution of average work done on the lungs per breath was obtained 7 (Figure 4). As indicated in the

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⁶ Although the data are not included in Table I, determinations of work of respiration of one newborn with congenital heart disease and two with borderline respiratory distress are included in Figures 7 and 8 for comparison of the three methods used to calculate pulmonary work.

⁶ An electromanometer and the Polyviso made by Sanborn Company, Cambridge, Massachusetts, were used.

⁷ As pointed out in the discussion, these measurements do not allow calculation of *total* "work done on the lungs" but do allow an apparently adequate approximation.

a - Pneumatic cuff

- b-Intraesophageal catheter
- c Stopcocks
- d-Krogh spirometer
- e-Tidal and minute volumes
- f Electric timer
- g-Kymograph
- h-Electrical manometer i - Calibration-syringe and pump





FIG. 1. DIAGRAM OF APPARATUS USED FOR RESPIRATORY STUDIES With the stopcock to the spirometer closed, the apparatus was used as a pressure plethysmograph. With the stopcock open to the spirometer, minute

volume was recorded with a photoelectric integrator (1).

diagram, this method of measuring work allows separation of pulmonary work into elastic and flow-resistive components. For purposes of comparison, pulmonary work for the same respirations was also estimated, using two formulae:

1. A simplified formula was suggested by one of the authors, (M. B. McI.), as a possibly adequate approximation of work done on the lungs during inspiration and expiration.

Work (in gm. cm. per min.) = 0.6 PV,

where $P = \text{total pressure change in cm. H}_2O$ during the respiratory cycle.

 \dot{V} = minute volume in ml.



Fig. 2. Method of Calculating Pulmonary Compliance

As shown in this diagrammatic representation of simultaneous pressure and volume recordings, compliance (C) is expressed as the ratio of tidal volume (V_T) to the change in intraesophageal pressure $(P_{\bullet 1})$ measured between points of no flow, *i.e.*, at the extremes of tidal volume. This formula is based on the fact that, if the intraesophageal pressure is represented by a sine wave, purely elastic work would be represented by the formula 0.5 $P\dot{V}$ (the area of a triangle), purely viscous work by the formula 0.79 $P\dot{V}$ (the area of an ellipse), and the fact that approximately 70 per cent of pulmonary work in normal adult respiration is elastic (5).⁸



FIG. 3. METHOD OF CALCULATING FLOW RESISTANCE

Respiratory resistance (R) is measured as the ratio of total pressure change (P_R) to the corresponding total flow change ($\nabla_{insp} + \nabla_{oxp}$) between points of equal volume (points a and b). Total flow change between points a and b was obtained by measuring the slopes (lines I and II) of the volume curve at these points.

⁸ The expression 0.6 PV should not be confused with the expression 0.7 PmaxV used by McIlroy and Eldridge (6) to obtain an approximation to the work of inspiration. In that case Pmax was the maximum pressure difference during inspiration. In the expression 0.6 PV used in this paper, P is the total intrathoracic pressure swing.

