A Developmental Study on Types and Frequency Distribution of Short Apneas (3 to 15 Seconds) in Term and Preterm Infants¹

DAVID LEE, REBECCA CACES, KIM KWIATKOWSKI, DON CATES, AND HENRIQUE RIGATTO

University of Manitoba, Department of Pediatrics, Section of Neonatal Medicine, Women's Hospital, Winnipeg, Manitoba, R3E 0L8 Canada

ABSTRACT. We measured the frequency distribution and the ventilatory correlates of the various types of apneas 3 to 15 s long during sleep in eight term infants (birth weight 3.65 ± 0.16 kg; gestational age 39.5 ± 0.3 wk) and eight preterm infants (birth weight 2.07 ± 0.18 kg; gestational age 34.3 ± 0.4 wk). Each infant was studied on five to seven occasions from birth to 56 wk of postconceptual age using a modified flow-through system. Sixty-six paired epochs of quiet sleep (1163 min) and rapid eye movement sleep (829 min) were analyzed in term infants and 85 paired epochs of quiet sleep (1553 min) and rapid eye movement sleep (1328 min) in preterm infants. Of the 783 apneas recorded in term infants 82% were central, 1.5% obstructive, 0.5% mixed, and 16% were of the breath-holding type; the corresponding figures for the 4086 apneas recorded in preterm infants were 93, 0.5, 1.0, and 5.5%. This distribution was similar in the two sleep states but term infants had a higher percentage of breath-holding apneas than preterm infants ($p < 0.01$). In preterm infants the rate of central apneas decreased with postnatal age ($p < 0.01$); in term infants the rate did not change significantly. The duration of apneas showed a modal distribution for central apneas at about 8 s for both groups during the 1st month of life ($p < 0.05$). The findings suggest: 1) apneas in the newborn and early infancy are primarily central and are more frequent in preterm than in term infants; 2) the higher rate of apnea in healthy preterm infants is accounted for almost entirely by the higher rate of central apneas; 3) a significant decrease in the rate of apnea occurs during the first 4 months after birth; and 4) preterm infants show longer respiratory pauses in both quiet sleep and rapid eye movement sleep when compared to term infants, and a maturation pattern can be discerned by 3 months of age. (*Pediatr Res* 22: 344–349, 1987)

Abbreviations

V_E , minute ventilation
 V_T , tidal volume
 f , respiratory frequency
 $P_A\text{CO}_2$, end-tidal PCO_2
 $P_A\text{O}_2$, end-tidal PO_2
QS, quiet sleep
REM, rapid eye movement sleep
 $T_c\text{PO}_2$, transcutaneous PO_2

EMG_{Di}, electromyogram of the diaphragm
BW, birth weight
GA, gestational age
ANOVA, analysis of variance
SIDS, sudden infant death syndrome

Although long and potentially pathologic apneas of more than 20 s in duration have been frequently studied, there is little known about the developmental pattern of shorter apneas of 3 to 15 s (1–6). There is increasing evidence that the presence of these short apneas reflect a disturbance of the respiratory control system which may lead to longer apneas and to SIDS (7–10). Furthermore, there are a paucity of data on the prevalence of the various types of apnea during the neonatal period and early infancy. The change in frequency distribution of these apneas with age and in different sleep states has not been determined.

We designed this study therefore to determine the types of apneas 3 to 15 s long and their frequency distribution according to sleep state at the various gestational and postnatal age.

SUBJECTS

Eight term infants [BW 3.65 ± 0.16 kg (SE); GA 39.5 ± 0.3 wk] and eight preterm infants (BW 2.07 ± 0.18 kg; GA 34.3 ± 0.4 wk) were studied after informed consent was obtained from one or both parents. All infants were born at the Women's Hospital, Winnipeg. Term babies had normal antenatal and postnatal course. Mothers of the preterm babies had various forms of complications during the last trimester. However, none of their babies showed any degree of asphyxia at the time of birth. None had evidence of intracerebral hemorrhage and all were neurologically normal on follow-up. All babies grew and developed normally for the duration of the study, and remained normal at 1 yr of age by telephone enquiry.

