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MEASUREMENT OF THORACIC GAS VOLUME IN THE NEWBORN INFANT *

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This paper presents the development of a plethysmographic method to measure the thoracic gas volume of the lungs of newborn infants (1). The technique is an adaptation of the method recently described by DuBois and co-workers (2) and is similar to that used by Klaus, Tooley, Weaver, and Clements (3). The method measures total thoracic gas volume (TGV), which in the normal subject is the same as the functional residual capacity (FRC). Berglund and Karlberg (4) and Geubelle and co-workers (5) have used a helium dilution method for the measurement of FRC in normal infants, but because of the relative simplicity of the plethysmographic method and because many measurements can be made in a few minutes, it was considered advantageous to apply it to normal newborn infants and to those with respiratory distress.

METHOD

Boyle's Law states that the volume of a gas is inversely proportional to the pressure applied to it. Thus, when the breathing of a subject in a body plethysmograph is obstructed at end-expiration and respiratory efforts are continued, the gas in the lungs will be compressed and decompressed, with a resultant change in volume. The ratio $\Delta V/\Delta P$ determines the thoracic gas volume: FRC or $TGV = (P_B - P_{H_2O})\ \Delta V/\Delta P$, where $P_B - P_{H_2O}$ equals the barometric pressure minus water vapor pressure, in centimeters of water. The derivation of this formula appears in the publication of DuBois and coworkers (2) which shows that in the seated adult subject the plethysmographic method gives FRC measurements comparable to those of the classical washout procedures (6).

The infant is placed on an adjustable canvas cot inside the body plethysmograph as shown in Figure 1. The infant's head is placed within the Plexiglas collar of the plethysmograph opening. This opening is closed with a circular Plexiglas lid through which a rigid tube of 20 mm i.d. may be moved vertically. The lower end of this tube is fitted with a Bennett infant mask lubricated with a glycerin-Aquaresin mixture and applied to the infant's face to enclose the nose and mouth securely. The upper end of the tube is left open until the time of obstruction. All possible sources of air leak are sealed with Plasticine. With care, the infant is usually not disturbed and continues to breathe quietly through the tube. Accumulation of CO_2 is avoided by applying suction at the open end of the tube until the TGV measurement is made. Leaks are checked by opening the plethysmograph tap A to the weighted (5 g) Krogh spirometer and noting any decrease in spirometer volume.

Lung volume change causes plethysmograph pressure change, which is registered through a pressure transducer D on one channel of a recorder and observed on the y-axis of an oscilloscope G. Pressure changes at the mouth are recorded through a Hathaway PS-8A pressure transducer E connected by a 15-mm length of 1.0 mm i.d. plastic tubing to an 18-gauge needle placed through a rubber stopper that fits into the open end of the Plexiglas tube. To avoid the volume drift that often occurs after obstruction of the airway, the plethysmograph is vented through the tap C for a few seconds immediately after obstruction. The infant is then allowed to make five or more respiratory efforts while volume and pressure changes are recorded. A pressure-volume line is also recorded on the oscilloscope. Each run includes one obstruction followed by several breaths, and in general five acceptable runs, as indicated by a straight line on the oscilloscope, are carried out in as short a time as possible.

During rapid breathing it is not always possible to obstruct the infant's breathing exactly at end-expiration, but since the average end-expiratory level as well as the exact point of the obstruction appear on the volume tracing, appropriate correction is easily made. At the completion of each study, calibration is done by moving a known volume of air in and out of the plethysmograph at approximately the rate of the infant's respirations to compensate for possible adiabatic effects (7). The transducer measuring airway pressure is calibrated in centimeters of water with a water manometer. The known volume of the Plexiglas tube is subtracted from the calculated value for TGV, which is corrected, if necessary, to the average end-expiratory position.