TABLE I

Data from studies on the mechanics of respiration in 23 normal newborn infants

No.	Birth wt. Kg.	Age	Resp. rate per min.	Tidal vol. <i>ml</i> .	ΔIEP [*] cm. H ₂ O	Com- pliance mean ml./cm. H ₁ O	Resistance mean cm. H ₂ O/ L./sec.	e Work per breath† gm. cm.	Work per minute† gm. cm.	% Elastic work†	Comments
P-30	3.7	6 d.	39	29	12.6	3.8	79	217	8,460	51	Restless
P-31	3.1	3 d.	44	16	2.9	9.1	13	20	885	70	Quiett
P-32	2.8	9 hr.	41	13	4.4	3.4	28	33	1.350	76	Õuiet
P-33	3.1	11 hr.	42	15	5.4	4.3	24	36	1.490	74	ÕuietI
P-33		6 d.	38	19	8.3	3.2	49	84	3,190	67	Restless
P-34	2.4	15 hr.	54	13	6.1	2.6	53	53	2,860	62	Ouiet-not basal
P-34		38 hr.	77	11	6.1	4.4	43	30	2,310	46	Restless
P-34		7 d.	40	24	12.4	4.0	70	139	5,560	52	Restless
P-35	3.8	8 hr.	70	14	5.0	3.4	25	43	3,010	67	Ouiet-not basal
P-38	2.4	10 hr.	51	9	5.4	4.6	45	17	840	53	Õuiet1
P-39	3.4	5 d.	51	15	8.4	4.1	50	51	2,600	54	Restless
P-41	3.0	2 d.	40	15	5.4	5.8	40	34	1,360	57	Ouiet 1
P-42	3.5	3 d.	31	21	4.5	7.1	42	55	1,700	57	Õuiet‡
P-43	3.6	2 hr.	28	20	10.4	3.8	131	113	3,160	47	Õuiet
P-43		4 hr.	48	15	4.1	5.1	18	30	1,445	73	Õuiet‡
P-44	2.7	12 hr.	38	14	5.5	3.9	45	39	1,480	65	Õuiet‡
P-45	2.9	16 hr.	24	25	5.3	9.3	43	60	1,440	56	Õuiet‡
P-47	2.5	4 hr.	35	11	3.3	4.0	24	19	675	78	Quiet‡
P-47		22 hr.	136	10	3.2	3.2	25	30	4,080	52	Restless
P-48	2.8	3 hr.	42	16	5.6	3.7	21	44	1,850	79	Quiet-not basal
P-48		22 hr.	37	18	2.9	8.6	7	22	810	85	Quiet‡
P-49	3.0	2 d.	41	18	4.5	7.4	17	31	1,270	71	Restless
P-51	3.3	1 hr.	44	13	7.7	2.2	7	60	2,635	64	Quiet‡
P-51		23 hr.	66	12	5.3	3.7	24	29	1,910	67	Restless
P-53	3.5	8 hr.	57	14	4.0	5.4	13	24	1,370	75	Restless
P-53		2 d.	49	12	5.2	2.5	36	39	1,925	73	Quiet‡
P-53		3 d.	98	28	5.9	6.8	22	126	12,100	46	Very restless
P-53		6 d.	53	15	4.6	4.6	32	40	2,120	61	Restless
P-54	3.1	21 hr.	29	21	3.9	7.9	13	35	1,020	80	Quiet
P-54		2 d.	25	19	5.2	6.9	21	34	850	77	Quiet‡
P-54		6 d.	27	24	5.5	7.1	37	64	1,700	63	Quiet
P-55	3.5	2 d.	64	13	6.7	5.9	75	48	3,070	30	Restless
P-55		3 d.	35	19	5.3	4.9	35	55	1,925	67	Quiet‡
P-56	2.9	6 hr.	30	16	7.0	3.4	19	44	1,310	86	Quiet‡
P-56		30 hr.	37	15	9.8	3.3	80	62	2,300	55	Restless
P-56		3 d.	51	15	5.5	3.1	41	56	2,840	65	Quiet-not basal
P-57	3.1	13 hr.	31	18	5.8	4.8	39	50	1,545	68	Quiet‡
P-60	2.8	6 d.	31	15	5.4	3.9	33	38	1,190	75	Quiet‡
Ave. all obs.	3.1					4.9					
Ave. 18 quiet infants	3.0		38	16	5.0	5.2 (S.E. ±0.4)§	29 (S.E. ±4)§	38	1,380	70	

* AIEP is the average of differences between maximal and minimal pressures occurring with each respiratory cycle

during periods of quiet breathing.
† Work per breath and per minute and per cent of work against elastic forces have been calculated from the simplified formula of Otis, Fenn, and Rahn (7).
† These 18 studies on 18 different infants were used for obtaining average values for quiet respiration.
§ S.E. = standard error of the mean of a series of 10 individual compliances or resistances. The standard deviation of a single determination was ±1.28 ml. per cm. H₂O for compliance and ±11 cm. H₂O per L. per sec. for resistance. These large individual variations are apparently due to the artifact in pressure recording introduced by the cardiac impulse.

2. Work was also calculated by substituting the determined elastic and resistive factors and tidal volume and respiratory rate in the formula of Otis, Fenn, and Rahn (7). In doing this, it was necessary to assume that the second order resistive factors were negligible. Thus the formula actually used was:

where $K_{e1} = \frac{1}{\text{compliance}}$ with compliance expressed as ml. per cm. H₂O

 V_T = tidal volume in ml.

f = breaths per min.

Work (in gm. cm. per min.) $= \frac{1}{2} f K_{e1} (V_T)^2 + \frac{1}{2} K_r \pi^2 f^2 (V_T)^2,$

 K_r = resistance in cm. H₂O per ml. per min.