METHODS

Polygraphic recording was done on five to seven sessions in each infant. Infants breathed a mixture of 21% O_2 in N_2 during the study. Term infants were studied within the 1st wk of birth and then at 4-wk intervals until the postconceptual age of 56 wk. Preterm infants were studied at 2-wk intervals during the 1st month and then at 4-wk intervals until the postconceptual age of 52 to 56 wk. All sleep-monitoring sessions were carried out in a neonatal respiratory laboratory. The babies slept in a supine position on an Ohio Neonatal Intensive Care Unit, shortly after a feed. The ambient temperature was kept at the thermal neutral range and skin temperature remained at $36.5 \pm 0.03^\circ\text{C}$.

Received October 2, 1986; accepted April 20, 1987.

Correspondence Dr. Henrique Rigatto, The University of Manitoba, Department of Pediatrics, Room WS108 Women's Hospital, 735 Notre Dame Avenue, Winnipeg, Manitoba R3E 0L8 Canada.

Supported by The Medical Research Council of Canada Grant MT-4980 and The Children's Hospital of Winnipeg Research Foundation.

¹ Presented in part at the FASEB meeting, Anaheim, CA April 1985.

Details of instrumentation and measurements have been described previously (11, 12). Briefly, ventilation was measured using a nose-piece and a flow-through system (13). Inspiratory flow was integrated to give volume. Breath-to-breath O_2 and CO_2 concentrations were measured continuously by sampling at one of the nostrils (Beckman O_2 and CO_2 analyzers). $TcPO_2$ (Narco Scientific Ltd.) and O_2 saturation (Biox II Ear Oxymeter) were also continuously recorded. EMG_{Di} was recorded with surface electrodes. Chest and abdominal excursions were monitored by mercury strain gauge (11). Electrocardiogram was monitored using standard leads.

Sleep states were defined as previously (11, 14). The definition depended on monitored EEG (F4-A1 leads), eye movements, and behavior. Movements of the eyes were recorded by two leads placed one superior to the left outer canthus and one inferior to the right outer canthus, both referenced to the right pinna. Behavioral changes as well as visible rapid eye movements were charted on the continuous readout tracing. Signals were filtered, amplified, and recorded on a multichannel EEG recorder (Nihon Kohden Inc.) and also stored on magnetic tape for future analysis. For each study the behavioral state of the infant was classified into periods (epochs) of recognizable wakefulness, QS, REM, transitional state, and indeterminate state. Wakefulness was defined by eye opening and restlessness, with or without crying. QS was defined by eye closure in the presence of high voltage EEG activity or "trace alternans," and the absence of eye movement and general body movement except for occasional myoclonic jerks ("startles"). REM was defined by the presence of rapid eye movements during sleep, irregular low voltage fast EEG activity, and frequent jerking movements of the body. As in previous studies (15) we avoided using respiratory pattern as a basis for defining sleep states. Transitional states were periods "sandwiched" between QS and REM without wakefulness. Periods that could not be thus classified were deemed indeterminate.

Of the five behavioral states, QS and REM epochs were further analyzed for the ventilatory variables and the presence of apneas of 3 to 15 s in duration. For each epoch, we calculated V_T , f , V_I , end-tidal PCO_2 and PO_2 , $TcPO_2$, O_2 saturation, and $\int EMG_{Di}$. These variables were meant to define the ventilatory correlates

of each state and served as independent assessment of sleep states. A representative tracing is shown in Figure 1.

The respiratory pauses, identified by the cessation of nasal air flow for 3 to 15 s not associated with gross body movements or stretching, were classified into one of four categories: 1) central apnea: an expiratory pause during which no respiratory output could be detected in the form of EMG_{Di} , chest or abdominal excursions; 2) obstructive apnea: a pause in nasal flow with persistent EMG_{Di} activity, and chest and abdominal excursions; 3) mixed apnea: pauses with elements of central and obstructive apneas; and 4) breath-holding apnea: an expiratory pause that is terminated by an expiration before the next breath (Fig. 2).

