0031-3998/92/3205-0589$03.00/0
PEDIATRIC RESEARCH

Vol. 32, No. 5, 1992
Printed in U.S.A.

Effects of Inspiratory Resistive Loading on Chest Wall Motion and Ventilation: Differences between Preterm and Full-Term Infants

KIRAN S. DEORAS, JAY S. GREENSPAN, MARLA R. WOLFSON, ESTEBAN N. KEKLIKIAN, THOMAS H. SHAFFER, AND JULIAN L. ALLEN

Departments of Pediatrics and Physiology, Temple University School of Medicine and St. Christopher's Hospital for Children, Philadelphia, Pennsylvania 19134-1095

ABSTRACT. The ability to maintain effective tidal volume and minute ventilation during resistive loaded breathing depends on both adequate central neural respiratory output response and respiratory system mechanical properties such as respiratory muscle strength and chest wall stability. We hypothesized that chest wall instability limits the ability of the preterm (PT) infant to respond to inspiratory resistive loading (IRL) compared with full-term (FT) infants. To test this hypothesis, we subjected eight FT and 10 PT infants to IRL with loads of 1.3, 2, and 6 times intrinsic lung resistance and measured steady state tidal volume (V_T), minute ventilation ($\dot{V}_E$), and chest wall motion. Thoracoabdominal asynchrony was measured by respiratory inductive plethysmography and quantitated by measuring the phase angle, θ, between rib cage and abdominal motion (0° = synchronous motion, 180° = paradoxic motion). At baseline, V_T/kg (mL/kg, mean ± SEM) was similar between PT (7.0 ± 0.7) and FT (7.5 ± 0.5) infants. $\dot{V}_E$/kg (mL/min/kg) was greater in PT (545 ± 50) than in FT (385 ± 33) infants ($p < 0.05$) as a result of increased respiratory frequency in the former. PT infants demonstrated significantly greater chest wall asynchrony (θ = 38 ± 9°) than FT infants (θ = 9 ± 3°) ($p < 0.01$). With the highest resistive loads, V_T decreased significantly in the PT but not the FT infants. Furthermore, during IRL, $\dot{V}_E$ decreased to 417 ± 50 mL/min/kg ($p < 0.05$) and θ increased to 56 ± 7 ($p < 0.05$) in the PT infants, whereas no significant change in either value was observed in the FT group. We conclude that IRL breathing significantly decreases V_T and $\dot{V}_E$ in PT infants. Chest wall instability in the PT group, as reflected by the increased asynchrony between rib cage and abdomen, contributes to the relative inability of PT infants to maintain ventilation during inspiratory resistive loaded breathing. (*Pediatr Res* 32: 589-594, 1992)

Abbreviations

IRL, inspiratory resistive load
FT, full-term
PT, preterm
V_T, tidal volume
$\dot{V}_E$, minute ventilation
f, respiratory frequency
P-P Pes, peak-to-peak esophageal pressure change
RC, rib cage
AB, abdomen
TAA, thoracoabdominal asynchrony
V.I., variability index (of phase angle, θ)
PNT, pneumotachograph (resistance 13.7 cm H_2O/L/s)
R1, resistive load 1 (63.7 cm H_2O/L/s)
R2, resistive load 2 (213.7 cm H_2O/L/s)

Received February 21, 1992; accepted June 18, 1992.
Correspondence and reprint requests: Julian L. Allen, M.D., Pulmonary Division, St. Christopher's Hospital for Children, Erie Avenue at Front Street, Philadelphia, PA 19134-1095.
Supported by The Foundation for Physical Therapy (M.R.W.), NIH HL32301 (T.H.S.), and NIH HL1R2941132 (J.L.A.).

Awake adults who are breathing through IRL can compensate for the increase in resistance by altering their pattern of breathing to maintain V_T and $\dot{V}_E$ (1). This compensation requires both an adequate respiratory control center response and an adequate mechanical system (respiratory muscle strength and chest wall stability) to be effective. The adequacy of this compensatory response, and factors that affect it, has been extensively studied in adults (2). Less is known about the response of infants to IRL. LaFramboise *et al.* (3) found a difference in the ability of 2-d- and 24-d-old infant monkeys to tolerate resistive loads; the newborn subjects were not able to maintain $\dot{V}_E$ with increasing loads of 2-6 times baseline respiratory resistance, whereas the older animals were. Although it appears that developmental changes in resistive load compensation occur during the neonatal period, there have been no direct comparisons between the PT and FT infant in this regard, nor has the role of chest wall instability been assessed. PT infants have a more compliant chest wall than FT infants (4). It is of interest in this regard that several studies have reported that PT infants are unable to maintain V_T and $\dot{V}_E$ when subjected to resistive loaded breathing (5-7).

In this study, we directly compare the ability of PT and FT infants to adapt to IRL breathing. We hypothesized that more chest wall distortion would occur in PT than in FT infants during IRL breathing. If this were true, we would expect that PT infants would be less able than FT infants to maintain V_T and $\dot{V}_E$. To test this hypothesis, we measured V_T, $\dot{V}_E$, and thoracoabdominal motion in PT and FT infants under three conditions of inspiratory resistive loading (14, 64, and 214 cm H_2O/L/s) to yield total resistive loads of approximately 1.3, 2, and 6 times baseline resistance.