Since in some infants the introduction of the intraesophageal catheter was followed by an increase in respiratory rate, the minute volume, rate, and tidal volume were obtained in most cases before or after the catheter was in place, utilizing a previously described technique for recording rate and minute volume (1) (see Figure 1). The resting rate and tidal volume were used in the simplified Otis formula for calculating the pulmonary work of the 18 quiet infants. Since these 18 infants had, when breathing quietly, an average respiratory rate of 38 per minute and an average minute volume of 570 ml. compared to 33 and 550 observed in another group of resting infants of comparable size (1), it was assumed that the average calculated pulmonary work per minute of these 18 infants approximated that of newborn infants in this weight range.

RESULTS

The results of the individual studies on normal infants are presented in Table I. The 23 normal infants averaged 3 Kg. in weight. The average tidal volume of the quiet infants was 16 ml. (range 9 to 25). Peak flow rates for individual infants averaged 61 ml. per sec. (range 44 to 111 ml. per sec.) during quiet respiration. The average compliance from 38 studies on the 23 normal infants was 4.9 ml. per cm. H₂O and for the 18 resting infants was essentially the same (5.2 ml. per cm. H₂O). Although there was considerable variability in both compliance and resistance determinations from breath to breath due to the cardiac component of the pressure recording, the standard error of the mean of a series of 10 compliances was only ± 0.4 ml. per cm. H₂O. The mean resistance was 29 cm. H₂O per L. per sec. (standard error of the mean of a series of $10 = \pm 4$ cm. H₂O per L. per sec.) for these 18 infants and the calculated average work done on the lungs was 1380 gm. cm. per min. In spite of occasional discrepancies, the proportion of work done against



FIG. 4. DIAGRAMMATIC AVERAGE NORMAL PRESSURE-VOLUME RESPIRATORY LOOP

Elastic work is represented by area of triangle ABC. Inspiratory and expiratory flow-resistive work are represented by areas I and II, respectively. Assuming that expiration is passive, total pulmonary work is represented by the sum of the elastic work (triangle ABC) plus the inspiratory flow-resistive work (area I).

elastic forces estimated from the pressure-volume diagram and from the Otis formula showed on the average a close correlation, being 71 and 70 per cent, respectively. As was expected, pulmonary work was greater in the restless infants primarily because of increases in respiratory rates. In the present study no significant relation between weight or age and compliance or resistance could be demonstrated, presumably because of the relatively small number of infants studied and the narrow weight and age range.

Data from serial observations on two infants severely ill with neonatal respiratory distress are

No.	Birth wt. (Kg.)	Age	IEP* (cm. H ₂ O)	Compliance (ml./cm. H ₂ O)		Resistance (cm. H ₂ O/L./sec.)		Work	Work per	Per cent	
				Mean	Range	Mean	Range	(gm. cm.)	(gm. cm.)	work†	Comments
P-40 P-40	3.0	2 d.	16.3	1.3	1.3-1.5	25	22-29	144	7,900	89 80	Severely ill
P-50 P-50 P-50	3.2	5 hr. 2 d. 10 d.	20.0 20.8 7.7	0.7 1.0 2.5	0.6-0.8 0.8-1.3 2.2-3.0	41 13 39	0-104‡ 0-27‡ 18-65	107 176 64	5,130 7,400 3.160	71 84 73	Severely ill Recovering

TABLE II Data on the mechanics of respiration in two infants with neonatal respiratory distress

* IEP is the average of differences between maximal and minimal pressures occurring with each respiratory cycle. † Pulmonary work per breath and per minute and per cent elastic work were estimated directly from the graphic pressure-volume loops for these two sick infants.

‡ Resistance calculated only on inspiration because of grunting expiration.



FIG. 5. PRESSURE-VOLUME LOOPS FOR INFANT WITH RESPIRATORY DISTRESS The marked increase in pulmonary work during respiratory distress is apparent. There is no increase in inspiratory flow resistance although the expiratory flow resistance is increased as a result of the grunting respiration.

shown in Table II. A typical pressure-volume loop for one of the infants during severe distress and a second loop during recovery are shown in Figure 5. These infants have, in contrast to normal newborn infants, a marked decrease in pulmonary compliance to 15 to 20 per cent of normal. Because of this and an increased respiratory rate, the work of respiration is increased by more than 400 per cent.

DISCUSSION

As in the one other report on the mechanics of breathing in newborn infants (8), the present data and calculations have been based on the assumption that intraesophageal pressure changes were reliable indices of intrapleural pressure changes. Although this concept has been based on studies in adults, the technique has a number of limitations in adults as well as newborn infants.

