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PULMONARY FUNCTION IN THE NEWBORN INFANT. V. TRAPPED GAS IN THE NORMAL INFANT'S LUNG *

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"Trapped gas" has been defined by Bedell, Marshall, DuBois, and Comroe (1) as "that component of the thoracic gas volume which, having entered the thorax, is present in the lungs or pleural space but is unable to leave owing to intrapulmonary mechanical factors which prevent gaseous outflow." By measuring the ventilated portion of the thoracic gas volume (i.e., the functional residual capacity, FRC) with conventional dilutional methods (2) and comparing it to the total (ventilated and nonventilated) thoracic gas volume (TGV) as determined by their compression-decompression plethysmographic technique (3), these investigators demonstrated trapped gas in several adult patients with blebs, cysts, pneumothorax, intrapulmonary tumors, and especially, emphysema. They conclude that gas which is trapped in alveoli (as opposed to intrapleural or cystic sites) must exist in regions that are in intermittent communication with the airway.

Recent measurements indicate a discrepancy between FRC (4) and TGV (5-7) in normal newborn infants. Thus, the data of Geubelle and associates (4) for infants over 1 hour of age yield an average FRC of 26.5 ± 5.7 ml per kg as determined by the closed-circuit, helium-dilution technique (8), while Klaus, Tooley, Weaver, and Clements (5) reported a mean TGV of 29 ± 7.0 ml per kg, and Auld and colleagues (7) reported 33.8 ± 7.3 ml per kg, as determined by

the plethysmographic method. Because these measurements were not made in the same infants, the suggestion of gas-trapping remains tentative on the basis of such evidence.

This paper presents concurrent measurements of TGV and FRC that indicate the possibility of gas-trapping in 10 of 23 normal newborn babies examined at random.

SUBJECTS AND METHODS

Twenty-three infants ranging in weight from 1.30 to 4.05 kg and in age from 16 hours to 71 days were studied. Although most of these babies were apparently normal in all respects, one (Subject 16) was recovering from mild respiratory distress due to the hyaline membrane syndrome, another had completed a clinical recovery from similar respiratory distress (Subject 12), and a third infant was postmature (Subject 21). Only occasional roentgenograms were obtained, and none of these revealed emphysema or pneumothorax. FRC was determined in duplicate followed within 3 hours by the TGV measurements. In certain infants (see Table II and Discussion), TGV was also determined after a period of O_2 -breathing.

Thoracic gas volume. This was determined by the plethysmographic method of DuBois and associates (3) as adapted for use in the newborn infant by Klaus and co-workers (5, 6) and Auld and colleagues (7). These publications should be consulted for details, but the principle of the procedure may be stated as: $TGV = \Delta V / \Delta P$ (barometric pressure-water vapor pressure). ΔV is registered as box pressure change and ΔP is measured as mouth (i.e., alveolar) pressure change after respiratory obstruction. In the present work the plethysmograph (65 L) and tare volume (150 ml) were filled with copper wire to minimize any adiabatic artifacts (9). The box was calibrated, after the infant was removed, by introduction and withdrawal of 5 ml air at a rate comparable to the infant's own respiratory frequency. Only the inspiratory slope of the $\Delta V / \Delta P$ trace was measured, to obviate the effect of possible compression of abdominal gas. These slopes were read both from the oscilloscope and from the paper traces, and the final measurement was taken from that record showing the least variation. For each study five or more acceptable

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runs (straight line PV traces) were averaged to constitute one determination of TGV. Next, a tare volume was switched in parallel to the TGV and three or more further acceptable runs were averaged as a determination of TGV plus tare volume. If the estimated tare volume was not correct $\pm 15\%$, the study was discarded. A coefficient of variation (SD/mean) for the individual runs of more than 20% was regarded as unacceptable.

Many measurements of model lungs yielded correct average estimates with a coefficient of variation amounting to $\pm 5\%$ of the known volume. In a previous series of 75 determinations of TGV in newborn infants by this method (7), the coefficient of variation for the several runs comprising one measurement averaged $11 \pm 6\%$.

Functional residual capacity. This was measured by the classical open-circuit, nitrogen-washout procedure of Darling, Cournand, and Richards (2) wherein: $FRC = [(spirometer\ volume + spirometer\ dead\ space) (\% spirometer\ N_2 - \% inspiratory\ N_2) - correction\ for\ N_2\ excretion] / [initial\ \% alveolar\ N_2 - final\ \% alveolar\ N_2]$.

