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**LIFE-THREATENING INFANTILE APNEA - RESULTS OF PRIMARY EVALUATION AND LONG-TERM FOLLOW-UP.**

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Management of the infant with severe infantile apnea remains controversial. Studies have suggested that home cardiorespiratory monitoring failed to prevent subsequent deaths from SIDS in as many as 10% of patients. In order to assess the effectiveness of home cardiorespiratory monitoring upon subsequent outcome in severe infantile apnea, 32 infants were evaluated and prospectively followed. These infants represented 8% (32/396) of the children seen at the Children's Hospital of Philadelphia during a two year period. All 32 infants had life-threatening apnea requiring cardiopulmonary resuscitation by parents, physicians, or paramedical personnel. Twenty-five (78.1%) were term infants, 7 (21.9%) were pre-term babies. Mean  $\pm$  SEM G.A. at birth was  $37.9 \pm 0.3$  wks. Age at the time of initial apneic episode was  $8.6 \pm 1.3$  wks. Initial thermistor-pneumocardiogram evaluation revealed respiratory pattern abnormalities in 16 (50%) infants: central apnea - 5 (15.6%); obstructive apnea - 1 (3.2%); periodic breathing - 6 (18.7%); gastroesophageal reflux associated apnea - 4 (12.5%). All infants were treated with home cardiorespiratory monitoring. Mean  $\pm$  SEM duration of monitoring was  $4.7 \pm 0.5$  months. Ten infants (31.3%) had apnea while monitored which required vigorous stimulation. Two infants (6.25%) required vigorous stimulation including CPR. Infants have been followed for a mean of  $21.3 \pm 6.3$  SEM months. No deaths have occurred. These results suggest that one-third of infants with severe infantile apnea will have subsequent respiratory episodes at home. Home monitoring appears to be an effective therapy in this group of babies at highest risk for continuing apnea.

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**MIXED APNEA OF INFANCY - SIGNIFICANCE OF RESPIRATORY PATTERN.**

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Mixed apnea of infancy is a respiratory pattern characterized by both central and obstructive apnea. In order to characterize this form of apnea more completely, 67 patients were evaluated in the Apnea Screening Program of The Children's Hospital of Philadelphia. These infants had predominantly mixed apnea and represented 8.1% (67/838) of the children evaluated for apnea during a two year period. Mean BW was  $1700 \pm 88.8$  SEM gms, mean GA was  $31.6 \pm 0.4$  SEM wks. The average age at the time of study was  $5.8 \pm 0.5$  SEM wks. Fifty-nine (88%) infants were premature, eight (12%) were term babies with infantile apnea or siblings of SIDS victims. Infants were evaluated for a minimum of 6 hours by thermistor-pneumocardiogram study. 279 episodes of mixed apnea were detected. 217 (77.8%) episodes began as central apnea and progressed to obstructive apnea. 62 episodes (22.2%) initially demonstrated obstructive apnea that subsequently became central. 155 (55.6%) episodes of mixed apnea were accompanied by bradycardia (decrease in heart rate  $>40$  bpm below baseline level). The duration of mixed apneic episodes tended to be prolonged with 85 (30.5%) 10-15 seconds duration, 120 (43%) 15-20 seconds duration, and 74 (26.6%)  $>20$  seconds duration. Children with predominantly mixed apnea had associated other apnea: 33 (49.3%) had central apnea, 11 (16.4%) obstructive apnea, and 24 (35.8%) had excessive periodic breathing ( $<5\%$  of sleep). These data suggest that in mixed apnea, central apnea most commonly precedes obstructive apnea. Approximately 70% of episodes of mixed apnea last for longer than 15 seconds. The majority of such episodes have associated bradycardia and therefore represent a significant clinical problem.

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**NALOXONE SIGNIFICANTLY DECREASES PERIODIC BREATHING OF INFANCY.**

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Periodic breathing in infancy represent an abnormal breathing pattern often associated with prolonged apnea. Although the etiology of periodic breathing is not well-established, it most likely represents an immaturity of respiratory control. In order to determine if endogenous endorphins and enkephalins affected periodic breathing, a group of infants who presented with markedly excessive periodic breathing were studied and treated with naloxone, a narcotic antagonist. Eight infants comprised the study population. Mean BW was  $2.2 \pm 0.3$  SEM kg (R = 1.0 - 3.2 kg), mean GA was  $33.8 \pm 15$  SEM wks (R = 30-40 wks). Mean age at initial study was  $17.2 \pm 6.0$  SEM days (R = 7-56 days). Initial study consisted of a 6 hour thermistor-pneumocardiogram. If periodic breathing greater than 15% of sleep time was detected, an IV was inserted and an additional 24 hours of recording were performed on the following day to determine baseline level of periodic breathing. Infants were then treated with IV naloxone .01 mgm/kg/dose q 4 hrs for 48 hrs. Respiration and heart rate were recorded continuously throughout this period and for 48 hours following discontinuation of naloxone. Baseline level of periodic breathing for infants was  $34.4\% \pm 3.3\%$  SEM of sleep. Naloxone decreased periodic breathing to  $15.1\% \pm 3.8\%$  SEM of sleep, a mean decrease of  $57.1\% \pm 11.1\%$  SEM (p  $<.01$ ). Following discontinuation of naloxone, periodic breathing remained at a lower level than baseline- $16.3\% \pm 3.8$  SEM, a mean decrease of  $50.2\% \pm 10.6$  SEM (p  $<.01$ ). No side effects were noted during the study. Follow-up of infants monthly after discharge demonstrated continuing reduction in the amount of periodic breathing. These data suggest that naloxone significantly decreases periodic breathing.