Statistical analysis consisted of pairing adjacent epochs of QS and REM in order to reduce the intrastudy variability (16). In eight term infants 66 paired epochs of QS (total duration 1163 min) and REM (829 min) were analyzed, while in the eight preterm infants 85 pairs were identified (QS, 1553 min; REM, 1328 min). The proportion of QS and REM were not different in the two groups.

For each epoch the rate of each type of apnea was expressed as number per h. Since apnea rate (r) had a non-Gaussian distribution a logarithmic transformation [$\ln(r + 1)$] was performed to normalize the data before comparing the means using the two-tailed paired t test. A p value of less than 0.05 was considered to be significant. Chi-square was used to detect differences in the proportion of the different types of apneas. Split-plot ANOVA was used to examine the effects of postconceptional age and sleep state on the rate of apneas and other respiratory measurements. Individual comparisons were then made using the least squares means test. The duration of the apneas showed a continuous distribution between 3 and 15 s. The relationship between rate and duration of apnea was examined using least squares curve fitting procedures (17).

RESULTS

A total of 783 apneas was recorded in term infants and 4086 in the preterm infants. Of these, central apneas predominated, accounting for 82% of the total in term infants and 93% in preterm (Table 1, Fig. 3). The next most frequent type was the

Fig. 1. Representative tracing during REM sleep in a preterm infant (33 wk gestation) at 25 days of age.

Fig. 2. Classification of apneas. Apneas were defined by the absence of nasal airflow and the absence (central type) or presence (obstructive type) of diaphragmatic activity and corresponding chest and abdominal movements. Mixed apneas showed both central and obstructive features. In breath-holding type the expired breath was delayed until just before the next inspiration.

breath-holding apnea which was more prevalent in the term group accounting for 16% of the total; only 5.5% of the apneas in the preterm group belonged to this type ($p < 0.02$). The other two types of apneas accounted for less than 3% of the total number of apneas. There was no difference between sleep states regarding this distribution.

Preterm infants had a significantly higher rate of central apneas in both sleep states than term infants ($p < 0.01$; Fig. 4). In preterm infants the rate fell rapidly postnatally; by 44 wk of postconceptional age it was comparable to that of term infants. After 44 wk there was a divergence in the rate of central apneas between the two sleep states, the rate during REM being higher at 47 wk and at 54 wk ($p < 0.05$). In term infants the change in rate of central apneas with increasing postnatal age was less pronounced and not significant. In these infants the mean rate of apneas in QS increased from an initial value of 9/h at 3 days to 24/h at 4 wk of age, and then decreased gradually over the next 2 to 3 months to levels below the initial value. In REM, a similar trend was observed during the 1st month. Again, after 44 wk of postconceptional age there was a divergence in the rate of apneas between the two sleep states in term infants, the rate becoming significantly higher in REM sleep at 48 wk ($p < 0.05$). The rate of breath-holding apneas in term infants decreased with age from 7/h at 40 wk to 0.5/h at 48 wk of postconceptional age ($p < 0.01$) and from 10/h at 35 wk to 0.9/h at 47 wk ($p < 0.05$) in preterm.

The duration of apneas was arbitrarily classified into intervals of 1 s (from 3 to 15 s) and the relationship between rate and duration was examined for central and breath-holding apneas. The longest apnea lasted for 15 s. For both term and preterm infants non-Gaussian distributions were obtained in both sleep states during the 1st and the 3rd month of life (Fig. 5). In preterm infants at 1 month of postnatal age, the distribution of rates of central apneas during QS demonstrated a modal tendency at around 8 s both in REM and in QS. Using least squares curve fitting procedures (17) the data were fitted to a combined quadratic curve (describing the primary decreasing rate/apnea duration relationship) and normal curve (describing the secondary peaked relationship present at duration of 6 to 10 s). The fit was excellent ($p < 0.001$) and the composite model accounted for 99.4% of the observed variation. The secondary normal curve had a peak at 8.13 s. At 3 months of age during REM and QS, the data also fitted quadratic models ($p < 0.001$) but a secondary peak was absent. Similarly, in term infants the data on central apneas fitted a composite quadratic/normal model at 1 month of age in QS ($p < 0.001$) and accounted for 92.9% of the observed variation. The peak for the secondary normal distribution was at 7.94 s. In REM sleep at 1 and 3 months and in QS at 3 months the data fitted quadratic models ($p < 0.001$) but a secondary peak was absent.

