

Influence of Light in the NICU on the Development of Circadian Rhythms in Preterm Infants

Majid Mirmiran and Ronald L. Ariagno

The fetal biological clock is an endogenous clock capable of generating circadian rhythms and responding to maternal entraining signals. By at least the third trimester of pregnancy fetal diurnal rhythms are entrainable by maternal day-night rhythms. Maternal illness during pregnancy and premature birth are obvious clinical factors that may adversely affect circadian rhythm development. Premature birth of the fetus has a most dramatic impact on maternal fetal interactions. The effect on biorhythms appears to be temporary and is greatest on the most immature infants. The results to date support the importance of fetal circadian rhythms and the relative lack of these rhythms in the preterm infant. It is well known that growth and development in the prematurely born infant are influenced by a multitude of factors; clearly, the neonatal intensive care unit is not a surrogate for the maternal placental unit. This article reviews what is known about circadian development in the human infant with an emphasis on the unique circumstances of the preterm infant. The research on the short- and long-term effects of environmental interventions on circadian, sleep, and neurologic development is discussed. Although an earlier onset of circadian development did not result with cycled lighting in the neonatal nursery, there may still be important biological effects that have not been studied. There are sufficient data to state that there is no reason for continuing a chaotic, noncircadian environmental approach for the care of the prematurely born infant.

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The origin of circadian rhythms development can be found during the fetal period.^{1,4} A fetal biological clock responsive to maternal entraining signals is already oscillating, at least in the last trimester of gestation in primates.⁵⁻⁸ A clear day-night rhythm of fetal heart rate synchronized with maternal rest-activity, heart rate, cortisol, melatonin, and body temperature rhythms is found in humans.^{9,10}

By comparing a discordant anencephaly twin pregnancy with 3 normal twin pregnancies, we were able to show that the fetal brain (most probably the fetal biological clock) is essential for expression of a diurnal rhythm in fetal heart rate.¹¹ These observations support the notion that, during fetal life and long before birth, the mother entrains the developing circadian rhythm of the infant to the light-dark cycle.^{2,4,12-18} Circadian rhythm of maternal melatonin, cortisol, and uterine activity are suggested to mediate the effect of light-dark cycle on the fetus (reviewed in Mirmiran and Lunshof⁹). Deguchi¹⁹ was the first to show that the fetal biological clock is already functional and entrainable by the mother in an even altricial mam-

mal such as the rat. Viswanathan and Chandrasekaran²⁰ elegantly show that even the presence and absence of the mother mouse can entrain the circadian clock of the immature pups.

Studies in human infancy have shown little or no evidence of circadian rhythmicity at birth. However, our recent studies, starting at 1 month of age in full-term infants, showed a significant circadian rhythm of body temperature. The amplitude of this rhythm increased by 3 months of age, to a level similar to 6 month or older children (Figs 1 and 2). A nocturnal trough of body temperature, which is a good marker of human circadian rhythms, is already present at 6 to 12 weeks of age in full-term infants.²¹

From the Division of Neonatology, Department of Pediatrics, Stanford University, Palo Alto, CA.

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Address reprint requests to Majid Mirmiran, MD, PhD, Visiting Professor of Pediatrics, Department of Pediatrics, Division of Neonatology, Stanford University, 750 Welch Rd, Suite 315, Palo Alto, CA 94305-5119; e-mail: mirmiran@stanford.edu

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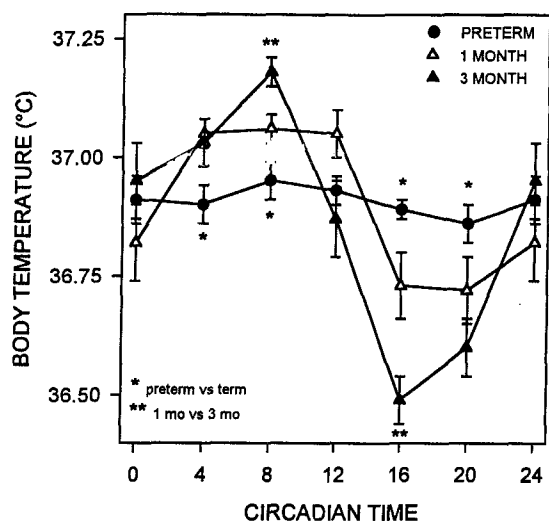


Figure 1. Mean rectal temperature circadian rhythms (recorded every 2 minutes over 3 consecutive days) plotted every 4 hours in 17 preterm infants at 36 weeks PCA, in 10 full-term infants at 1 month, and at 3 months of age. Note the significant increase in rhythm amplitude in the 1-month-old full-term infants during day (circadian time 0 to 12; 0 = 8 a.m.) versus night (circadian time 12 to 24) and the pronounced drop in temperature nadir at 3 months of age. (Reprinted with permission of Pediatrics.³³)