Compliance was determined by the method originally suggested by Drorbaugh and co-workers (8) and subsequently used by Karlberg, Cherry, Escardó, and Koch

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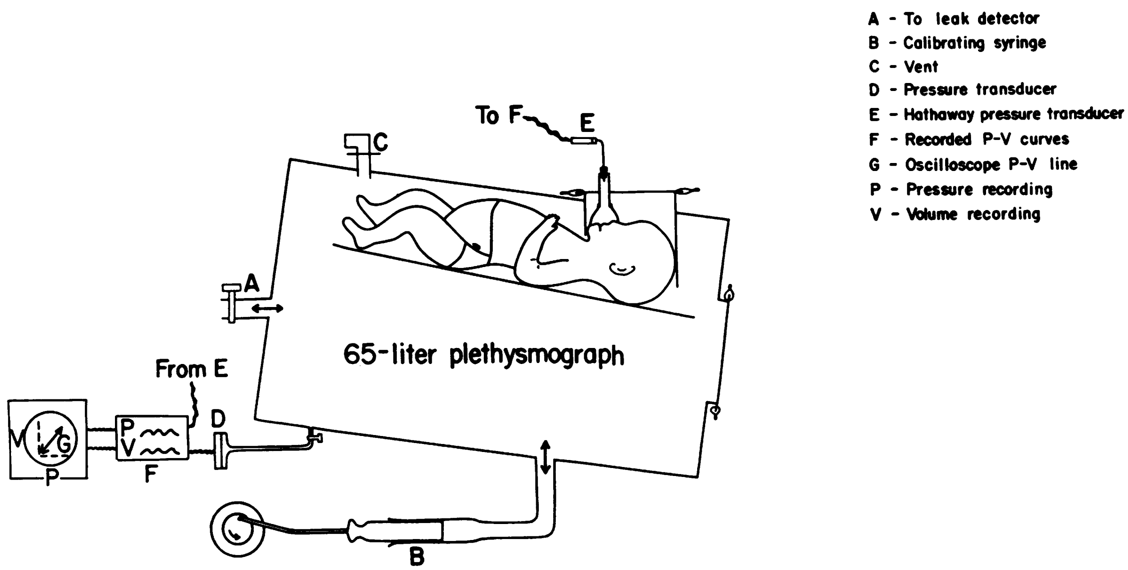

FIG. 1. ARRANGEMENT OF THE PLETHYSMOGRAPH FOR DETERMINATION OF THORACIC GAS VOLUME.

(9). Total lung capacity (TLC) was obtained by adding TGV to inspiratory capacity (10).

Selection and analysis of data. The thoracic gas volume measurement, or run, was considered acceptable only when the oscilloscope recorded a straight line. If a loop was observed, closure of the glottis or mouthing movements were considered responsible. Often sick infants grunted during the studies, and in these a straight line was recorded during inspiration only, with such irregularities in expiration that it seemed best to use inspiratory slopes in analyzing data from all children. It was felt that such selection might also minimize errors from compression of abdominal gas.

Because of the very small and often rapid volume changes of infants during the brief periods of obstruction, the slope observed on the oscilloscope was less useful for accurate calculation of $\Delta V/\Delta P$ than a plotted slope from the recorded volume and pressure curves. Five satisfactory runs were selected from each observation for such plotting, and their mean value and standard deviation calculated.

Infants studied. Twenty-seven newborn infants were studied, ten of them infants of diabetic mothers. Seventy-five acceptable measurements of TGV were made on the 27 infants at various ages; 61 estimates of TLC were made, and compliance was determined on 33 occasions. The infants were divided into three groups. The first group was clinically well. The second group consisted of infants who exhibited some initial respiratory distress, but who recovered in the first 24 hours. Mild hyaline membrane disease could not be ruled out, but the clinical courses of these infants were more typical of intrauterine aspiration, and the roentgenograms of some substantiated that diagnosis. The third group was clinically and roentgenologically diagnosed as having idiopathic respiratory distress, or in other terms, "hyaline membranes and atelectasis," or the "hyaline membrane syndrome." None of these infants died, so that the definite diagnosis possible only at autopsy could not be made.

RESULTS

The data appear in Tables I, II, and III. In the normal infants, both TGV and TLC appear to correlate better with body length than with birth weight.[1] The average value for these infants (Table I) for TGV is 1.8 ml per cm length (36 ml per kg) and for TLC is 3.4 ml per cm length (63 ml per kg). Because of the better correlation with length and also because premature infants and those of diabetic mothers are known to have large variations in body weight throughout the first week of life, the data are presented with respect to length except where comparison with results of other workers is desired.