In preterm infants at 1 month of age, the distribution of breath-holding apneas during QS also fitted a composite quadratic/normal curve model ($p < 0.001$), which accounted for 84.0% of

the observed variations. The peak for the secondary normal curve was at 8.05 s. At 1 month of age in REM sleep the data also fitted a composite model ($p < 0.001$) but a secondary peak was absent. At 3 months the breath-holding apneas were too few to be subjected to statistical analysis. In term infants the frequency of breath-holding apneas was also low for statistical analysis.

There was no significant change in V_E over the period of the study but values in REM were significantly higher than those in QS for all ages ($p < 0.05$) (Table 1, Fig. 6). This was due primarily to a higher f in REM ($p < 0.05$) in the preterm group with V_T remaining unchanged between the states. In term infants the higher V_E in REM was also primarily attributed to an increase in f , but V_T was also significantly larger at 48 and 52 wk of postconceptional age. P_aCO_2 remained unchanged in both groups of infants over the period of study as was $TcPO_2$ in term infants. $TcPO_2$ in the preterm group showed a significant increase with age, from 60 mm Hg at 37 wk postconceptional age to 77 mm Hg at 47 wk postconceptional age ($p < 0.05$).

DISCUSSION

We examined the frequency distribution of the various types of short apneas (3 to 15 s) during the first 3 months of life in healthy preterm and term infants. We found that central apneas predominated, obstructive, or mixed apneas being rare. Breath-holding apneas, surprisingly, were relatively common in term infants. The distribution of apneas according to length was continuous showing a modal tendency at about 8 s in preterm infants during the 1st month of life. Despite the high prevalence of apneas, particularly in the preterm group of infants, ventilatory correlates remained remarkably unchanged. Sleep states affected the prevalence of apneas only after 44 wk of postconceptional age. The findings suggest that oscillations of the respiratory control system producing short apneas during early postnatal life are common. Because they are more frequent in preterm than in term infants, we suggest that they reflect immaturity of the respiratory control system, possibly involving the respiratory "centers" and the peripheral mechanical properties of the respiratory pump.

The frequency distribution of short apneas has not been examined sequentially during the early neonatal period. We were surprised to see that they are commonly seen also in term infants. Kelly and Shannon (18) suggested that the presence of apneas in term infants increases the risk of SIDS. Steinschneider (19) suggested that early neonatal apnea was commonly followed by SIDS. In subsequent reports this investigator examined the frequency of apneas in neonates and used discriminant analysis to identify a population at risk for SIDS. The present study specifically examined short apneas longitudinally in preterm and term infants. Sleep state did not affect the incidence or rate of apnea before 44 wk of postconceptional age. This observation was

Table 1. Prevalence of central apneas and ventilatory correlates in term and preterm infants during sleep