MATERIALS AND METHODS

Study Population. Lung mechanics and thoracoabdominal motion were evaluated in 10 PT and eight FT infants who had no clinical evidence of lung disease at the time of study and did not, on visual inspection, demonstrate paradoxic breathing at rest. In addition, these infants had not required supplemental oxygen or ventilatory support for more than 48 h. Age and weight characteristics of the infants are given in Table 1.

Assessment of Lung Mechanics. Transpulmonary pressure,

Table 1. *Subject characteristics**

Group	*n*	Gestational age (wk)	Postconceptional age (wk)	Study wt (kg)
FT	8	39.8 ± 0.2	40.1 ± 0.1	3.3 ± 0.2
PT	10	31.6 ± 0.6	35.5 ± 0.5	1.6 ± 0.1

* Values are mean ± SEM.

airflow, and inspired and expired volumes were recorded during tidal breathing. Transpulmonary pressure was determined as the difference between airway (mouth) pressure and esophageal pressure. The latter was measured using an esophageal balloon, filled with 0.2–0.4 mL of air, connected to a differential pressure transducer (Celesco P7D, Canoga Park, CA). Proper balloon placement was assessed by the occlusion technique (8, 9). Mouth pressure was measured at the side port of the face mask pneumotachometer (Fleisch 00, Epalinges, Switzerland) used to measure airflow. The airflow signal was digitally integrated to determine V_T. The above measurements were collected over 60 to 120 s and stored for analysis (PeDS, Medical Associated Services, Hatfield, PA). Signals of airflow were also recorded on a polygraph recorder (model 7CPB, Grass Instrument Co., Quincy, MA), amplified, and integrated to yield V_T.

Pulmonary mechanics were determined by the least mean squares technique (10). Pressure, flow, and volume measurements were used to calculate lung compliance and resistance, P-P Pes, f, and $\dot{V}_E$.

Assessment of Chest Wall Motion. Movement of the RC and AB were assessed for TAA using respiratory inductive plethysmography (Respitrace Corporation, Ardsley, NY). Briefly, this device measures changes in the self-inductance of coils of wire woven into elastic bands that are placed around the RC and AB. The inductance changes reflect alterations in the cross-sectional area of the RC and AB during the respiratory cycle.

The inductance bands were fitted to the infant before the study, with the upper edge of the RC band placed below the axillae and the AB band placed midway between the lower border of the RC and the iliac crest. A cotton mesh jersey was used to maintain the bands in place during the study. The voltage changes occurring with RC and AB motion were recorded simultaneously on a strip chart recorder (Grass polygraph 7CB) to obtain scalar tracings and an *x-y* recorder (Hewlett-Packard 7035B, Hewlett-Packard Co., Palo Alto, CA) to obtain "Lissajous figures" of RC (*y* axis) *versus* AB (*x* axis) motion (11). RC and AB signals were adjusted so that they were readily visible and approximately equal to each other. The respiratory inductive plethysmograph was not calibrated for volume, as we were interested in evaluating asynchrony, not in measuring absolute volume (12).

The resulting Lissajous figures (Fig. 1) were analyzed as described previously (12, 13) for at least 10 breaths under baseline and each loading condition (see below). Briefly, when RC and AB motion are synchronous, a narrow or closed loop is produced that widens with increasing asynchrony. Paradoxic breathing, in which RC and AB motion are 180° out of phase, results in a closed loop with a negative slope. The phase angle (θ) was computed as $\theta = \sin^{-1}$ (m/s) for $\theta < 90°$ and as $\theta = 180° - \sin^{-1}$ (m/s) for $\theta > 90°$, where m = width of the Lissajous figure at mid RC excursion and s = width of the Lissajous figure at its largest AB excursion (12). Thus, θ ranged from 0° (synchronous) to 180° (paradoxic), with increasing angles indicating increasing TAA. The Lissajous figure was also evaluated for counterclockwise or clockwise direction, *i.e.* whether outward motion of the AB preceded or lagged, respectively, motion of the RC.

The breath-to-breath variability of phase angle within each subject was calculated at each resistive load as an index of changing "strategies" of chest wall motion. The V.I. was determined by adding the differences (Di) in θ between at least 10 consecutive breaths and dividing by the number (n) of breaths examined (14):

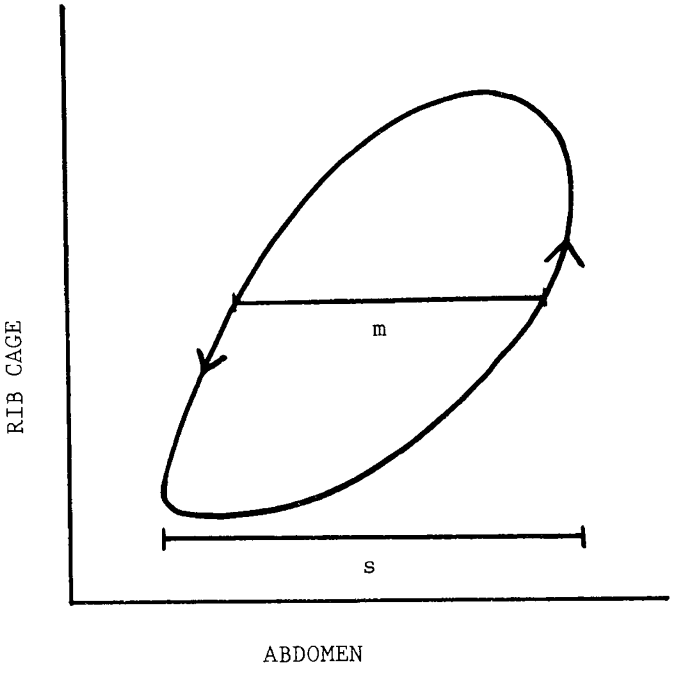

Fig. 1. RC and abdominal motion plotted against each other in a Lissajous figure. The ratio of m/s is used to calculate the phase angle, θ (see text).