Figure 2 shows TGV in milliliters per centimeter plotted with respect to age for both well infants (Table I) and infants with distress presum-

[1] Correlations and regressions for data from normal infants follow. TGV: Birth weight $r = 0.56$, TGV in milliliters $= 8.95 + 32.08$ birth weight in kilograms; TGV: Length $r = 0.79$, TGV in milliliters $= -276.73 + 7.85$ length in centimeters. TLC: Birth weight $r = 0.56$, TLC in milliliters $= 32.71 + 49.65$ birth weight in kilograms; TLC: Length $r = 0.74$, TLC in milliliters $= -381.41 + 11.68$ length in centimeters.

TABLE I

Lung volume measurements in normal infants

Infant	Age	Birth wt	Length	Thoracic gas volume				Inspiratory capacity	Total lung capacity		
		kg	*cm*	*ml*	*ml/kg body wt*	*ml/cm body length*	*ml/g estimated lung wt*	*ml*	*ml*	*ml/kg body wt*	*ml/cm body length*
1	18 hours	1.82	42	51± 4	28	1.2	1.3				
	39 hours			56± 5	31	1.3	1.4	43	99	54	2.4
	3 days			62±13	34	1.5	1.6	48	110	60	2.6
	9 days			46±11	25	1.1	1.2	56	102	56	2.4
2	38 hours	2.10	48	95± 7	45	2.0	2.1				
3	9 hours	1.96	44	51±15	26	1.2	1.2	88	139	71	3.2
4	2 hours	2.30	45	92± 8	40	2.0	2.0	72	164	71	3.6
	21 hours			80±17	35	1.8	1.7	83	163	71	3.6
5	2 hours	2.27	45	88± 9	39	1.9	1.9	65	153	67	3.4
	26 hours			75±12	33	1.7	1.6	60	135	60	3.0
	4 days			81± 5	36	1.8	1.7	74	155	68	3.4
6	4 hours	2.35	48	126± 4	54	2.6	2.6				
	26 hours			91± 9	39	1.9	1.9				
	13 days			120± 6	51	2.5	2.5				
7	5 hours	3.18	49	99± 5	31	2.0	1.7	57	156	49	3.2
	27 hours			81± 8	25	1.7	1.4	58	139	44	2.8
	3 days			92±10	29	1.9	1.6	73	165	52	3.4
8	28 hours	2.89	50	137±10	47	2.7	2.5	112	249	86	5.0
	6 days			124± 8	43	2.5	2.3	119	243	84	4.9
9	7 hours	2.77	47	82± 9	30	1.7	1.5	74	156	56	3.3
	29 hours			84±14	30	1.8	1.6	82	166	60	3.5
10*	10 hours	2.04	46	75± 5	37	1.6	1.7				

* Compliance at this age was 2.1 ml per cm H_2O.

TABLE II

*Lung volume and compliance measurements in infants with minimal respiratory distress**

Infant	Clinical condition	Age	Birth wt	Length	Thoracic gas volume				Compliance	Inspiratory capacity	Total lung capacity		
			kg	*cm*	*ml*	*ml/kg body wt*	*ml/cm body length*	*ml/g estimated lung wt*	*ml/cm H_2O*	*ml*	*ml*	*ml/kg body wt*	*ml/cm body length*
11	RD, recovered	29 hours	2.46	49	109±13	44	2.2	2.2					
12	RD	1 hour	2.01	48	106± 8	53	2.2	2.4		49	155	77	3.2
	RD, recovered	26 hours			56± 3	28	1.2	1.3		51	107	53	2.2
		10 days			104± 9	52	2.2	2.4		80	184	92	3.8
		15 days			81±10	40	1.7	1.8		84	165	82	3.4
13	RD	2 hours	2.54	47	113±19	45	2.4	2.3		74	187	74	4.0
14	RD	4 hours	3.51	51	122± 4	35	2.4	2.0	2.7	68	190	54	3.7
	RD, recovered	32 hours			100±12	29	2.0	1.7	4.7	96	196	56	3.8
		56 hours			142± 9	40	2.8	2.4	4.2	120	262	75	5.1
		6 days			110±10	31	2.2	1.8		92	202	58	4.0
15	RD	5 hours	2.25	46	85± 5	38	1.9	1.8					
	RD, recovered	33 hours			110± 7	49	2.4	2.3					
		5 days			106± 9	47	2.3	2.3					
16	RD	2 hours	3.20	50	82± 2	26	1.6	1.4		62	144	45	2.9
	RD, recovered	28 hours			126±12	40	2.5	2.2		67	193	60	3.9
		4 days			108±10	34	2.2	1.9		106	214	67	4.3
17	RD	7 hours	3.90	52	112±11	29	2.2	1.8		78	190	49	3.7
	RD, recovered at 24 hours	5 days			105± 7	27	2.0	1.7		87	192	49	3.7