Many factors including feeding (scheduled versus on demand, mother's milk versus formula milk), environmental lighting (indoor versus outdoor, regular versus irregular light-dark cycle) and chronological/postconceptional age of the infant influence the experimental outcome. Moreover, short recordings and other methodological pitfalls (including sampling every 4 hours versus continuous recording; averaging all infants vs. individual analysis of the data) may

have, indeed, resulted in earlier negative findings. For instance, in Lodmore et al's 1992 study²² some infants showed circadian rhythm of body temperature as early as by 8 weeks and others not until 16 weeks. Breastfed infants, girls, and first born infants showed earlier rhythm development.

Recio et al²³ have discussed a number of important issues influencing the development of circadian rhythm especially during the first 3 months of postnatal life. They indicated that newborns are often kept in a dark room during the day so that they can sleep and may also be exposed to bright light during nightly feeding periods. Indeed, an environmental light-dark cycle conflicting with the infant endogenous rhythm. Human milk contains melatonin. The change from breast milk to commercial milk usually starts with substituting the nocturnal one; on the other hand mothers use breast milk usually pumped during the day for night-time feeding. In both cases the newborn is deprived of the maternal melatonin signal because the melatonin peak in maternal milk is between midnight and 4 a.m.²⁴

Recently, McGraw et al²⁵ carefully studied a full-term infant from the moment of birth. They recorded hourly body temperature, daily sleep-wake patterns and weekly 24 hour melatonin. The infant was fed only on demand and left undisturbed by the mother (McGraw). Careful attention was paid to having outdoor daytime lighting and dim light at night. Even during feeding at night no extra lighting was used to avoid disturbing the circadian rhythm of the infant. These investigators found a clear circadian rhythm in body temperature within 1 week

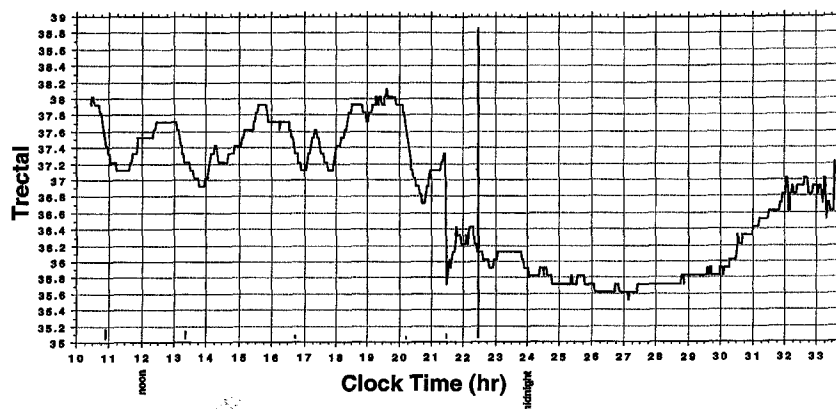


Figure 2. Rectal temperature (Trectal), recorded every 2 minutes from a 6-month-old full-term infant, as a function of 24 hour day-night cycle. Temperature trough and nadir in the evening and night with gradual increase in early morning hours are pronounced at this age. Note that the Clock Times of 25 through 33 correspond to 1 a.m. to 9 a.m.

of life. Circadian rhythm of both wake episodes and melatonin emerged by 6 weeks. The last rhythm to develop was sleep, attaining significance after 9 weeks. Their study clearly shows that the results from earlier circadian research in human infancy were confounded by maternal/environmental factors as well as by only recording sleep-wake cycle. These results show that the already functional fetal biological clock is able to continue oscillating after birth if not disturbed by interfering ex-utero environmental factors (including scheduled feeding every 2 to 4 hours and night-time bright light).

Kennaway²⁶ found no evidence of circadian rhythm in melatonin before 9 to 12 weeks of age in full-term infants. They also found a delay of 2 to 3 weeks in development of melatonin circadian rhythm in preterm (corrected for age) versus term infants. A recent study showed the development of cortisol circadian rhythm by 10 weeks of age.²⁷

Many investigators have also indicated individual differences in development of circadian rhythms both in preterm and in full-term infants.^{26,28-32} To what extent these individual differences are the results of differences in prenatal