$$\text{V.I.} = \sum_{i=1}^{n} \text{Di}/n$$

Experimental Protocol. Infants were evaluated at least 30 min after feeding, lying supine with the head placed in the midline and neck extended. This position was maintained throughout the study. All data were collected during nonsedated quiet sleep as determined by behavioral criteria (15, 16).

Baseline lung mechanics. To measure lung mechanics, a soft rubber mask was placed over the infant's nose and mouth, ensuring a good seal, and a PNT (dead space: 1.7 mL) was attached. Baseline lung mechanics measurements were repeated in duplicate or triplicate to ensure consistent measurements.

Measurement of thoracoabdominal motion at baseline and after application of external IRL. Baseline thoracoabdominal motion was assessed before and after application of the face mask. Because of the theoretical effect of face mask application on respiratory pattern during tidal breathing (17, 18), measurements made with the face mask in place were used as the basis for all subsequent comparisons with loaded breaths, as the face mask was required for attachment of the loads. After the collection of baseline data, the PNT was attached to the face mask, acting as the first resistive load (13.7 cm H_2O/L/s, or approximately 30% of baseline resistance in these infants). Subsequently, a one-way nonrebreathing valve was attached to the PNT, and inspiratory flow resistive loads of 50 and 200 cm H_2O/L/s (Hans Rudolph Inc., Kansas, MO) were randomly applied to the inspiratory port for up to 3 min. The 50 and 200 cm H_2O/L/s loads were linear over flow rates of 0–0.5 and 0–0.1 L/s, respectively. Taking into account the resistance of the PNT, the infants were thus subjected to resistive loads of 13.7 cm H_2O/L/s (PNT), 63.7 cm H_2O/L/s (R1), and 213.7 cm H_2O/L/s (R2). Infants were allowed to rest for 2–3 min between loads. Whenever possible, measurements were repeated with each of the three loads. RC and AB motion were recorded continuously throughout the study period. During all breathing studies, the PNT was used to provide airflow and volume signals, which were recorded on the strip chart recorder and used for the calculation of f and $\dot{V}_E$.

A transcutaneous pulse oximeter (N200, Nelcor, Inc., Hay-

ward, CA) was used to monitor the infant's heart rate and oxygen saturation throughout the protocol, and a study was terminated if heart rate fell below 90/min or O_2 saturation fell below 90%.

This protocol was approved by the St. Christopher's Hospital for Children and Temple University Hospital committees for the protection of human subjects, and informed parental consent was obtained for each study.

Statistical Analysis. Baseline studies. Differences in θ, V.I., and lung mechanics (V_T, f, $\dot{V}_E$, resistance, compliance, and P-P Pes) between PT and FT infants were analyzed for significance by a two-tailed t test for unpaired data, and significance was accepted at the $p < 0.05$ level.

Acute IRL studies. A multifactor randomized design analysis of variance was used to evaluate the effect of gestational age (PT *versus* FT) and IRL on θ, V.I., V_T, f, and $\dot{V}_E$. Data were further analyzed within each age group using single-factor repeated measure analyses of variance with appropriate post hoc tests to evaluate the effects of IRL. In all cases, significance was accepted at the $p < 0.05$ level.

RESULTS

Baseline studies. Summarized values for baseline pulmonary mechanics and RC-AB phase angle for PT and FT infants are shown in Table 2. There was no significant difference in V_T/kg between PT and FT infants; however, f, and hence $\dot{V}_E$/kg, were significantly higher in the PT infants. There were no significant differences in lung resistance and compliance between the two age groups. Although the peak-to-peak pleural pressure changes (P-P Pes) were slightly lower in the PT infants, this difference was not statistically significant.

Evaluation of thoracoabdominal motion by the *x-y* plots of AB-RC motion demonstrated predominantly counterclockwise loops in all infants. Phase angles (θ) were significantly greater in the PT than in the FT infants. Furthermore, chest wall motion breath-to-breath variability, as quantitated by the V.I., was significantly greater in the PT than in the FT group.

Acute inspiratory resistive loading. Summarized values for ventilation and thoracoabdominal motion indices with inspiratory resistive loading for PT and FT infants are given in Table 3. Because application of a face mask has been shown to influence ventilatory pattern (17, 18), baseline values of θ were remeasured with the face mask in place, and these values were used in all subsequent comparisons of IRL breathing. Both the PT and FT infants maintained V_T, f, and $\dot{V}_E$ upon application of load R1. PT infants showed significant decreases in V_T, f, and $\dot{V}_E$ upon application of load R2, whereas FT infants did not.