* RD = respiratory distress; recovery occurred within 24 hours.

TABLE III

*Lung volume and compliance measurements in infants with respiratory distress**

Infant	Clinical condition	Age	Birth wt	Length	Thoracic gas volume				Compliance	Inspiratory capacity	Total lung capacity		
			kg	*cm*	*ml*	*ml/kg body wt*	*ml/cm body length*	*ml/g estimated lung wt*†	*ml/cm H_2O*	*ml*	*ml*	*ml/kg body wt*	*ml/cm body length*
18	RD	12 hours	3.01	49	73± 9	24	1.5	1.3		40	113	38	2.3
	RD, recovering	37 hours			70±10	23	1.4	1.3		54	124	41	2.5
19	RD	16 hours	2.03	45	43± 4	21	1.0	1.0	1.0	48	91	45	2.0
		40 hours			64± 6	32	1.4	1.5	1.3	45	109	54	2.4
		64 hours			57± 6	28	1.3	1.3	2.4	49	106	52	2.4
	RD, recovered	7 days			88± 4	43	1.9	2.0		55	143	70	3.2
		14 days							2.5	70			
20	RD	3 hours	2.18	47	78± 3	36	1.7	1.7					
		26 hours			61± 2	28	1.3	1.3	1.8	59	120	55	2.6
	RD, recovered	6 days			85±12	39	1.8	1.8	2.7	75	160	73	3.4
21	RD	2 hours	2.09	46	61± 4	29	1.3	1.4	0.8	44	105	50	2.3
		53 hours			50± 6	24	1.1	1.1		36	86	41	1.9
	RD, recovering	5 days			74±14	35	1.6	1.6	1.5	47	121	58	2.6
	RD, recovered	10 days			64±17	30	1.4	1.4	2.1	87	151	72	3.3
22	Rd	8 hours	2.55	48	72± 7	28	1.5	1.4	1.5	53	125	49	2.6
		22 hours			104± 9	41	2.2	2.0	1.4	44	148	58	3.1
23	RD	16 hours	2.74	46	53± 7	19	1.2	1.0	1.1				
		40 hours			74± 5	27	1.6	1.4	1.0	47	121	44	2.6
	RD, recovered	7 days			47±13	17	1.0	0.9	2.6	99	146	53	3.2
		8 days			70±11	26	1.5	1.3					
24	RD	3 hours	3.77	51	68± 6	18	1.3	1.1	1.1	62	130	35	2.5
		27 hours			74± 3	20	1.5	1.2	0.9	60	134	36	2.6
		76 hours			89±10	24	1.8	1.4	1.0	37	126	33	2.5
		29 hours							1.1	50			
	RD, recovering	7 days			100± 8	27	2.0	1.6	1.6	81	181	48	3.5
	RD, recovered	14 days			136±13	36	2.7	2.2					
		15 days							2.7				
25	RD	4 hours	2.69	49	63±10	24	1.3	1.2	1.9	37	100	37	2.0
		31 hours			65± 3	24	1.3	1.3	1.2	49	114	42	2.3
		56 hours			61± 5	23	1.2	1.2	1.1	57	118	44	2.4
	RD, recovering	3 days			58± 9	22	1.2	1.1		86	144	54	2.9
	RD, recovered	10 days			87± 8	32	1.8	1.7	2.4	90	177	66	3.6
26	RD	5 hours	2.90	48	50± 7	17	1.0	0.9	0.9	42	92	32	1.9
		29 hours							1.2	38			
		4 days			37± 6	13	0.8	0.7	1.6	34	71	25	1.5
27	RD	6 hours	3.15	49	99± 7	31	2.0	1.8	2.7	79	178	57	3.6
		26 hours			79± 5	25	1.6	1.4		70	149	47	3.0
	RD, recovered	3 days			90± 8	29	1.8	1.6		64	154	49	3.1
		7 days			92± 3	29	1.9	1.6	3.4	90	182	58	3.7