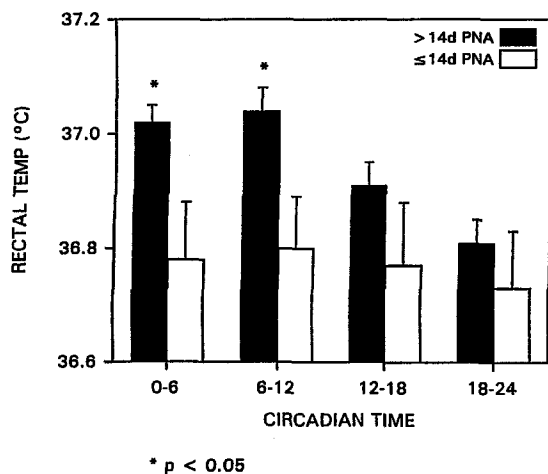


Figure 3. Mean rectal temperature, recorded every 2 minutes and averaged every 6 hours, of a circadian day (circadian time 0 = 8 a.m.) in preterm infants. Data are plotted separately for preterm infants more than 14 days and preterm infants less than 14 days postnatal age (PNA). Rectal temperature was significantly greater during the first half of each circadian day (circadian time 0 to 12) in the more than 14 days PNA preterm infants (Reprinted with permission of Pediatrics.³³)

Table 1. The Presence of Circadian Rhythms in Body Temperature and Heart Rate in Appropriate for Gestational Age (AGA) Versus Small for Gestational Age (SGA) Preterm Infants

Circadian Rhythm	AGA (n = 18)	SGA (n = 17)	P-value
Body temperature	13 (72%)	9 (53%)	<.05
Heart rate	14 (78%)	6 (35%)	<.05

circadian rhythms and/or postnatal environmental condition is yet to be studied. For example, in our own studies in preterm infants before discharge from the nursery,³³ it was found that although no day night differences were present in body temperature at less than 14 days postnatal age, a small but significant rhythm of body temperature emerged in infants older than 14 days of age (Fig 3). The presence or absence of circadian rhythms in preterm infants is also influenced by their intrauterine growth. The percentage of preterm infants with circadian rhythms of body temperature and heart rate was significantly greater in the appropriate for gestational age group compared with the small for gestational age group (Table 1). Postconceptional age (maturational effect) is also important to consider. In our own studies, infants with postconceptional age of 35 to 37 weeks had much higher amplitude of body temperature rhythm compared with 32 to 34 weeks postconceptional age (PCA) infants³³ (see also ref 32). Although preterm infants before discharge from the hospital at 36 weeks postconceptional age, slept as much during the night as during the day, by 3 months corrected age the same infants showed a clear day-night rhythm of sleep (Table 2).

Based on the new findings (reviewed above) several propositions could be made on the development of circadian rhythms in infancy:

Table 2. Sleep Percentage of Recording Time During the Day and Night Periods in 12 Preterm Infants Averaged Over 2 Consecutive Days at 36 weeks PCA and 3 Months Corrected Age

36 Weeks PCA		3 Months Corrected Age	
Day	Night	Day	Night
65 ± 12	71 ± 10	18 ± 12	65 ± 11

NOTE. Day-night effect significant only at 3 months of age ($P < .001$).

1. The fetal biological clock is an endogenous clock capable of generating circadian rhythms and responding to maternal entraining signals.
2. Maternal circadian rhythms influence fetal overt rhythms and entrain these rhythms to the light-dark cycle.
3. The presence or absence of circadian rhythms in the infant after birth results from the combined influence of prenatal and postnatal environmental conditions.

Role of Infant Entrainment

An important function of maternal entrainment during the perinatal development may be to prepare the fetus circadian timing system for later independent adaptation to the light-dark cycle. It is possible that the postnatal development of human circadian rhythms may be hampered by maternal, fetal, or perinatal disturbances. This is observed clinically when the intimate mother-fetus relationship is dramatically altered by premature birth or by maternal illness. Furthermore, preterm infants are exposed to continuous or unpredictable light illumination for several weeks or months in the Neonatal Intensive Care Unit (NICU) and intermediate nursery³⁴ (Figs 4 and 5).

Preterm infants are deprived of several potentially important maternal entrainment factors. This lack of maternal entrainment and random/unpredictable environmental condition in the nursery may induce disturbances in sleep, body temperature, feeding, and other rhythms in preterm infants. Mann³⁵ reported improved development, sleep and growth in preterm infants subjected to day-night nursery; but this finding was not evident until 6 weeks postdischarge. Tenreiro et al³⁶ found some beneficial effect of light-dark cycle in the nursery on development of circadian rhythms of heart rate and skin temperature before discharge. Kennaway et al²⁶ also found that the delayed development of the melatonin rhythm in some preterm infants could be advanced by home cycled light. Hao's recent study⁸ is important because it shows that the biological clock is responsive to light as early as 125 days in prematurely born baboons (baboon gestational age is 180 days). When extrapolated to human, this means that as early as 25 weeks,

preterm infants might be responsive to the biological effects of light on circadian system.