Data of Cherniack, Farhi, Armstrong, and Proctor (9) show that this indirect technique does not provide a reliable measure of absolute intrapleural pressure even in adults. However, their data indicate that pressure changes determined directly and indirectly during quiet breathing were on the average comparable. Secondly, recent work has shown that both intrapleural and intraesophageal pressure changes are influenced by the position of the patient, being more reliable and consistent in the upright position than in the supine (10). This position factor may or may not be applicable to studies in the newborn. In any case it would be difficult to study infants in any other than a supine position.

One further source of error may be related to the use of a water-filled catheter rather than an air-filled balloon. In a comparative study, Mead, McIlroy, Selverstone, and Kriete (11) have shown that the balloon is superior but the differences were least in the upper portion of the esophagus. In

TABLE III Average data on mechanics of respiration for newborn infants and adults

	In	fant	Adult			
Weight (Kg.)	3.	0	70			
Respiratory rate	38		15			
(per min.)						
Compliance	5.	2(2–9)	170 (Ref. 14)			
(ml./cm. H2O)			-			
Compliance		08	.15			
(per gm. lung)						
Compliance	.065		.063			
$(per \ ml. \ V_{FRC})^*$						
Resistance	29	(7-45)	2 (1-3)(Ref. 17)			
(cm. H ₂ O/L./sec.)						
Pulmonary minute work (gm. cm.)	1,380		15,700†			
Per cent elastic work	71		67†			

* Based on VFRC from references 15 and 16.

† Calculated from simplified formula of Otis, Fenn, and Rahn (7).

the present work, this error was presumably minimized by placing the tip of the catheter in the upper third of the esophagus.

In regard to the pulmonary work calculations, it has been pointed out by Otis (12) that the work represented by the pressure-volume diagram described above is not the total work done on the lungs. To the extent that end-expiratory intrapleural pressure is less than atmospheric, additional elastic work must be done during inspiration. Part of the energy for this additional work is supplied by the elastic recoil of the thorax, and the remainder by the respiratory muscles. A more complete measurement of pulmonary work can be accomplished only if both the absolute intrapleural pressure and the elastic characteristics of the thorax are known.

Obviously, further observations comparing intrapleural and intraesophageal pressure changes in infants and studies of the effect of various factors on these measurements are desirable, but difficult to obtain. Pending these, it seems necessary to assume that intraesophageal pressure measurements are acceptable indices of intrapleural pressure changes in newborn infants, as in small experimental animals (3) and in adults (13).

The data from quiet normal infants (average weight = 3.0 Kg.) have been summarized in Table III and compared with similar observations for adults (14, 17). On a weight basis adult lungs are approximately 18 times as heavy as infant lungs. However, adult lungs are 33 times as compliant. Thus, expressed per kilogram of lung tissue, infant lungs would appear to be less compliant than those of the adult. However, using functional residual volume as a basis of comparison, adult lungs are similar in compliance to those of infants (compliance/FRC ratio = 0.065 in infants and 0.063 in adults).

While comparison of compliance can logically be made on the basis of lung weight or lung volume, adult and infant lung resistances are more difficult to compare. Even the comparative effect on flow resistance of nose-breathing in the infant



FIG. 6. CALCULATED PULMONARY WORK VERSUS RESPIRATORY RATE

Using the present data on mechanics of respiration in newborn infants and previously determined values for respiratory dead space (5.5 ml.) and alveolar ventilation (385 ml.), the theoretical pulmonary work at constant alveolar ventilation was calculated for various respiratory rates from the simplified formula of Otis, Fenn, and Rahn (7). The value used for compliance was 5.2 ml. per cm. H₂O and for resistance was 29 cm. H₂O per L. per sec. The theoretical minimum work of respiration occurs at a rate of 37 per minute.



FIG. 7. PRESSURE-VOLUME DIAGRAM VERSUS SIMPLIFIED FORMULA OF OTIS, FENN, AND RAHN FOR DETERMINATION OF PULMONARY WORK

Work was estimated by the two methods from the same respirations. Using the loop method as the basis for comparison, there was an average difference of -0.6 per cent and standard deviation of ± 11 per cent. If there were perfect agreement in each case, all points would fall on the 45° line.

and mouth-breathing in the adult cannot be properly assessed. The present data have shown that the resistance to air flow in the infant's lungs is only 15 times that of the adult, considerably less than would be expected if infant air passages were reduced in size and length in proportion to weight. More detailed comparison of resistance seems impossible without further accurate knowledge of the many factors involved.