Certain modifications of the original method were necessary for use in newborn infants. The open circuit employed in the present study has been described separately (10); a 7-L bell spirometer with a dead space of approximately 0.8 L was used. To insure accurate spirometer samples, a 5-L anesthesia bag parallel with the spirometer bell was used as a mixing chamber. The N_2 content of the spirometer and the O_2 tank was measured in duplicate $\pm 0.04\%$ by the method of Darling, Cournand, Mansfield, and Richards (11) as adapted to the Scholander gas analyzer (12). N_2 -excretion figures were taken from an empirical curve derived from four O_2 -breathing infants (12) by an adaptation of the method of Shaw and associates (13). The initial alveolar N_2 was assumed to be 80%, and the final figure, 1%.

These assumptions were necessary because of technical difficulties in obtaining spot alveolar samples from an essentially untrainable subject. Attempts at simultaneous monitoring of alveolar N_2 with a N_2 -meter¹ led to unmeasurable losses of expired N_2 . The assumption of an initial alveolar N_2 of 80% has been justified as leading to less than 2% error in the final estimate of FRC (14). The assumption of a final alveolar N_2 of 1% is justified with insignificant error from a separate study (15) in

¹ Nitralyzer model #300 AR, Custom Engineering and Development Co., St. Louis, Mo.

TABLE I
Thoracic gas volume (TGV) and functional residual capacity (FRC) in normal infants

Infant	Age	Birth weight	TGV		TGV/kg	FRC			FRC/kg	TGV-FRC
			Mean	SD		Mean	Duplicate			
	days*	kg	ml		ml/kg		ml		ml/kg	ml
1A	12	1.30†	93	9	71.4					
1B	13		86	6	65.9	87	83	90	66.9	-1
2	16	1.48†	67	4	45.2	59	53	65	39.9	8
3A	5	1.83	68	5	37.2	66	62	69	36.1	2
3B	12		78	5	42.7	79	71	87	43.2	-1
3C	22	2.13†	92	3	43.1	62	62		29.1	30†
4	19	2.10	61	7	29.0					
5	23 hrs	2.16	87	11	40.3	46	42	50	21.3	41†
6	8	2.16	100	5	46.3	87	80	93	40.3	13
7	6	2.16	69	5	31.9	64	61	66	29.6	5
8	39	2.21†				39	36	41	17.6	
9	9	2.22	93	16	41.9	62	60	63	27.9	31†
10	71	2.24†	63	5	28.1	70	68	72	31.3	-7
11A	18 hrs	2.30	126	8	54.7	89	87	90	38.7	37†
11B	2		95	5	41.3					
12	23	2.34†	159	8	68.0	63	58	67	26.9	96†
13A	16 hrs	2.36	108	12	45.8	80	79	81	33.9	28†
13B	3		112	8	47.5					
14	4	2.44	84	4	34.4	93	87	99	38.1	-9
15	2	2.65	112	17	42.3	121	116	126	45.7	-9
16	2	2.73	73	7	26.8	88	82	94	32.2	-15
17	2	3.06	75	5	24.5	53	50	55	17.3	22†
18	25 hrs	3.08				65	58	71	21.3	
19	4	3.23	105	4	31.0	77	74	80	23.9	28†
20	36 hrs	3.32	121	6	36.4	91	82	100	27.4	30†
21	2	3.32	92	7	27.6	82	79	85	24.6	10
22	5	4.04	87	5	21.5	88	82	93	21.8	-1
23	4	4.05	127	9	31.4	70	68	72	17.2	57†
Mean					40.6				31.3	40.0†
SD					13.1				11.3	21.9†

* Except where age in hours is indicated.

† Weight at examination.

‡ Trapped gas.

which every one of 58 N₂-washout curves in 21 newborn infants (including some with respiratory distress) became asymptotic at about 1% alveolar N₂ within 2 minutes of O₂-breathing.

Satisfactory gas collections of at least 2 to 3 minutes were demanded for each determination. Although a washout period of 2 to 3 minutes may seem insufficient, the turnover rate of newborn infants is so fast that alveolar washout is essentially complete within this time (15-17). Moreover, washout periods of more than 4 to 5 minutes proved technically difficult. Duplicate determinations of FRC were repeated after 30 minutes of air breathing and were required to agree within $\pm 7\%$ of the mean in most cases. Each determination was corrected to average end-expiratory level as indicated by a bag-in-box recording system (pressure plethysmograph) to which the inspiratory line of the open circuit was connected before O₂-breathing commenced. The known volumes of model lungs were repeatedly measured within $\pm 5\%$ by this method.