Stanford Cycled Light Trials

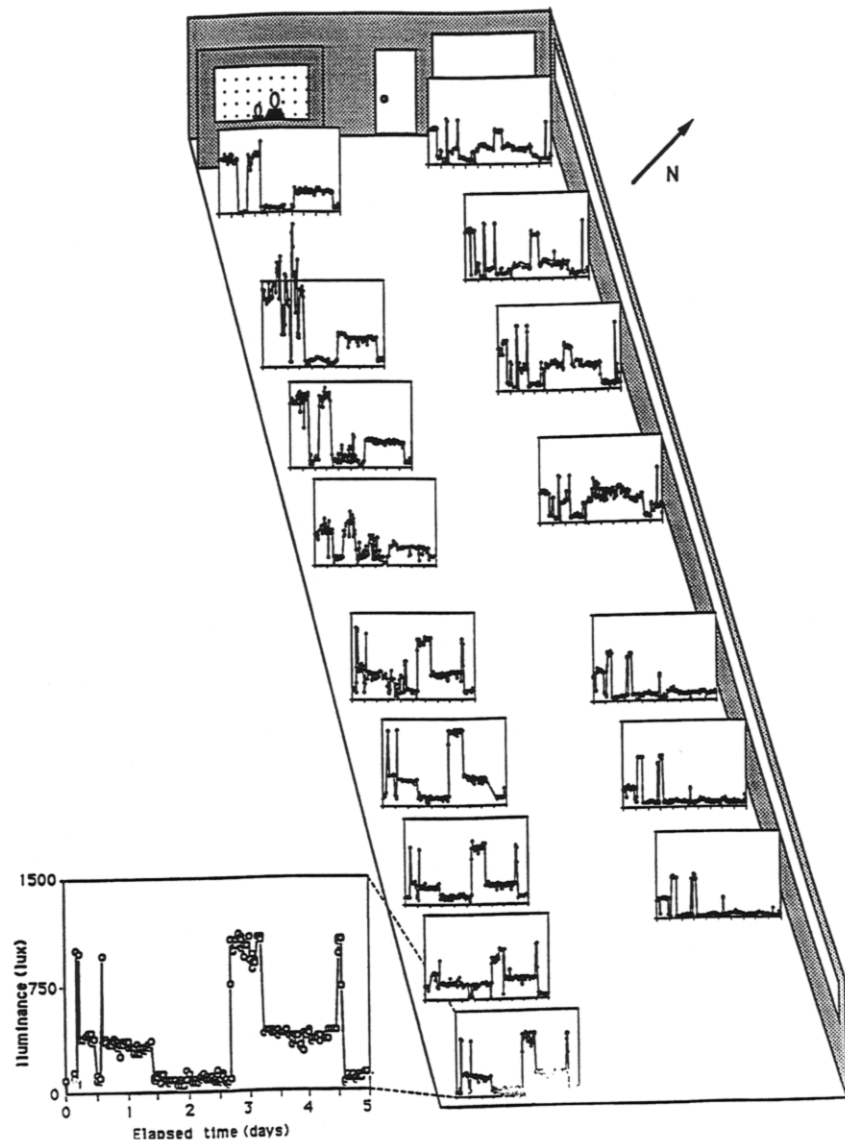
We have recently investigated the influence of a regular light-dark cycle in the nursery on the development of circadian rhythms in preterm infants. From the moment that the clinical condition of these infants were stable the infants in the study were randomly assigned to 1 of 2 groups. In the Dim group, the infant's incubator/bassinet was covered by a thick blanket except during feeding or other interventions by parents and care givers. This is the routine recommended by NIDCAP (Neonatal Individualized Developmental Care Program) and is followed in our practice at Stanford. Infants in the Cycled group were exposed to a regular environmental light-dark cycle in which the incubator/bassinet was covered only from 7 p.m. until 7 a.m. A representative plot in Figure 6 shows the level of light experienced by each group for at least 2 weeks until discharge home.

At 36 weeks postconceptional age (just before discharge) as well as at 1 and 3 months corrected age, rectal temperature was recorded for 1 to 3 days continuously and a 24 hour time lapse videosomnography was made. Figures 7 and 8 summarize the results of the light intervention on development of circadian rhythms of body temperature and sleep. Although a significant maturation was found for both overt rhythms, no beneficial environmental light effects were observed on the development of circadian rhythms.