Chest wall motion became more asynchronous in the PT group, but not in the FT group, during IRL breathing (Figs. 2 and 3, Table 3). AB outward motion preceded RC outward motion in all infants under all conditions of loading (Fig. 2). Chest wall motion breath-to-breath variability was greater in PT than in FT infants under all conditions of loading (Fig. 3, Table 3).

Table 2. *Summarized baseline lung mechanics and RC-AB phase angles**

	FT infants	PT infants
V_T (mL/kg)	7.46 ± 0.48	7.03 ± 0.66
f (breaths/min)	56 ± 6	77 ± 4†
$\dot{V}_E$ (mL/min/kg)	385.6 ± 33.5	545.2 ± 50.5†
Compliance (mL/cm H_2O/kg)	1.36 ± 0.14	1.33 ± 0.22
Resistance (cm H_2O/L/s)	44.9 ± 6.0	55.0 ± 4.7
P-P Pes (cm H_2O)	7.0 ± 0.7	5.5 ± 0.6
Phase angle, θ (degrees)	9.3 ± 2.6	38.0 ± 8.7‡
V.I. (degrees)	4.9 ± 1.5	19.6 ± 3.4‡

* Phase angle measurements were made without the face mask. Values are mean ± SEM.

† $p < 0.05$, PT infants different from FT infants.

‡ $p < 0.01$, PT infants different from FT infants.

DISCUSSION

The principal findings of this study are as follows: *1*) During resting tidal breathing in quiet sleep, PT infants with normal lung function display substantially more asynchronous RC-abdominal motion than FT infants. *2*) In FT infants, acute external inspiratory resistive loading causes relatively little change in RC-abdominal synchrony, V_T or $\dot{V}_E$. *3*) In contrast, in PT infants, acute external inspiratory resistive loading causes increased TAA and decreased V_T and $\dot{V}_E$. The implication is that chest wall instability plays a role in the inability of the PT infant to sustain $\dot{V}_E$ during loaded breathing.

Methodologic considerations. Prior studies comparing the response of PT and FT infants to resistive loaded breathing have concentrated on the first loaded breath to compare indices of respiratory drive such as mechanical inspiratory time, neural inspiratory time as reflected by diaphragmatic electromyogram, and strength of the Hering-Breuer reflex (19, 20). We were interested in the functional consequences of resistive loads on $\dot{V}_E$ and therefore chose to study breaths that occurred after the infant had time to "adapt" to the load. Significant adaptation to loaded breathing can occur within five to 10 breaths; recovery of V_T, for example, can occur between the first and subsequent five loaded breaths in infants (21) and adult humans (2). We chose to examine breaths between 2 and 5 min into a given loading run because prior studies have shown that a steady state ventilatory level is achieved by then (1, 3, 7). Furthermore, all of our infants had achieved a stable pattern of frequency and V_T by the time we initiated measurements.

Sleep state can affect the response to resistive and elastic loading (2, 21) and can affect RC-abdominal timing relationships (22–24). We therefore studied all our infants in clinically determined quiet sleep (15, 16).

We chose to measure baseline thoracoabdominal motion during breathing through the face mask without the PNT attached, because the PNT presented a substantial resistive load by itself (up to 30% of intrinsic lung resistance). The resistive loads we used were the same for the PT and FT infants; if PT infants have higher baseline resistance than FT infants, this could theoretically result in a lower "load" for the PT infants compared to baseline. However, the baseline resistance values were not significantly different between the two groups of infants. Furthermore, the loads of PNT, R1, and R2 represented relative resistance increases over intrinsic lung resistance of 25%, 114%, and 387%, respectively, for the PT infants and 31%, 143%, and 473%, respectively, for the FT infants. One might expect this should result in greater ventilatory effects on the FT than on the PT group; therefore, our findings that the greater effects were seen in the PT group cannot be explained by relative differences in load.

We used esophageal manometry to measure baseline lung mechanics. Technical problems associated with the use of this technique have recently been described (8, 9, 25, 26). Thompson *et al.* (25) found that pleural pressure swings could be underestimated by this technique in intubated PT infants, whereas LeSouef *et al.* (26) found that pleural pressure swings could be overestimated during periods of maximal chest wall paradox associated with active sleep. We feel, however, that our lung mechanics results are accurate for the following reasons: *1*) In the Thompson study (25), the occlusion technique verified accurate pleural pressure measurement in the healthy PT infants but not in the sick intubated infants. The PT infants that we studied were healthy; furthermore, we verified our esophageal manometry measurements by the occlusion test, thus indicating that our pleural pressure measurements were accurate (8, 9). *2*) We excluded infants with obvious chest wall paradox from the study (see Materials and Methods) and only studied infants

Table 3. *Inspiratory resistive loading**

	Face mask	PNT	R1	R2
FT infants				
V_T (mL/kg)		7.5 ± 0.5	7.5 ± 0.9	6.9 ± 0.9
f (breaths/min)		55.9 ± 5.7	55.5 ± 4.6	54.9 ± 4.7
$\dot{V}_E$ (mL/min/kg)		385.6 ± 33.5	387.1 ± 20.0	354.2 ± 27.0
θ (degrees)	16.5 ± 3.3	20.8 ± 4.5	26.5 ± 4.9	22.3 ± 5.9
V.I. (degrees)	6.3 ± 1.6	6.8 ± 1.2	7.9 ± 1.7	10.9 ± 3.1
PT infants				
V_T (mL/kg)		7.0 ± 0.7	7.5 ± 0.4	6.1 ± 0.6†
f (breaths/min)		77.4 ± 4.2	74.7 ± 2.3	68.5 ± 4.2†
$\dot{V}_E$ (mL/min/kg)		545.2 ± 50.5	555.2 ± 28.3	417.9 ± 50.9†
θ (degrees)	36.4 ± 6.9‡	44.3 ± 6.0‡	43.9 ± 6.7‡	55.5 ± 7.4†‡
V.I. (degrees)	13.9 ± 3.4‡	18.9 ± 2.8‡	15.9 ± 2.7‡	19.4 ± 2.8‡