RESULTS

These are presented in Table I and are summarized in Figure 1, where it is seen that in full-term infants (approximately 2.5 to 3.5 kg) the

present measurements of FRC by open-circuit N₂-washout agree well with those of Geubelle and associates (4) derived from the closed-circuit, He-dilution technique. Moreover, the average value of Klaus and co-workers (5) for TGV in newborn infants (29 ± 7.0 ml per kg) is in close agreement with our own estimates for babies of comparable size (2.55 to 4.12 kg). Lung volume apparently decreases with increasing body weight. The individual values and the 95% confidence limits for the three studies have been omitted from Figure 1 for simplification, but none of these separate estimates is significantly different from another throughout the weight range of the infants examined (see legend for Figure 1). Figure 1, however, shows only the over-all trend of measurements.

When the present concurrent measurements of FRC and TGV in the same infants are compared as in Figure 2, it is apparent that several babies (Subjects 3C, 5, 9, 11A, 12, 13A, 17, 19, 20, and 23) show a significant discrepancy between the

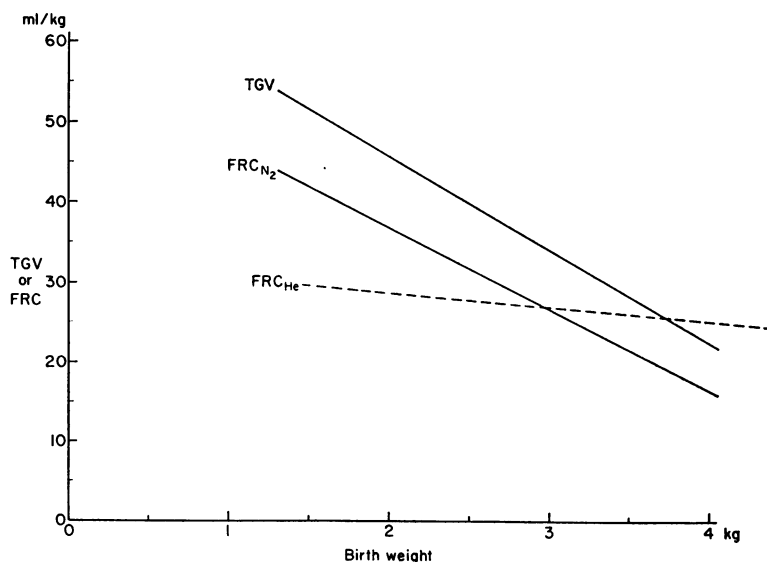


FIG. 1. THORACIC GAS VOLUME (TGV) AND FUNCTIONAL RESIDUAL CAPACITY (FRC) IN NEWBORN INFANTS. Regression line equations:

TGV (present data) in milliliters per kilogram = $69.2 - 11.7$ body weight in kilograms, where $n = 26$, $r = -0.62$ ($t = 3.9$, $p \approx 0.001$), and $SE = \pm 10.3$ ml per kg.

FRC_{N₂} (present data) in milliliters per kilogram = $57.5 - 10.3$ body weight in kilograms, where $n = 24$, $r = -0.62$ ($t = 3.7$, $p < 0.01$), and $SE = \pm 8.8$ ml per kg.

FRC_{He} [Geubelle and associates (4)] in milliliters per kilogram = $32.6 - 1.9$ body weight in kilograms, where $n = 44$, $r = -0.28$ ($t = 1.9$, $p > 0.05$), and $SE = \pm 5.0$ ml per kg.