Comparing these results with our earlier studies in term infants (see Fig 1), it seems as if circadian rhythms in preterm infants develop endogenously as a function of postconceptional age, independent of prematurity and/or environmental intervention, to a level comparable to term infants when corrected for age. Endogenous perinatal development of sleep-wake rhythmicity, based more on maturation of the brain rather than environment, has already been suggested in earlier studies.³⁷⁻³⁹

One factor that may have contributed to the lack of light-dark intervention effect on circadian development in our study is that our controls were not experiencing a chaotic lighting in the nursery but indeed were exposed to a continuous dim light condition. Other long-term

Figure 4. Bed-site differences in illumination over a 5-day study in a NICU. Each plot represents a bedside at which measurements were obtained at 240 contiguous 30-minute intervals. One bedside (lower left) is expanded to show details of the time (0-5 days) and illuminance (0 to 1,500 lux) scales, which are identical on all plots. Note the differences in the patterns of illumination at different parts of the nursery, and the similarity in the patterns at some contiguous bedsides. The highest recorded illumination levels corresponded with the presence of photo-therapy lights. Room dimensions are approximately 22 feet \times 82 feet (Reprinted with permission.³⁴)



follow-up studies including our own (Fig 9), without a controlled cycled light nursery environment, also failed to show differences in sleep distribution between preterm and term infants when corrected for age.³⁹⁻⁴¹ These infants were exposed to continuous and unpredictable illumination in the NICU before discharge home. However, it is important to realize that no attempt was made (or could be made) to modify the light-dark cycle at home in any of these studies. It could be argued that any effect of our early intervention has been masked by the home environment. For instance, infants from the Dim group could have gone home to a much regular light-dark cycle than

infants in the Cycled group. This could indeed diminish the real differences between the two groups. Nevertheless, it is important to find that preterm infants, despite differences in the nursery and home environment, do not show a substantial difference in maturation of circadian rhythms compared with full-term infants.

Other Cycled Lighting Studies

McMillen et al⁴² found that the circadian rhythm of sleep in the preterm infants entrained after a similar duration of exposure (6 to 10 weeks) to the home environment (with regular

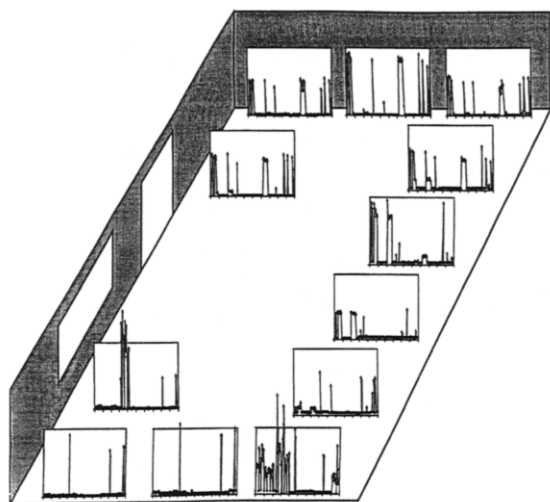


Figure 5. Bed-site differences in illumination over the 5-day study in an Intermediate Care nursery. Plot dimensions are identical to those in Figure 4. Room dimensions are approximately 12 feet \times 44 feet (Reprinted with permission.³⁴)

day-night rhythm, a single care giver, and “on-demand” feeding) when compared with the full-term infants. However, since preterm infants were discharged home around 35 weeks in their study, the entrainment to light-dark cycle took place at significantly earlier postconceptional age (47 weeks) in these infants compared with the term group (49 weeks).

Interestingly, they also found an inverse rela-

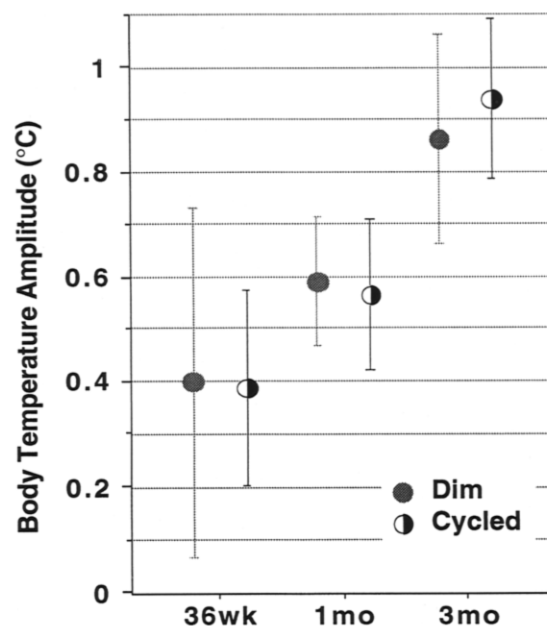


Figure 7. Mean (\pm SEM) amplitude of body temperature circadian rhythm of preterm infants subjected to Dim and to Cycled lighting in the nursery is shown at 36 weeks PCA (before discharge), at 1 month and at 3 months corrected age. Note the increase in body temperature amplitude as a function of age in both groups. No significant differences were found between the 2 groups at any age.