* RD = respiratory distress.
† From data of Potter (14).

ably due to the hyaline membrane syndrome (Table III). TLC in milliliters per centimeter is shown in Figure 3. In normal infants, there is little change in either of these volumes with age, and no trend is apparent. The average value for either volume during the first 24 hours is essentially the same as that for the same volume at 3 days and over.

Compared with the first measurements of normal infants, initial TGV of the sick ones (average 1.4 ml per cm) was low, but TGV increased with clinical improvement during the next few days (Figure 2, right). Infant 27 was an exception in that the second TGV was reduced, but subsequent ones did rise with recovery. Average TGV of 1.8 ml per cm in the sick infants after they had recovered was identical with the average for the normal infants. TLC in sick and normal infants showed similar relationships.

In Table IV, which summarizes the lung volumes in respiratory distress compared with the normal state, the lowest single value for each in-

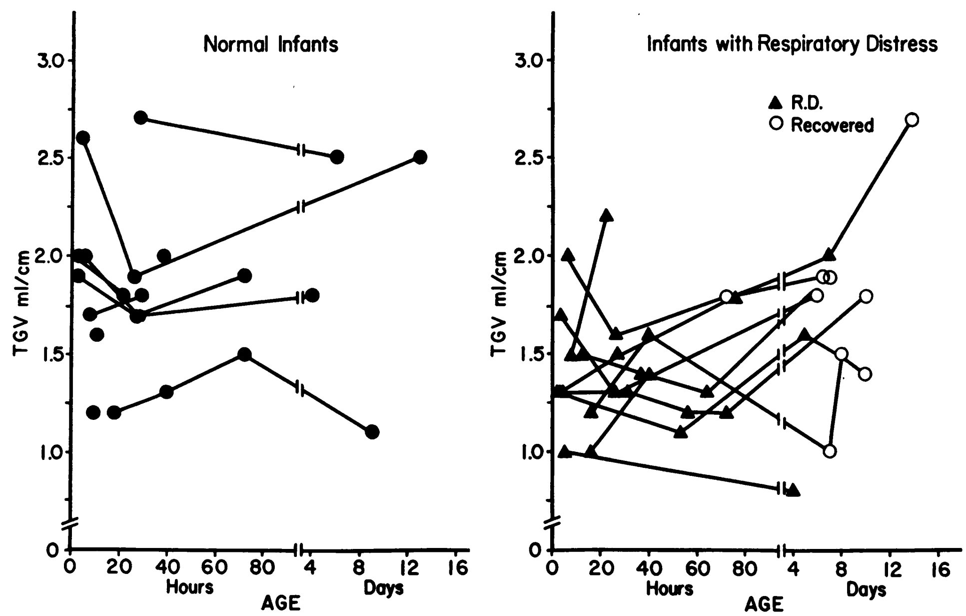

FIG. 2. THORACIC GAS VOLUME, TGV, IN MILLILITERS PER CENTIMETER BODY LENGTH WITH RESPECT TO AGE FROM BIRTH IN NORMAL INFANTS AND INFANTS WITH RESPIRATORY DISTRESS.

fant during distress and the lowest value obtained for each normal infant were used for calculation of means. This allowed the most marked effect during the distressed state to be compared with the normal, regardless of any possible variations due to age. Infants with hyaline membrane disease had lung volumes significantly less than normal.