* Summarized values of ventilatory and thoracoabdominal motion indices in FT and PT infants during the following conditions: with face mask alone, application of the PNT, R1, and R2. Values are mean ± SEM.

† $p < 0.05$, R2 different from baseline.

‡ $p < 0.05$, PT different than FT.

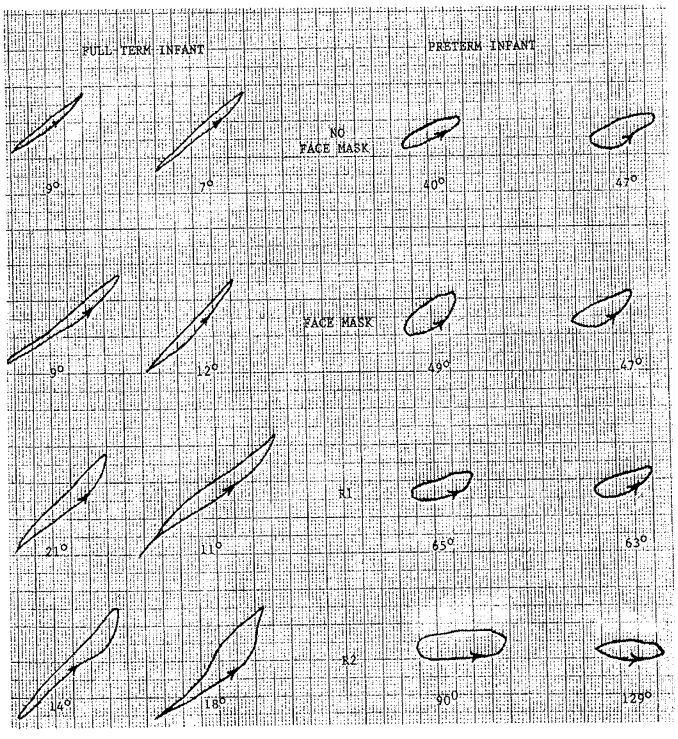

Fig. 2. Typical quiet sleep Lissajous figures from an FT infant and a PT infant when breathing *1*) without a face mask, *2*) with a face mask, *3*) with R1, and *4*) with R2 applied to the mask. The PT infant has more chest wall motion asynchrony than the FT infant. In addition, IRL breathing increases asynchrony in the PT infant but not the FT infant.

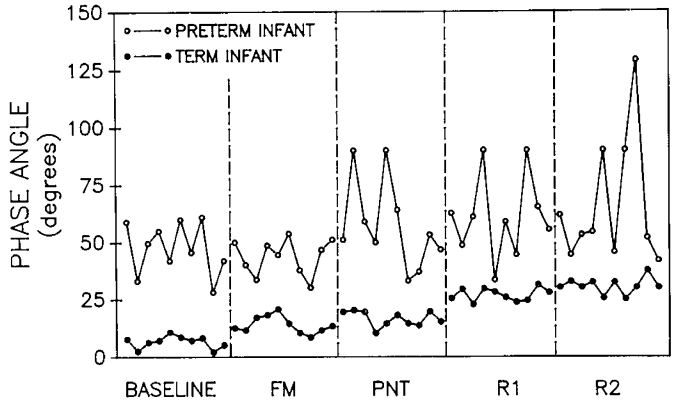

Fig. 3. Phase angles of 10 consecutive breaths in a PT and an FT infant during each of the following conditions: *1*) baseline (no face mask), *2*) application of face mask (*FM*), *3*) FM + pneumotachograph (*PNT*), *4*) R1, and *5*) R2. Asynchrony and breath-to-breath variability of phase angle is greater in the PT than in the FT infant at all levels of IRL breathing.

during quiet sleep. The FT infants all displayed synchronous chest wall motion. The degree of asynchrony that our PT infants displayed during measurement of lung mechanics (mean phase angle 38°) was no where near the 180° out of phase motion that has been reported to interfere with esophageal manometry measurements (26).

TAA in normal PT infants. The finding of asynchronous breathing at baseline in PT compared to FT infants (Figs. 2 and 3, Table 2) is consistent with the former having increased intrapleural pressure swings, increased chest wall instability, or both. Infants with increased intrapleural pressure swings during tidal breathing, *e.g.* patients with increased airflow resistance, display asynchronous breathing with abdominal dimensions increasing before RC dimensions during inspiration; the negative pleural pressure impedes outward RC motion as the descending diaphragm moves the abdominal wall outward (12). Although the PT infants that we studied had slightly higher resistance than the FT infants, the difference was not significant; additionally, because of their lower absolute V_T and flow rates, pleural pressure swings were actually lower in the PT group (Table 2). Thus, these data support the concept that increased asynchrony in PT infants is due to increased chest wall distortability, a finding that is in agreement with prior studies of chest wall compliance in PT and FT infants (4) and of developmental changes in minute volume displacement of the diaphragm and of diaphragmatic work (27, 28).