tionship between gestational age and the postnatal age at which the entrainment occurred in preterm infants. They interpreted this postnatal

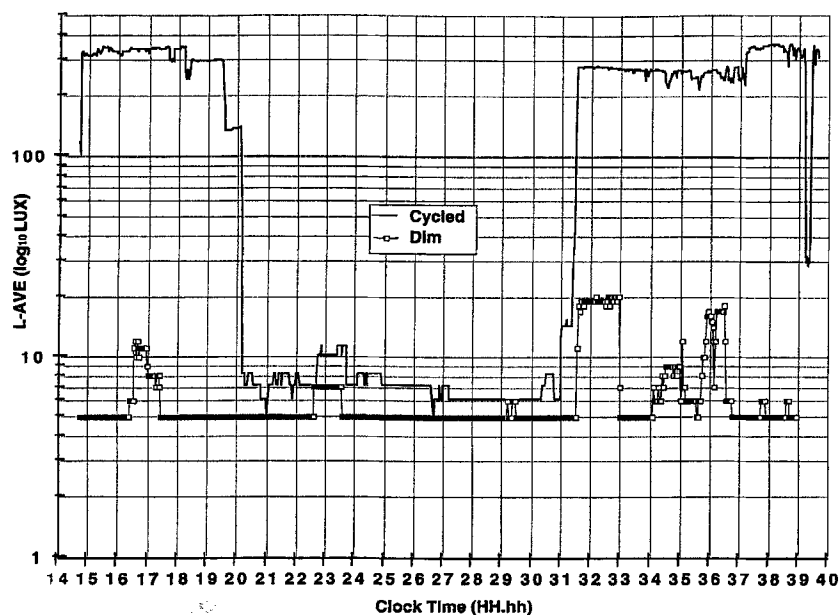


Figure 6. Light intensity (L-AVE) (logarithmic scale) experienced for at least 2 weeks in the nursery by preterm infants subjected to a Dim lighting condition (open symbol, thin line) and by preterm infants subjected to Cycled lighting (no symbol, thicker line) as a function of time of 24-hour day. Note the cyclicity from 300 lux to less than 10 lux in the Cycled group compared with little or no cyclicity in the Dim group. Recording started at 2 p.m. and continued until 4 p.m. next day. Note that the Clock Times of 25 through 40 correspond to 1 a.m. to 4 p.m.

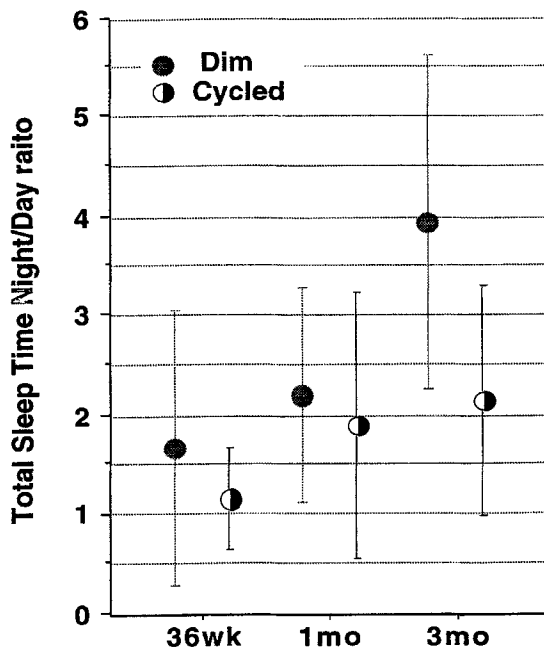


Figure 8. Mean (\pm SEM) total sleep time Night/Day ratio of sleep in preterm infants subjected to Dim and Cycled lighting in the nursery is shown at 36 weeks PCA (before discharge), at 1 month and at 3 months corrected age. Note the increase in the ratio (more sleep at night vs. day) as a function of age in both groups. No significant differences were found between the 2 groups at any age.

delay in entrainment of the younger preterm infants to be due to the longer period of non-entraining stimulation in the nursery environment. Their results suggest that regular environmental entraining factors are more important than preterm/full-term delivery in later adaptation of the infant to light-dark cycle.

It is also interesting to note that 1 infant in this 4 month study never developed a sleep circadian rhythm. This term infant was fed at night with full bright light. McMillen's findings suggest that early exposure of preterm infants to a cycled light would result in earlier development of circadian rhythms. However, our findings do not support this hypothesis.