The average pulmonary work during quiet respiration estimated for the hypothetical infant of 3 Kg. is approximately 1 per cent of the total basal metabolism, as in the adult, if the efficiency of the respiratory muscles is assumed to be between 5 and 10 per cent for both age groups (7).

It has been shown by Otis, Fenn, and Rahn (7) that the rate and depth of breathing in normal adults are adjusted with the result that alveolar ventilation is accomplished with the minimum expenditure of total respiratory work. When only pulmonary work was estimated by the pressure-volume method, McIlroy, Marshall, and

Christie (5, 18) have shown a similar adjustment in normal adults during rest and exercise, as well as in patients with heart disease. If previously published data on alveolar ventilation and physiologic dead space (1) are combined with the present information on compliance and resistance, the theoretical minimum of work of respiration in the normal newborn infant occurs at approximately 37 respirations per minute. The average observed resting values were 38 in the present studies compared with 33 in a previous series of observations (1). Figure 6 shows graphically the theoretical work of respiration at various respiratory rates. It is possible that the wide variation in normal respiratory rates recorded for newborn infants is related to the small change in pulmonary work between respiratory rates of 30 and 50 per minute.

In addition to establishing elastic and viscous resistance constants and approximations of the pulmonary work for newborn infants, the present study allowed comparison of the three methods of calculating pulmonary work. The results of these comparisons are shown in Figures 7 and 8. It can be seen that the three methods have a close correlation over the wide range of compliance, resistance, respiratory rate, and tidal volumes observed. Using the graphic solution of the pressure-volume diagram as the basis for comparison, the formula of Otis, Fenn, and Rahn gave an average difference of -0.6 per cent with a standard deviation of ± 11 per cent. This close correlation suggests that second order resistive factors are relatively unimportant in the respiration of newborn infants. On the same basis of comparison, the simplified formula (0.6 PV) differed on the average by -6 per cent and showed a standard deviation of ± 13 per cent. These data show that, at least in infants, pulmonary work can be approximated by application of a simplified Otis formula and even with considerable accuracy on the basis of simple measurements of pressure and volume.

This series of studies on newborn infants was undertaken not only to investigate respiratory physiology, but also to try to delineate the pathophysiology of neonatal respiratory distress. The results of observations on two infants initially studied during severe neonatal respiratory distress (or the hyaline membrane syndrome) and again during recovery have shown that respiratory difficulty of this sort is accompanied by a marked decrease in compliance to 1.3 ml. and to 0.7 ml. per cm. H.O. a moderate increase in viscous work and a marked increase in the work of respiration. These observations, which have been borne out by non-simultaneous pressure-volume studies in three infants and pressure studies alone in 17 others with respiratory distress (19), would appear to explain the marked sternal retraction observed clinically. As one would predict from the compliance and resistance measurements in these sick infants (if the minimum work concept of Otis, Fenn, and Rahn is applicable), they adjust to their pulmonary insufficiency by increasing their respiratory rate with relatively little change in tidal volume (19). Presumably, another



FIG. 8. PRESSURE-VOLUME DIAGRAM VERSUS 0.6 PV FORMULA FOR DE-TERMINATION OF PULMONARY WORK

Work was estimated by the two methods from the same respirations. Using the loop method as the basis for comparison, there was an average difference of -6 per cent and standard deviation of ± 13 per cent. If there were perfect agreement in each case, all points would fall on the 45° line.

result of the decreased compliance is the inability of these infants to achieve more than approximately half of normal "crying vital capacity" (20, 21). The demonstration of a marked increase in the work of respiration in neonatal respiratory distress supports the clinical impression that these infants frequently die of exhaustion and indicates that, until this condition can be prevented or specifically treated, therapy should, at least in part, be directly toward support of respiratory efforts.

SUMMARY

In summary, 43 observations on the mechanics of respiration in 23 normal newborn infants and 2 infants with respiratory distress have been reported. The resistance for an average 3-Kg. infant breathing quietly was found to be 29 cm. H_2O per L. per sec. and the average compliance 5.2 ml. per cm. H_2O . The resting pulmonary work for such an infant was approximately 1,400 gm. cm. per minute or 1 per cent of basal metabolism. In addition, it was shown that three methods of calculating pulmonary work correlated well. Finally, it was demonstrated that infants with neonatal respiratory distress have a marked decrease in compliance, and a striking increase in the work of respiration.

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