Postconceptional age (wk)	No. of paired epochs	Duration of epoch (min)		Apnea rate (no./hour)		$\dot{V}_i$ (liter/min/kg)		f (breaths/min)		$\dot{V}_i$ (ml/kg)		P_ACO_2 (mm Hg)		P_AO_2 (mm Hg)		T_cPO_2 (mm Hg)	
		Q	REM	Q	REM	Q	REM	Q	REM	Q	REM	Q	REM	Q	REM	Q	REM
Term infants																	
40.0	17	15.7	18.4	9.0	11.8	0.159	0.188*	37	43*	4.4	4.5	36	35†	95	98	70	64*
±0.5†		±1.3	±1.9	±2.0	±2.1	±0.004	±0.005	±2	±1	±0.2	±0.2	±1	±1	±4	±4	±3	±2
43.3	16	16.5	13.5	24.2	26.3	0.158	0.190*	35	40*	4.7	4.8	42	41†	100	104*	61	60
±0.6		±1.5	±2.1	±6.9	±5.8	±0.009	±0.010	±2	±2	±0.4	±0.3	±1	±1	±3	±3	±3	±3
47.7	11	20.4	9.5*	9.6	28.2	0.158	0.206*	31	37*	5.4	5.7	42	40*	103	106	66	71
±0.6		±2.3	±2.0	±2.8	±8.3	±0.008	±0.009	±2	±2	±0.5	±0.4	±1	±1	±2	±2	±6	±5
51.9	12	18.0	7.8*	11.3	19.8	0.155	0.210*	30	36*	5.3	6.0*	42	41	107	110†	67	71*
±0.7		±2.4	±0.9	±4.0	±4.3	±0.008	±0.010	±2	±1	±0.4	±0.4	±1	±1	±3	±3	±2	±3
56.4	11	19.2	8.9*	4.9	12.7	0.153	0.183*	30	38*	5.1	4.9	40	40	101	103	64	63
±0.6		±1.3	±1.4	±1.7	±2.8	±0.006	±0.007	±1	±2	±0.3	±0.2	±1	±1	±3	±4	±4	±5
Preterm infants																	
35.1	18	20.3	18.5	89.5	95.0	0.162	0.186*	27	33*	6.4	5.9	41	39*	99	103*	61	58
±0.2		±2.3	±2.5	±20.4	±17.3	±0.010	±0.012	±2	±2	±0.3	±0.3	±1	±1	±2	±2	±2	±2
36.8	20	18.8	19.6	86.3	71.0	0.178	0.205*	32	36†	6.3	5.8	44	41*	96	100*	60	60
±0.2		±1.8	±2.5	±21.3	±15.9	±0.009	±0.011	±3	±2	±0.6	±0.2	±1	±1	±2	±2	±2	±2
39.5	15	19.7	12.9†	88.6	64.0	0.181	0.216*	30	36*	6.3	6.1	40	39*	107	105	64	65
±0.3		±1.9	±1.6	±26.7	±16.1	±0.017	±0.018	±3	±2	±0.4	±0.2	±1	±1	±4	±4	±3	±3
43.4	13	17.4	10.7†	45.3	43.3	0.166	0.203*	33	35	5.7	6.1	41	40*	102	105†	70	68
±0.4		±1.6	±1.9	±15.0	±10.3	±0.010	±0.011	±4	±3	±0.5	±0.4	±1	±1	±2	±2	±4	±4
47.7	18	15.3	13.7	7.8	30.0†	0.174	0.205*	32	35†	5.8	6.2*	42	41*	107	109	77	76
±0.6		±1.6	±1.0	±2.1	±8.0	±0.010	±0.012	±2	±2	±0.5	±0.5	±1	±1	±4	±4	±2	±2
53.8	17	15.8	7.0*	15.4	33.6	0.163	0.188*	26	29	6.3	6.4	39	36†	106	110	73	72
±0.6		±1.7	±1.0	±6.1	±20.0	±0.010	±0.018	±1	±2	±0.4	±0.5	±1	±1	±3	±6	±3	±2

* $p < 0.01$.† $p < 0.05$, for significance of the differences between quiet and REM sleep.

‡ SEM.

Fig. 3. Prevalence of various types of apneas. Central apneas predominated. Next in prevalence were breath-holding type of apneas. Obstructive and mixed apneas were rare.

Fig. 4. The effect of postnatal age on the rate of central apneas. The rate of apneas decreased with postnatal age in preterm infants but did not change in term infants. After 44 wk of postconceptional age apneas were more frequent in REM than in quiet sleep both in term and preterm infants.