Shimada et al,^{39,41} in a large study, found no differences between term and preterm infants in the circadian rhythm of sleep, duration of day and night sleep, or the time of onset of the longest sustained sleep time after home discharge when corrected for age. Preterm infants (low risk 28 to 36 weeks gestational age) in their

study were exposed to continuous light ranging from 420 to 500 lux in the NICU.

On the other hand the light intensity at home was similar for both groups and varied substantially during day versus night: ranging from 650 to 3,000 lux during the day to 10 to 100 lux at night. There were also no significant differences between the two groups regarding the frequency of on-demand vs. scheduled feeding or the time of parents bedtime. Both groups showed entrainment to day-night rhythm by 48 weeks PCA.

Contrary to McMillen, they concluded that environmental factors (both entraining and perturbing) are not able to influence the endogenous time course of circadian rhythm maturation before the innate biological clock is mature enough to respond to these stimuli. The continuous lighting exposure of preterm infants for several weeks before discharge home does not appear to retard the development of sleep-wake circadian rhythms if an appropriate lighting regime is experienced at home.

In a recent report they studied sleep habit of 44 preterm and 40 full-term infants longitudinally from birth for more than 16 weeks at home. Seventy five percent of the infants initially showed either ultradian or irregular sleep-wake pattern. Only 7% of the infants showed a free-running sleep-wake rhythm before entrainment. The mean age of the entrainment to light-dark cycle was 44.8 weeks postconceptional age,

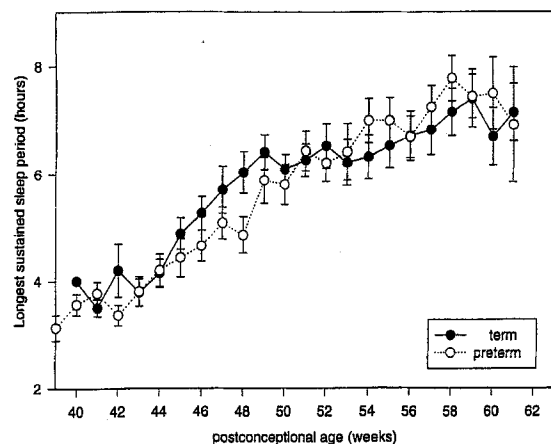


Figure 9. Mean (\pm SEM) longest sustained sleep period (always included midnight until 5 a.m.) as a function of postconceptional age in preterm and full-term infants. No significant differences were found between the 2 groups through 6 month of age in this follow-up study.

much earlier than in their earlier publication and very similar to our own data in preterm and term infants (see above). There were no significant differences in either the frequency of each pattern or the mean age of the entrainment between preterm and term infants.⁴¹

Reports from Gabriel⁴³ and Mann et al³⁵ are among the first to show the beneficial effects of a regular and less disturbed nursery on development of preterm infants. Mann et al³⁵ randomly assigned 20 preterm infants to the day-night nursery and 21 infants to the control nursery. Equal numbers of infants were born before or after 30 weeks gestational age in both groups. Infants stayed at least 10 days in each nursery. These nurseries were identical in size and the number and distribution of windows.

During the daytime, the environment was identical in the 2 nurseries. But at night (from 7 p.m. until 7 a.m.) the windows in the day-night nursery were covered by dark curtains, the lights were turned out, the radio was off, and the staff and visitors were urged to make as little noise as possible. Light intensity in the control nursery was about 200 lumen/m² throughout the 24 hours, however, at night in the day-night nursery the light intensity was 1 lumen/m². Background noise was about 10 db lower at night in the day-night nursery.

Sleep-wake patterns of infants were observed immediately before discharge, at the expected date of delivery, and at 6 and 12 weeks corrected age. Observations were made over 2 successive 24 hour periods. After discharge from the hospital infants in the day-night nursery slept an average of 2 hours more. This extra daily sleep, however, was evenly distributed over 24 hours and was not due to an increase in nocturnal sleep. Both groups equally showed less sleep by day and more sleep at night with increasing age.

Day-night nursery infants, despite fewer feeding/24 hours, gained significantly more weight and were, on average, 0.5 kg heavier than the controls by 3 months corrected age. Any differences between the 2 groups in light and noise intensity at home were not known. However, because no differences in development of circadian rhythms were found before or after discharge, it is unlikely that their longterm sleep and weight gain results were the results of a direct influence of day-night rhythm on the development of the circadian system. It is possible

that the parents of these infants had more confidence in the health and well being of their infants, as the medical and nursing staff left them alone in a quiet and dark room for long periods. Whatever the explanation as stated by Mann et al,³⁵ because it is beneficial for infants to sleep longer, spend less time feeding and gain weight faster, it is recommended that the preterm infants not be subjected to continuous light and noise and disturbed as little as possible.