Both TGV and TLC are related to compliance, although the regressions calculated from all values

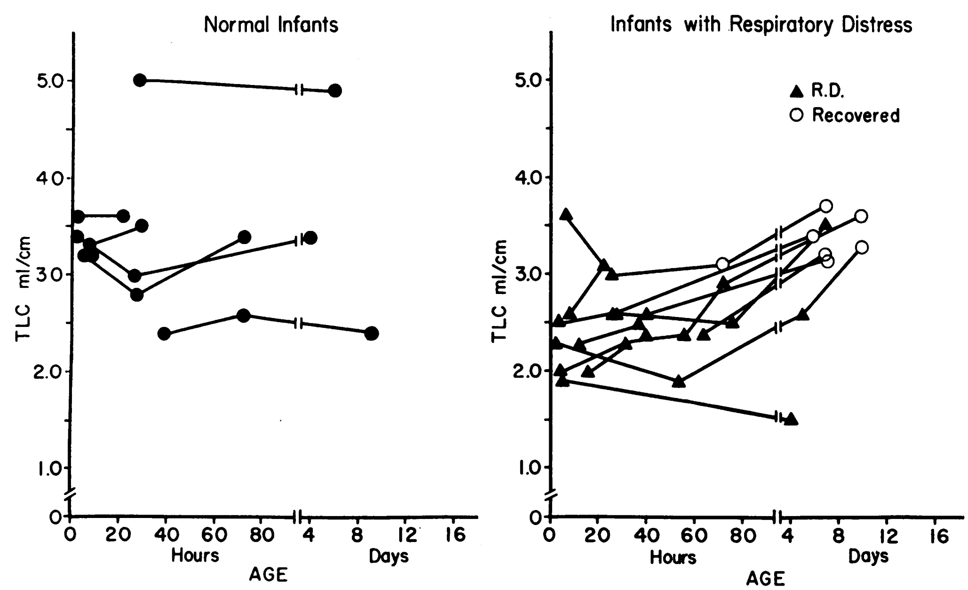

FIG. 3. TOTAL LUNG CAPACITY, TLC, IN MILLILITERS PER CENTIMETER BODY LENGTH WITH RESPECT TO AGE FROM BIRTH IN NORMAL INFANTS AND INFANTS WITH RESIRATORY DISTRESS.

TABLE IV

Lung volumes in normal infants and in those with respiratory distress

	n	Thoracic gas volume		n	Total lung capacity	
		ml/cm body length			*ml/cm body length*	
Well (Table I)	10	1.72 ± 0.39	33.8 ± 7.3	7	3.31 ± 0.80	62.9 ± 13.3
Sick (Table III)	10	1.24 ± 0.24 ($p \leq 0.01$)	22.1 ± 4.6 ($p \leq 0.001$)	10	2.30 ± 0.44 ($p \leq 0.01$)	41.4 ± 8.6 ($p \leq 0.01$)

of compliance in Tables I, II, and II show a better correlation with TLC than with TGV.[2]

DISCUSSION

Although pulmonary physiologic data from normal newborn infants are usually expressed per unit of weight, better correlation with length was obtained in this study, and this agrees with the better correlation with height in adults.

In sick infants, the data agree with the autopsy finding of extensive atelectasis in association with hyaline membranes in the newborn. That atelectasis and reduction of lung volumes occur early and not entirely as terminal effects is suggested by the roentgenological appearance (11) and by the demonstration (12) that an antiatelectatic surface active factor is lacking from the lungs of premature infants. The current investigations do not prove that atelectasis is primary, although the early decrease of lung volumes in the sick infants studied favors this probability.

If expressed in milliliters per gram of estimated lung weight, the data can be compared with those obtained by Gribetz, Frank, and Avery (13) from

[2] C_L (compliance) in milliliters per centimeter $H_2O = 0.079 + 0.024$ TGV in milliliters, $r = 0.57$; C_L in milliliters per centimeter $H_2O = -0.733 + 0.019$ TLC in milliliters, $r = 0.74$.