Fig. 5. Frequency distribution of central apneas at 1 and 3 months of postnatal age. Apneas were longer during the 1st month than during the 3rd month in preterm infants ($p < 0.005$). This difference disappeared at 3 months of age.

interesting, considering that REM sleep is frequently quoted as being associated with more apneas than QS (1, 9, 20). The reason for this lack of difference is unknown, but we would like to speculate that the inherent imbalance of the respiratory control system at this early age, may preclude the appearance of differences related to sleep states. In favor of this hypothesis is the similarity in the distribution of duration of apnea in the term and preterm groups, independent of sleep state. The modal tendency at about 8 s appearing in preterm infants only, probably reflects the increased instability of the respiratory control system in this group of infants. This increased imbalance may be consequence of their relative hypoxemia, for example. Previous work in the area of apnea, periodic breathing, and respiratory control suggest that these short apneas are likely related to the oscillations in arterial blood gases (21). Waggener *et al.* (10) suggested that prolonged apneas have the same etiology as short apneas.

Our classification of the types of apnea followed conventional terminology present in the literature (7, 22-24). Two major findings were of interest. First, the predominance of central apneas both in term and preterm infants argues against a major role for peripheral mechanisms on the cause of apnea in healthy infants. In infants recovering from RDS the prevalence of mixed apneas is greater than in the present study and is likely related to residual lung disease (22). Second, the large percent of breath-holding apneas in term infants suggest an important underlying control element which is missing in preterm infants. Breath-holding apneas may represent activation of laryngeal adductors while the short burst of expiratory flow following apnea represents abductor activation. Adductor activity such as that of the thyroarytenoid muscle, is abolished in REM sleep (25-27). Be-

Fig. 6. The effect of postnatal age on ventilatory variables. Ventilation did not change with postnatal age despite major change in respiratory pattern both in term and preterm infants.

cause preterm infants spend most of their time in REM sleep, it is possible that the mechanism controlling breath-holding apneas is inactive most of the time.

V_E remained remarkably stable despite the oscillating nature of breathing pattern. Previously, we suggested that infants having periodic breathing and apnea had lower V_E than those breathing regularly (2). Those were infants in whom apneas were long, usually more than 15 s and frequently more than 20 s duration. In that same report we suggested that in a system oscillating between apnea and breathing periods, the resulting respiratory V_E would greatly depend on the ventilation/apnea ratio. If this ratio is more than 2, hyperventilation occurs in relation to regular breathing; if less, hypoventilation results. In the present investigation we studied short apneas, the ventilation/apnea ratio therefore being more than 2. Under these circumstances V_E tended to remain unchanged as breathing became regular with an increase in postnatal age. Alveolar ventilation was also stable as reflected by unchanged alveolar PCO_2 . Transcutaneous PaO_2 tended to increase with age in preterm infants, probably reflecting large V/Q abnormalities which improved with age (28).

In conclusion, we measured the frequency distribution of short apneas in preterm and term infants during sleep during the early postnatal period. Central apneas predominated in preterm and term infants, but breath-holding apneas accounted for 16% of the apneas in term infants and only 5.5% in preterm infants. Obstructive and mixed apneas were rare. The rate of apneas decreased with postnatal age to a level that was statistically the same in preterm and term infants at 3 months of age. Sleep state did not affect the prevalence of short apneas before 44 wk of

gestation and ventilation remained unchanged despite a decrease in the prevalence of apnea with age. The findings suggest that short apneas are common in these newborn infants, more so in preterm than in term infants, and are likely to represent a baseline instability of the respiratory control system at this age.

Acknowledgements. The authors thank Debbie Bialek for her invaluable help in preparing and typing the manuscript. We also thank Tom Hassard and Mary Cheang for their help with the statistical analysis.