Effects of acute resistive loading in FT infants. Upon application of acute external IRL, the FT infants were able to maintain $\dot{V}_E$ surprisingly well compared with prior studies in newborn monkeys. In our study, the change in $\dot{V}_E$ upon applications of loads of 1.3, 2, and 6 times baseline resistance was insignificant (Table 3). In contrast, term newborn monkeys have been shown to decrease $\dot{V}_E$ by 10% and 25%, respectively, upon application of similarly graded loads (3).

FT infants also displayed no increase in TAA upon application of resistive loads; indeed, this may in part explain their ability to maintain $\dot{V}_E$. This finding, too, was somewhat surprising in view of earlier studies of TAA in infants with chronic lung disease in which it has been shown that the degree of TAA in such infants is proportional to the degree of elevation of airways resistance (12, 29). We therefore expected the addition of graded IRL to lead to increasing degrees of TAA. Although we do not have direct evidence, we surmise that the mechanical forces that lead

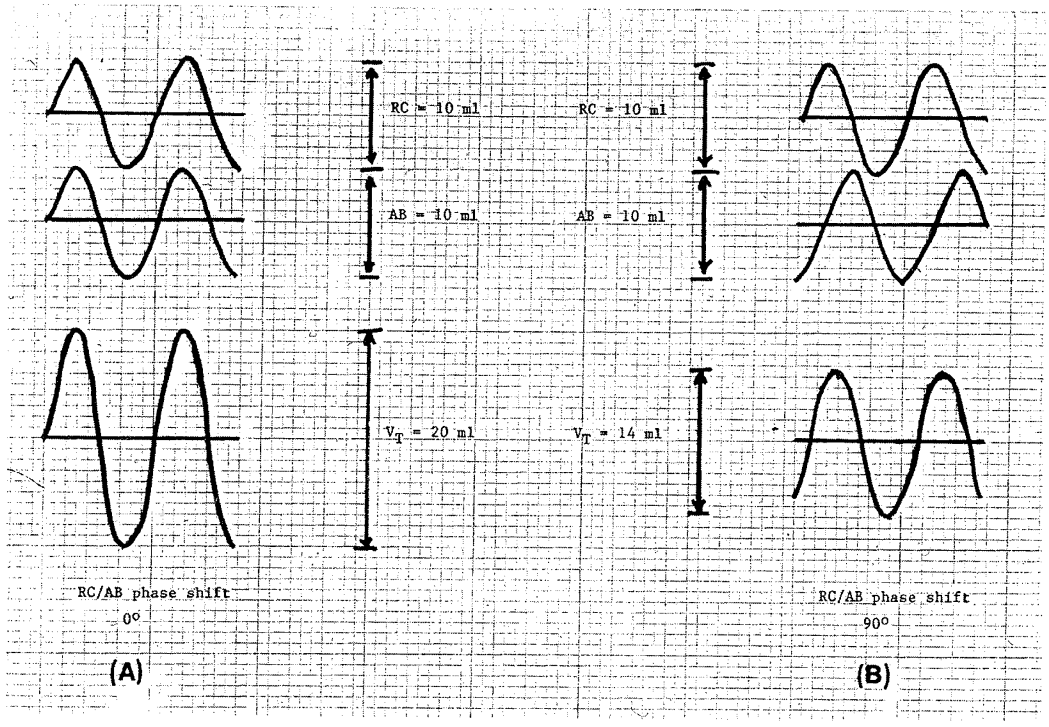

Fig. 4. Idealized figure of RC and AB contributions to total V_T under conditions of synchronous (*A*) and asynchronous (*B*) chest wall motion. *A*, Sum of peak-to-peak swings of RC + AB equals swings of V_T. *B*, Although RC and AB individual volume contributions are unchanged, V_T is less than sum of peak-to-peak RC + AB.

to TAA were overshadowed by increased respiratory drive tending to drive the RC and AB in a more synchronous fashion. This compensation was maintained for the relatively short duration of loaded breathing that we studied (several minutes). Mortola *et al.* (30) have shown that RC distortion in sleeping FT infants decreases V_T to half that obtained during passive inflations and that, when infants breathe along the relaxation curve of the chest wall, this RC distortion is not absent but merely compensated for by extradiaphragmatic muscles expanding the RC. They further speculate that the distorted pattern is more advantageous to the infant in that it may provide an energetic advantage by decreasing negative intrapleural pressure. This speculation is consistent with our finding that term infants are able to maintain synchronous breathing for short-duration resistive loads, but that when confronted with a long-term resistive load (as seen in chronic lung disease) they adopt an asynchronous pattern that allows inspiratory RC distortion.

Effects of resistive loading in PT infants. We have shown that PT infants do not sustain V_T and $\dot{V}_E$ as well as FT infants in response to graded inspiratory resistive loading. Concomitantly, PT infants display substantially greater TAA in response to resistive loading than do FT infants.