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**THERMISTOR-PNEUMOCARDIOGRAMS: PREDICTIVE VALUE IN INFANT APNEA.**

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Controversy exists as to whether initial evaluation of the infant with apnea is predictive of future apneic episodes. To determine if thermistor-pneumocardiograms were predictive of future apnea, 53 children who presented with infantile apnea were studied and home monitored. Twenty-one (39.6%) had normal initial studies. Thirty-two (60.4%) children were selected on the basis of both initially abnormal thermistor study and at least one subsequent abnormal home pneumocardiogram. The two groups were matched for birthweight ( $2.76 \pm .2$  SEM kg vs.  $2.75 \pm .2$  SEM kg) and GA ( $36.6 \pm 1.1$  SEM wks vs.  $37.1 \pm 0.7$  SEM wks). Abnormalities seen on recording were: prolonged central apnea-13, excessive periodic breathing ( $>5\%$ )-11, mixed apnea-4, obstructive apnea-3. All infants had home pneumocardiograms performed a 2-3 mo. intervals. In the group with normal initial studies, all subsequent pneumocardiograms were normal. The infants with abnormal initial studies had a mean of  $1.7 \pm .2$  SEM abnormal follow-up studies (R 1-5). Of the infants with normal studies, 2/21 (9.5%) had further episodes of apnea detected by monitor at home; both were self-revived. In the babies with abnormal initial study and abnormal home pneumogram, 15/32 (46.9%) had further apnea (p  $<.005$ ). Five infants (15.6%) required vigorous stimulation and three were hospitalized. Infants in the normal group were monitored until  $24.8 \pm 1.8$  SEM wks of age compared to  $33.7 \pm 2.3$  SEM wks (p  $<.005$ ) in the group with abnormal studies. These results suggest that children with abnormal initial thermistor-pneumocardiograms who continue to show respiratory abnormalities on home pneumograms are highly likely to have significant clinical apnea. Home monitoring is warranted until all studies are normal.

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**NATURAL HISTORY OF PERIODIC BREATHING IN TERM AND PRETERM INFANTS.**

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Periodic breathing in infancy represents immaturity of respiratory control commonly associated with prolonged apnea. It is therefore important to assess which infants appear to be at greatest risk with periodic breathing and the age at which periodic breathing resolves. To examine these issues, 61 infants (38 pre-term, 23 term) were initially assessed with thermistor-pneumocardiograms and found to have excessive periodic breathing for age. Periodic breathing was defined as respiration  $<20$  seconds duration, separated by periods of apnea of  $<10$  seconds duration occurring at least three times in succession. All infants in this study demonstrated periodic breathing  $>5\%$  of sleep time. The 61 children were prospectively followed with pneumocardiograms every 6-8 weeks. Mean GA was  $34.4 \pm 0.6$  SEM wks. All children had apnea, cyanosis, or bradycardia that prompted initial evaluation. Twenty-nine (47.5%) had 5-10% of sleep in periodic breathing, 24 (39.3%) had 10-20% of sleep in periodic breathing, and 8 (13.1%) had more than 20% of sleep in periodic breathing. Forty-nine (83.5%) resolved their periodic breathing ( $<5\%$  of sleep) by 5 months post-natal age. Fifty-nine (96.7%) had normal sleep studies by 9 months of age. No infant demonstrated periodic breathing beyond 10 months of age. Infants with 5-10%, 10-20% and greater than 20% of sleep in periodic breathing showed no differences in the time it took to resolve their periodic breathing. These results suggest that most (83.5%) of infants resolve their periodic breathing by five months of age. The degree of initial periodic breathing does not influence the age at which this respiratory pattern resolves.

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**NEONATAL GLUCOSE HOMEOSTASIS: A NEW LOOK.**

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To reexamine and establish normal values for plasma glucose (G) during the first week of life, 564 plasma G. values were done in 344 normal AGA full term newborns (NB) who weighed from 2.5-4.0 kg. Mean $\pm$ S.D. for gest. age was  $39.6 \pm 0.6$  wk; birth wt:  $3292 \pm 365$ g; Hct  $62 \pm 6\%$ ; Apgar (5 min)  $9.1 \pm 0.5$ . Serial samples were taken in 60 NB at 0 (cord), 1, 2 and 3 hr. Milk feedings were started at 3-4 hrs and cross sectional samples were taken in the other 284 NB. Results are shown in table:

Hour	0	1	2	3	4	6	24	48	72	96	168
Mean	T16	55	59	70*	68	65	67	71	73	83*	80
S.D.	48	18	11	12	14	13	14	10	13	12	12
Range	55-	17-	32-	39-	40-	40-	46-	48-	50-	56-	54-
(mg%)	280	119	96	97	112	101	117	98	114	102	102
N	60	60	58	57	49	69	40	55	55	35	26

Plasma G reached its lowest level at 1 hr, was sig. higher by 3 hrs; remained stable until 72 hrs and then rose sig. higher at 73-96 hrs. Thirteen percent of NB had  $G < 35$ mg% at 1-3hr; only 5% had symptoms of hypoglycemia. All symptomatic infants had plasma  $G < 25$ mg% and were treated by I.V. glucose. The remaining NB recovered spontaneously within one hour. None of the NB had  $G < 40$ mg% after 3 hrs of age. In view of these findings, current definitions for hypoglycemia need to be reevaluated.

\*p $<.01$