REFERENCES

- Gabriel M, Albani M, Schulte FJ 1976 Apneic spells and sleep states in preterm infants. *J Pediatr* 57:142-147
- Rigatto H, Brady JP 1972 Periodic breathing and apnea in preterm infants. I. Evidence of hypoventilation possibly due to central respiratory depression. *Pediatrics* 50:202-218
- Rigatto H, Brady JP 1972 Periodic breathing and apnea in preterm infants. II. Hypoxia as a primary event. *Pediatrics* 50:219-228
- Daily WJR, Klaus M, Meyer HBP 1969 Apnea in premature infants: Monitoring incidence, heart rate changes and effects of environmental temperature. *Pediatrics* 43:510-518
- Schulte FJ 1977 Apnea. *Clin Perinatol* 4:65-76
- Steinschneider A 1972 Prolonged apnea and the sudden infant death syndrome: clinical and laboratory observations. *Pediatrics* 50:646-654
- Wealthall S 1983 The natural history of short breathing pauses. *Aust Paediatr J* 19:262(abstr)
- Kelly DH, Shannon DC 1979 Periodic breathing in infants with near-miss sudden infant death syndrome. *Pediatrics* 63:355-360
- Guilleminault C, Ariagno R, Korobkin R, Nagel L, Baldwin R, Coons S, Owen M 1979 Mixed and obstructive sleep apnea and near miss for sudden infant death syndrome: 2. Comparison of near miss and normal control infants by age. *Pediatrics* 64:882-891
- Waggener TB, Stark AR, Cohan BA, Frantz III ID 1984 Apnea duration is related to ventilatory oscillation characteristics in newborn infants. *J Appl Physiol* 57:536-544
- Moriette G, Van Reempts P, Moore M, Cates D, Rigatto H 1985 The effect of rebreathing CO_2 on ventilation and diaphragmatic electromyography in newborn infants. *Respir Physiol* 62:387-397
- Aizad F, Bodani J, Cates D, Horvath L, Rigatto H 1984 Effect of a single breath of 100% oxygen on respiration in neonates during sleep. *J Appl Physiol* 57:1531-1535
- Rigatto H, Brady JP 1972 A new nose-piece for measuring ventilation in preterm infants. *J Appl Physiol* 32:423-424
- Prechtl HFR 1974 The behavioural states of the newborn infant (a review). *Brain Res* 76:185-212
- Rigatto H, Kalapesi Z, Leahy FN, Durand M, MacCallum M, Cates D 1980 Chemical control of respiratory frequency and tidal volume during sleep in preterm infants. *Respir Physiol* 41:117-125
- Miller JC, Horvath SM 1976 Cardiac output during human sleep. *Aviat Space Environ Med* 47:1046-1051
- Kleinbaum DG, Kupper LL, Morgenstern H 1982 Epidemiologic Research Principles and Quantitative Methods. The Lifetime Learning Publications, Belmont, CA
- Shannon DC, Kelly DH 1982 Sids and near-sids. *N Engl J Med* 306:1022-1028
- Steinschneider A 1977 Prolonged sleep apnea and respiratory instability: a discriminative study. *Pediatrics* 59:962-970
- Haddad GG, Lai TL, Mellins RB 1982 Determination of the ventilatory pattern in REM sleep in normal infants. *J Appl Physiol* 53:52-56
- Cherniack NS, Longobardo GS, Levine OR, Mellins R, Fishman AP 1966 Periodic breathing in dogs. *J Appl Physiol* 21:1847-1854
- Thach BT, Brouillette RT, Abu-Osha YK, Wilson SL, Matew OP 1980 Prevalence of mixed and obstructive apneic spells in preterm infants. *Pediatr Res* 14:637(abstr)
- Flores-Guevara R, Plouin P, Curzi-Dascalova L, Radvanyi ME, Guidasci S, Pajot N, Monod N 1982 Sleep apneas in normal neonates and infants during the first 3 months of life. *Neuropediatrics* 13:21-28
- Albani M, Bentele KHP, Budde C, Schulte FJ 1985 Infant sleep apnea profile: preterm vs. term infants. *Eur J Pediatr* 143:261-268
- Kosch PC, Stark AR 1984 Dynamic maintenance of end-expiratory lung volume in full-term infants. *J Appl Physiol* 57:1126-1133
- Kosch PC, Davenport PW, Wozniak JA, Stark AR 1985 Reflex control of expiratory duration in full-term newborn infants. *J Appl Physiol* 58:575-581
- Harding R, Johnson P, McClelland ME 1980 Respiratory function of the larynx in the developing sheep and the influence of sleep state. *Respir Physiol* 40:165-179
- Krauss AN, Auld PAM 1969 Ventilators perfusion abnormalities in the premature infant: triple gradient. *Pediatr Res* 3:255-264