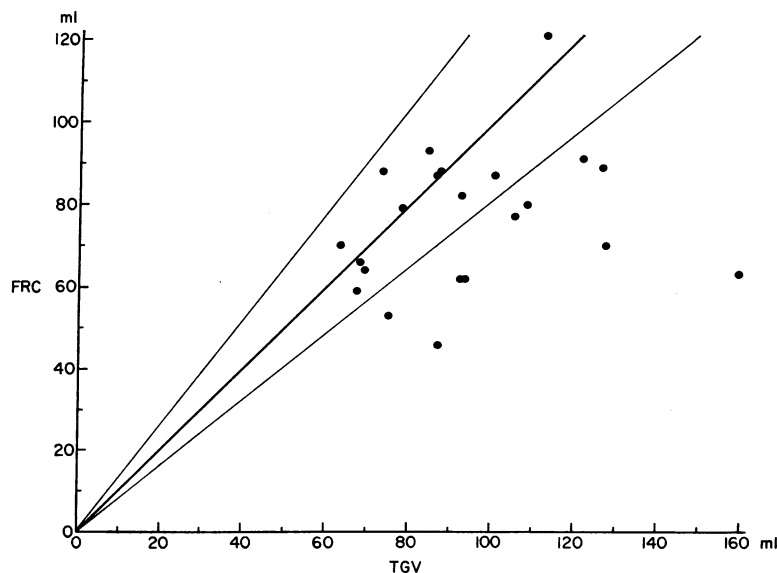


FIG. 2. TRAPPED GAS IN NORMAL NEWBORN INFANTS. The line of identity (thick line) is shown as well as the range encompassed by $\pm 23\%$ of TGV (thin lines). FRC is significantly less than TGV in 10 infants.

two. The line of identity $\pm 23\%$ clearly separates these infants in whom TGV exceeded FRC. In no instance did the reverse occur. Since the coefficient of variation of the TGV determination is $11 \pm 6\%$, any infant whose TGV exceeded the FRC by more than 23% (mean coefficient of variation ± 2 SD) was regarded as demonstrating the phenomenon of "trapped gas." The average amount of "trapped gas" so detected was 40 ± 22 ml and amounted to 25 to 60% of TGV, a volume comparable to that of adult patients with emphysema (1).

In each of three infants having "trapped gas" (Subjects 3C, 19, and 20), the TGV could be significantly lowered by a 10- to 20-minute period of O_2 -breathing by funnel while in the plethysmograph, whereas three infants without "trapped gas" (Subjects 7, 10, and 15) had no change in TGV; this is shown in Table II.

Figure 3 plots the frequency distribution of "trapped gas" against the age and weight of the infants. No clear trend is apparent, but the number of studies is admittedly small.

DISCUSSION

Possible sources of error. The reliable estimates of model lungs by both TGV and FRC methods and of tare volumes during each TGV

study would appear to preclude gross errors. Since both TGV and FRC measurements were made in the supine position, diaphragmatic shifts are unlikely to account for the differences seen in Figure 2.

The most accurate method for calibration of box pressure change is the rapid introduction and withdrawal of a known gas volume while the subject remains in the plethysmograph (1). This proved to be impractical in the present work because the infants' respirations interfered with accurate measurements of the record, so that calibration had to be performed with the infant removed. The inclusion of a tare volume estimation with each determination of TGV (6) checked any inaccuracy so introduced.

TABLE II
Effect of O_2 -breathing in infants with and without trapped gas

Infant	TGV-air	FRC	TGV- O_2
	ml	ml	ml
3C*	92 ± 3	62	47 ± 3
19*	105 ± 4	77	62 ± 11
20*	121 ± 6	91	100 ± 7
7	69 ± 5	64	57 ± 5
10	63 ± 5	70	51 ± 8
15	112 ± 17	121	104 ± 8

* Infants with trapped gas.

Boyle's law, which is the basis of the plethysmographic method for estimating TGV, assumes an isothermal compression of gas, and insofar as compression of the TGV during obstruction is nonisothermal, Boyle's law may not be strictly applicable to the conditions of this method. This objection, however, has been thoroughly examined by Mean and Collier (18) and denied as a source of measurable error.

Figure 2 indicates that any error involved in the TGV measurement must systematically lead to overestimation, for TGV was never significantly less than FRC. Abdominal gas compressed by the respiratory efforts following obstruction must be included in the estimate of TGV and could produce such a systematic overestimation; it does not do so in the trained adult (3), and Klaus considers it unlikely to be a source of significant error in the newborn (6). Gentle injections of up to 40 ml of air into the rectal ampullae of several infants in this laboratory led to no consistent change in TGV. Furthermore, as noted above, only inspiratory slopes were measured to preclude errors owing to unobserved abdominal compression by these infants.

Gross systematic errors in the determination of FRC were checked by satisfactory estimates of model lungs, but erroneously low measurements

of the infants' FRC could occur if the N_2 -excretion figure were too high, the assumed final alveolar N_2 too low, or the amount of alveolar N_2 washed out too low.

Sample calculations reveal that an error of $\pm 200\%$ in the N_2 excretion estimate is necessary to produce a significant error in the FRC. Such an error seems unlikely.