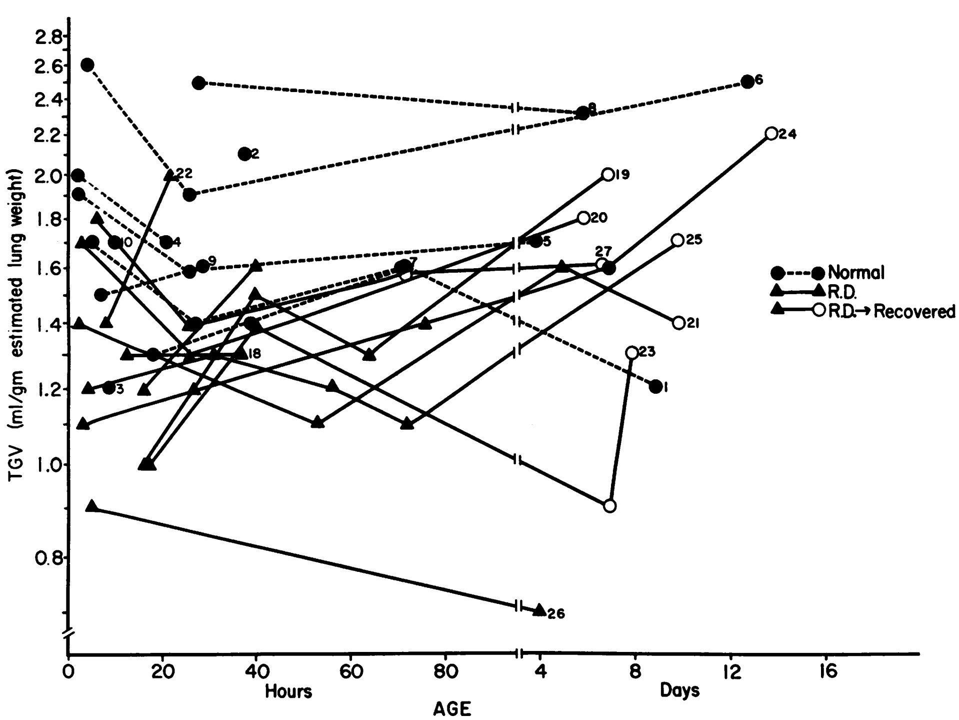

FIG. 4. GRAPH OF THORACIC GAS VOLUME, IN MILLILITERS PER GRAM ESTIMATED LUNG WEIGHT, RELATED TO AGE FROM BIRTH IN NORMAL INFANTS AND INFANTS WITH RESPIRATORY DISTRESS DURING ILLNESS AND AFTER RECOVERY.

the lungs of infants who died with hyaline membranes. In Figure 4, TGV in milliliters per gram estimated lung weight (14) is plotted against age. Thoracic gas volumes of most sick infants are below 1.4 ml per g and rise with recovery; two of the sick infants had initial values within the range of the normal infants. Gribetz and co-workers (13), however, found a smaller gas-containing volume that was well below 1.0 ml per g in excised lungs of infants with hyaline membranes at all airway pressures used. This difference between lung volume/lung weight figures may be explained by inclusion of upper airway volume in the *in vivo* TGV measurements.

Several authors (15, 16) have shown a relationship between compliance and FRC in normal children and adults. In the present study, data obtained from infants with hyaline membranes or minimal respiratory distress showed significant correlation between compliance and TGV, with rather better correlation between compliance and TLC. Since compliance is more easily measured than either of these volumes, its determination immediately after birth might be of value in assessing lung volume changes.

Geubelle and co-workers (5) measured functional residual capacity of newborn infants by means of helium dilution and expressed the results per unit of body weight. The average TGV of the present data for normal infants (35.8 ml per kg) is significantly greater than the average FRC obtained by helium dilution (25.7 ml per kg). Since the helium dilution method measures only that portion of the lung volume in continuity with the airway and since the plethysmographic method measures total thoracic gas, this difference might be interpreted as indicating a considerable amount of "trapped air" in the normal newborn infant's lung.

Data from infants with minimal respiratory distress and early recovery (Table III) showed no evident reduction of lung volumes. Indeed, several had rather high TGV values. Aspiration may not only have produced their symptoms, but also have caused some trapping of air.

SUMMARY

The thoracic gas volume (TGV) of newborn infants has been measured by a plethysmographic method. Total lung capacity (TLC) has also been estimated by adding TGV to the inspiratory capacity obtained during crying.

The results suggest the following conclusions. *1*) TGV and TLC are established within a few hours after birth in normal infants and increase little during subsequent neonatal life. *2*) There is a significant decrease in TGV and TLC in newborn infants with the hyaline membrane syndrome. *3*) This decrease in volume occurs early in the course of the disease. *4*) Compliance and TLC or TGV are related in sick infants. *5*) "Trapped gas" may exist in the lungs of some normal newborn infants.

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