The ability of the infant to sustain $\dot{V}_E$ in the face of resistive loads depends on both adequate respiratory control center output and adequate respiratory system mechanical stability. Although no prior studies have directly compared the abilities of PT and FT infants to maintain $\dot{V}_E$ and V_T during resistive loaded breathing, several studies have compared the effects of either resistive loads or total occlusions on inspiratory timing and volume of the first loaded breath (19, 20, 31–34). Interestingly, for the same relative decrease in V_T, PT infants of greater than 32 wk gestation prolong inspiratory effort to the same degree (19, 20, 32, 34) as or to a greater degree (31, 33) than FT infants. This prolongation of inspiratory effort is one manifestation of the Hering-Breuer reflex (33, 35) and serves as a compensatory response to resistive loading; if inspiratory flow is diminished due to the resistive load, prolonging inspiratory time will tend to preserve V_T (3). Why, then, are PT infants not as able as FT infants to maintain V_T and $\dot{V}_E$? We speculate that although PT infants may have a respiratory drive that is adequate to maintain ventilation under loaded conditions, the mechanical inefficiency of the highly compliant chest wall prevents adequate compensation from occurring; this is reflected in the increased degree of TAA that the PT infants displayed under both baseline and loaded conditions. In addition, there may be differences in the abilities of PT and FT infants to recruit respiratory muscles in response to IRL breathing such that PT infants cannot further recruit the intercostal muscles as well as FT infants, resulting in less stability of the RC. Diaphragmatic and intercostal electromyographic studies would be interesting in this regard. In any event, the resultant TAA can directly decrease V_T even if the individual compartments' volume excursions remain the same (Fig. 4). Thus, TAA could decrease $\dot{V}_E$ independently of changes in respiratory center neural output.

There is an additional way that TAA can lead to decreased V_T. Inward distortion of the RC during inspiration has been shown to lead to early termination of inspiration in infants (36); whether this intercostal-phrenic inhibitory reflex is as strong in FT infants as in PT infants is controversial (34, 36). In either case, it could help explain the difference between the PT and the FT infant's ventilatory response to resistive loading. Because resistive loading results in more RC distortion in the PT than in the FT infant, this reflex would be expected to result in a greater decrement in $\dot{V}_E$ in the former.

Our findings of increased TAA with IRL breathing are similar to those of Tobin *et al.* (37) in awake adults. They differ in an important respect, however. Whereas Tobin demonstrated paradoxic motion primarily of the AB during loaded breathing and clockwise loops indicating that RC outward motion preceded AB outward motion, we have demonstrated the reverse (Fig. 2). Our findings are consistent with the highly compliant chest wall of the PT infant being unable to withstand the distorting force of negative pleural pressure during inspiration. Our finding of greater variability of chest wall motion synchrony in PT than in FT infants (Tables 2 and 3, Fig. 3), both at baseline and during IRL breathing, suggests that recruitment and derecruitment of

intercostal muscles and diaphragm (38) may occur in PT infants. This strategy has been suggested as one that may postpone respiratory muscle fatigue in adults (37), and it may similarly be a way that the PT infant deals with the inefficiencies inherent in a highly compliant chest wall.

In summary, the greater degree of TAA in PT than in FT infants under resting conditions probably results from the increased RC compliance in the PT infants. During resistive loading, TAA significantly increases in the PT, but not the FT infant; PT infants also experience significant declines in V_T and $\dot{V}_E$. Our findings provide a mechanism for why nasal occlusion, for example, may have ventilatory consequences in the PT infant (39). We suggest that the inefficiency of chest wall motion that is induced in the PT infant by resistive loads may play a role in its inability to maintain $\dot{V}_E$ that is independent of considerations of central respiratory drive.