The lack of actual alveolar samples in these studies is perhaps not so serious an omission as would at first appear, for considerable doubt exists as to what constitutes a representative alveolar sample during N_2 washout (19). Although the assumed final alveolar concentration of 1% N_2 admittedly leads to a minimal estimate of FRC, sample calculations show that the actual final alveolar concentration of N_2 would have to be as high as 20% to produce a 20% error in the final estimate of FRC. Because of the washout curves of normal infants previously mentioned (15), this also seems unlikely.

The probable reason for underestimation of FRC by the method used is an insufficient washout of N_2 from poorly ventilated areas. The fact that no important maldistribution of inspired gas has been seen in many studies of normal infants (15) renders an error of this nature unlikely in the present investigation.

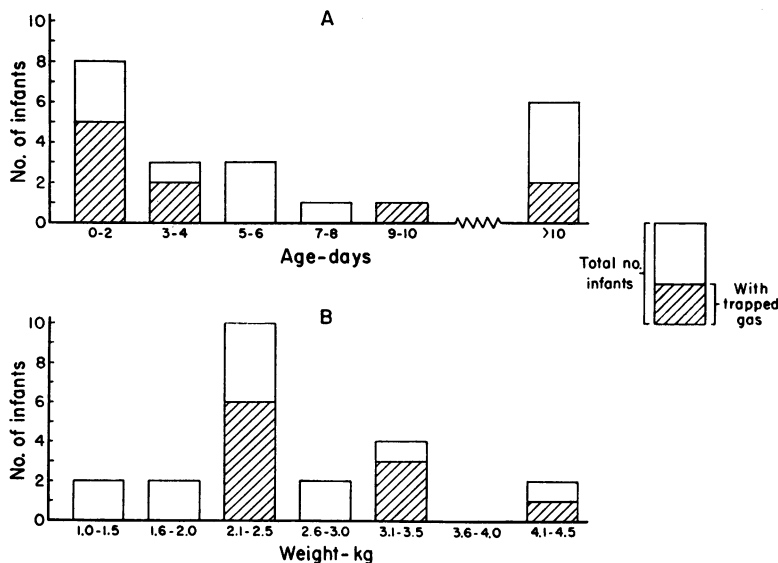


FIG. 3. FREQUENCY DISTRIBUTION OF TRAPPED GAS IN 22 NORMAL NEWBORN INFANTS. Infants with trapped gas are indicated by height of shaded bars. A—with regard to age. B—with regard to birth weight.

No systematic errors in the methods for measurement of TGV and FRC offer a reasonable explanation for the discrepancies noted in Figure 2, and the phenomenon of gas-trapping seems to be demonstrated in these infants.

Interpretation. The term "trapped gas" implies the presence of some mechanical obstruction to gas flow (1) leading to very poor ventilation of some portions of the TGV. Since no direct examinations of the mechanics of breathing were made, we can only claim to have demonstrated that a significant portion of the TGV in many of the normal infants examined was so poorly ventilated as to escape representation in the FRC measurement. Washout curves in similar normal infants (15-17) have not shown significant maldistribution of ventilation. Thus, the very poorly ventilated gas detected here must be essentially isolated from the airway.

Poorly ventilated gas might be totally isolated from the airway as in cysts, blebs, pneumothorax, and so forth. These may have existed in the present infants, but unfortunately, routine roentgenograms of these clinically normal infants were omitted. It would seem unlikely, however, that such pathology could be sufficiently widespread in a random sample of newborns to occur in all of the infants manifesting "trapped gas."

Interstitial emphysema has been described in the lungs of babies dying from nonpulmonary causes (20) and could represent a site for gas-trapping in these infants. Unless such areas were relatively avascular, or at least poorly perfused, they would rapidly diffuse N_2 into the pulmonary capillary blood and be rendered gas-free during O_2 -breathing, thus producing a discrepancy between TGV and FRC. Such areas once gas-freed should not reaerate, and one would expect stable FRC measurements, whereas we have noted that FRC measurements in the same infant tended to increase if the baby had been restless or crying immediately before the period of O_2 -breathing. In short, the very poorly aerated portion of the TGV may well be in intermittent communication with the airway.