REFERENCES

1. Freedman S, Campbell EJM 1970 The ability of normal subjects to tolerate added inspiratory loads. Respir Physiol 10:213–235
2. Wiegand L, Zwillich CW, White DP 1988 Sleep and the ventilatory response to resistive loading in normal men. J Appl Physiol 64:1186–1195
3. LaFramboise WA, Standaert TA, Guthrie RD, Woodrum DE 1987 Developmental changes in the ventilatory response of the newborn to added airway resistance. Am Rev Respir Dis 136:1075–1083
4. Gerhardt T, Bancalari E 1980 Chest wall compliance in full term and premature infants. Acta Paediatr Scand 69:359–364
5. Boychuk RB, Seshia MMK, Rigatto H 1977 The immediate ventilatory response to added inspiratory elastic and resistive loads in preterm infants. Pediatr Res 11:276–279
6. Abbasi S, Duara S, Shaffer T, Fox WW 1984 Effect of external inspiratory loading on ventilation of premature infants. Pediatr Res 18:150–154
7. Duara S, Abbasi S, Shaffer TH, Fox WW 1985 Preterm infants: ventilation and P_{100} changes with CO_2 and inspiratory resistive loading. J Appl Physiol 58:1982–1987
8. Beardsmore CS, Helms P, Stocks J, Hatch DJ, Silverman M 1980 Improved esophageal balloon technique for use in infants. J Appl Physiol 49:735–742
9. Coates AL, Stocks J 1991 Esophageal pressure manometry in human infants. Pediatr Pulmonol 11:350–360
10. Bhutani VK, Sivieri EM, Abbasi S, Shaffer T 1988 Evaluation of neonatal pulmonary mechanics and energetics: a two factor least mean squares analysis. Pediatr Pulmonol 4:150–158
11. Kono K, Mead J 1967 Measurement of the separate volume changes of the rib cage and abdomen during breathing. J Appl Physiol 22:407–422
12. Allen JL, Wolfson MR, McDowell K, Shaffer TH 1990 Thoraco-abdominal asynchrony in infants with airflow obstruction. Am Rev Respir Dis 141:337–342
13. Agostoni E, Mognoni P 1966 Deformation of the chest wall during breathing efforts. J Appl Physiol 21:1827–1832
14. Klemfuss H, Tallarida RJ, Adler CH, Adler MW 1979 Morphine induced mydriasis and fluctuation in the rat: time and dose relationships. J Pharmacol Exp Ther 208:91–95
15. Prechtl HFR 1974 The behavioural states of the newborn infant. Brain Res 76:185–212
16. Shulte FJ 1981 Developmental neurophysiology. In: Davis J, Dobbins J (eds) The Scientific Foundations of Pediatrics. University Park Press, Baltimore, pp 785–789
17. Fleming PJ, Levine MR, Goncalves A 1982 Changes in respiratory pattern resulting from the use of a face mask to record respiration in newborn infants. Pediatr Res 16:1031–1034
18. Dolfin T, Dufty P, Wilkes D, England S, Bryan H 1983 Effects of a face mask and pneumotachograph on breathing in sleeping infants. Am Rev Respir Dis 128:977–979
19. Kosch PC, Davenport PW, Wozniak JA, Stark AR 1986 Reflex control of inspiratory duration in newborn infants. J Appl Physiol 60:2007–2014
20. Fox RE, Kosch PC, Feldman HA, Stark AR 1988 Control of inspiratory duration in premature infants. J Appl Physiol 64:2597–2604
21. Knill R, Andrews W, Bryan AC, Bryan MH 1976 Respiratory load compensation in infants. J Appl Physiol 40:357–361
22. Carlo WA, Martin RJ, Versteegh FGA, Goldman MD, Robertson SS, Fanaroff AA 1982 The effect of respiratory distress syndrome on chest wall movements and respiratory pauses in preterm infants. Am Rev Respir Dis 126:103–107
23. Rome ES, Miller MJ, Goldthwait DA, Osorio IO, Fanaroff AA, Martin RJ 1987 Effect of sleep state on chest wall movements and gas exchange in infants with resolving bronchopulmonary dysplasia. Pediatr Pulmonol 3:259–263
24. Gaultier C, Praud JP, Canet E, Delaperche MF, D'Allest AM 1987 Paradoxical inward rib cage motion during rapid eye movement sleep in infants and young children. J Dev Physiol 9:391–397
25. Thompson A, Elliot J, Silverman M 1983 Pulmonary compliance in sick low birthweight infants. Arch Dis Child 58:891–896
26. LeSouef PN, Lopes JM, England SJ, Bryan HM, Bryan CA 1983 Influence of chest wall distortion on esophageal pressure. J Appl Physiol 55:353–358
27. Heldt GP, McIlroy MB 1987 Distortion of chest wall and work of diaphragm in preterm infants. J Appl Physiol 62:164–169
28. Heldt GP, McIlroy MB 1987 Dynamics of the chest wall in preterm infants. J Appl Physiol 62:170–174
29. Allen JL, Greenspan JS, Deoras KS, Keklikian E, Wolfson MR, Shaffer TH 1991 Interaction between chest wall motion and lung mechanics in normal infants and infants with bronchopulmonary dysplasia. Pediatr Pulmonol 11:37–43
30. Mortola JP, Saetta M, Fox G, Smith B, Weeks S 1985 Mechanical aspects of chest wall distortion. J Appl Physiol 59:295–304
31. Kirkpatrick SML, Olinsky MB, Bryan MH, Bryan AC 1976 Effect of premature delivery on the maturation of the Hering-Breuer inspiratory inhibitory reflex in human infants. J Pediatr 88:1010–1014
32. Thach BT, Frantz III ID, Adler SM, Taeusch Jr HW 1978 Maturation of reflexes influencing inspiratory duration in human infants. J Appl Physiol 45:203–211
33. Olinski A, Bryan MH, Bryan AC 1974 Influence of lung inflation on respiratory control in neonates. J Appl Physiol 36:426–429
34. Gerhardt T, Bancalari E 1981 Maturational changes of reflexes influencing inspiratory timing in newborns. J Appl Physiol 50:1282–1285
35. Grunstein MM, Younes M, Milic-Emili J 1973 Control of tidal volume and respiratory frequency in anesthetized cats. J Appl Physiol 35:463–476
36. Knill R, Bryan AC 1976 An intercostal-phrenic inhibitory reflex in human newborn infants. J Appl Physiol 40:352–356
37. Tobin MJ, Perez W, Guenther SM, Lodato RF, Dantzker DR 1987 Does rib cage-abdominal paradox signify respiratory muscle fatigue? J Appl Physiol 63:851–860
38. Roussos C, Fixley M, Gross D, Macklem PT 1979 Fatigue of inspiratory muscles and their synergic behavior. J Appl Physiol 46:897–904
39. Martin RJ, Miller MJ, Siner B, DiFiore JM, Carlo WA 1989 Effects of unilateral nasal occlusion on ventilation and pulmonary resistance in infants. J Appl Physiol 66:2522–2526