Thus, it appears that the alveoli themselves are the sites for whatever gas-trapping occurred in these infants. Some further evidence was obtained indicating that gas may be trapped in alveoli only intermittently ventilated (Table II). Fur-

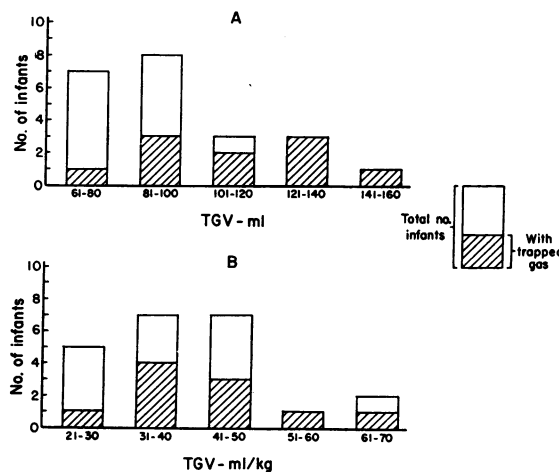


FIG. 4. FREQUENCY DISTRIBUTION OF TRAPPED GAS IN INFANTS WITH REGARD TO THORACIC GAS VOLUME. Infants with trapped gas are indicated by height of shaded bars. A—Total TGV. The only significant difference is between classes between 121-140 and 61-80. B—TGV per unit weight. There is no significant difference between any classes.

thermore, although no significant slow spaces were seen in a separate study of washout curves in normal infants quietly breathing O_2 (15), an occasional deep breath of O_2 was followed by a sudden increase in the constantly monitored alveolar N_2 concentration, thus denoting a group of terminal lung units isolated from the airway during quiet breathing, yet opening into it during briefly increased lung expansion.

These considerations raise doubt concerning the validity of the discrepancies detected between TGV and FRC because the measurements were not properly controlled in that FRC was always determined before TGV. Since the very act of O_2 -breathing may well diminish FRC (and possibly did in infants 3C, 19, and 20 of Table II), a preferable procedure would have been to determine FRC and TGV at random. After measurement of TGV, however, these babies were often fatigued and uncooperative, which made satisfactory gas collections for FRC measurements exceedingly difficult. Therefore, a minimal period of 1 hour following FRC determination was allowed for N_2 washin and possible re-expansion of alveoli before measurement of TGV.

The use of a nonabsorbable indicator gas such as He for FRC measurements would answer the question of whether trapped gas is actually pres-

ent in air-breathing infants or whether it is an artifact introduced by O_2 -breathing and subsequent alveolar collapse. The available data for FRC_{He} in newborn infants indicate a discrepancy between TGV and FRC_{He} similar to that reported here for TGV and FRC_{N_2} . The differences appearing in Figure 1, however, are not significant.

The usual cause for gas-trapping in alveoli is simple expiratory obstruction such as occurs in emphysema (1). Without the critical evidence of expiratory flow rates, resistance measurements, and so forth, we can only speculate as to whether expiratory obstruction existed in these infants. Typical signs of expiratory obstruction (such as variations in end-expiratory level and slow return to base line after deep breathing) were not apparent in the bag-in-box tracings from these babies. Furthermore, although end-expiratory obstruction should lead to hyperinflated lungs, Figure 4 shows no significant trend towards increasingly frequent trapped gas at high lung volumes.

Previous investigations have shown that although TGV (5) and FRC (4) are rapidly attained in the first minutes to hours after birth, variations of 20 to 100% may occur in both measurements during subsequent days. This evidence, coupled with the present indications of intermittently nonventilated alveoli and subsequent degassing, suggests a high degree of instability of lung volume during the first few days of life.

Agostoni's work (21) offers an explanation for such instability in that, owing largely to the highly compliant fetal thorax, the rest volume of the fetal (dog) thorax and lung is near the collapse volume of the latter. A small increase in rest volume occurs during air breathing after birth (21), but during the period when alveolar fluid is replaced by air (22), surface active forces may produce collapse of alveoli, particularly if the antiatelectasis factor (surfactant) is missing or inhibited (23); but since airway resistance tends to become infinite as lung volume decreases (24), gas-trapping may well develop. The relatively high lung volumes in premature infants and the close approximation of average TGV and FRC values in full-term infants (Figure 1) suggest that the stability of the newborn's lung improves as the thoracic cage stiffens and the alveolar surfactant appears with advancing gestational and postnatal (Figure 3A) age. Gas-trapping might then be an

expression of the tenuous balance existing between the compliant thoracic cage of the newborn and the retractive forces of his lung.

SUMMARY

1) The total thoracic gas volume (TGV) and its ventilated component, the functional residual capacity (FRC), have been measured concurrently in 23 normal newborn infants.

2) The TGV was significantly larger than the FRC in 10 babies, indicating the presence of a very poorly ventilated portion of the lung amounting to 25 to 60% of the TGV.

3) This very poorly ventilated gas is probably "trapped" in terminal lung units that are intermittently nonventilated, especially during quiet breathing.

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