Blackburn and Patterson⁴⁴ studied the direct effect of light in the nursery on motor activity and cardiac function in 18 preterm infants born at less than 34 weeks gestational age. Half of these infants experienced, on average, 11 hours dimmed lighting during each 24 hours. No attempt was made to control the time when the lights were turned off for each infant. Nevertheless all infants in the intervention group had the lights off ranging from 4 p.m. until 12 a.m. The 24 hour time-lapse video combined with analog/digital recording of the infant monitor output allowed longitudinal and naturalistic recording of the infant and his/her responses to its environment.

Infants in the intervention group had significantly lower motor activity levels and heart rate during the periods when the lights were off compared to the period when the lights were on. There were no significant day-night differences in activity, respiratory rate or heart rate for control infants. The results of this study suggest that decreasing light levels during the evening and night hours may facilitate rest and subsequent energy conservation in preterm infants. They suggested a separate lighting regime for each infant to allow the nurse to individualize lighting according to the needs of the infant. Strauch et al⁴⁵ also found that the implementation of quiet (low noise) hour in the NICU increased sleep and reduced crying in preterm infants. Lotas⁴⁶ has reviewed the light and sound in the NICU and its impact on preterm infants. She emphasized the significant role nurses can play in improving the developmental outcome of preterm infants by minimizing the adverse effects of light and sound.

Fajardo et al⁴⁷ have studied short- and long-term influences of an intervention in the nursery. They studied 24 low risk, low birth weight preterm infants. At 32 weeks PCA infants were alternately assigned to a regular nursery or an

alternative (intervention) nursery. The control nursery was an open floor with 18 beds and many disruptive stimuli around the clock. The alternative nursery was an 8-bed room organized to (1) reduced unpatterned stimuli, (2) to introduce a well defined day-night cycle, and (3) to provide patterned stimuli and state-contingent nursing care. There were no statistically significant differences in the level of noise between the two nurseries.

Infants were observed for organization of behavioral states at 32 weeks as well as at 1 to 3 days before discharge at 36 weeks. One year outcome measures included: morbidity, growth, pediatric complications, Bayley scores and state regulation in the strange situation. Mean duration of each behavioral states showed a significant age effect from 32 to 36 weeks. This increase in mean duration of each state as a function of age was significantly greater in the intervention group compared with the controls. However, neither of the long-term outcome measures showed significant effect of intervention. Furthermore, it was interesting to find that there was a significant correlation between good neonatal state organization and better outcome measures irrespective of the nursery condition.

These findings indicate that normal neonatal state regulation may serve as an index for later self-organization. At 1 year of age, a better capacity to maintain stable organized waking episodes in the strange situation was related to good neonatal state organization. None of the infants classified as good organized state at 36 weeks PCA had major medical or developmental dysfunction at 1 year of age.

Miller et al⁴⁸ subjected 20 preterm infants till discharge to a cycled and 20 infants to control nurseries. The intervention took place in the NICU. During the day both cycled and non cycled NICU had the same amount of illumination. From 11 p.m. until next morning the illumination decreased by half in the cycled NICU. There were no statistically significant differences in the level of noise between the 2 nurseries. Compared with controls, infants from cycled nursery had a greater rate of weight gain, were able to be fed orally sooner, spent fewer days on the ventilator and on phototherapy, and displayed enhanced motor coordination. In addition to light, the significance of behavioral entrainment of newborn was shown several years

ago in a study by Pinilla and Birch.⁴⁹ These investigators instructed the parents to gradually increase the interval between the middle of night feeds and maximize the differences between day and night. By 3 weeks, all infants in the intervention group showed significantly longer sleep episodes at night compared with controls. Milk intake for 24 hours did not differ between the two groups. Babies in the intervention group also were rated as more predictable on Bates Infant Characteristics Questionnaire.

Summary

In conclusion, it appears that the fetal biologic clock functions endogenously early in development. Fetal diurnal rhythms are entrainable by maternal day night rhythms by the third trimester of pregnancy if not earlier. After birth the synchronizing effect of light may be ineffective when the circadian system is not mature enough to detect/or integrate changes in environmental lighting.^{23,39}

Based on animal and human studies, Recio et al²³ hypothesized that melatonin circadian rhythm in maternal circulation prenatally and in maternal milk postnatally may be an important factor in perinatal entrainment of circadian rhythms. This temporal signal may be altered when the mother's circadian system is desynchronized or poorly synchronized, eg, when the mother's nightly melatonin surge is blunted by nocturnal bright light during either late pregnancy or nightly feedings of breast milk.

Clearly, premature birth of the fetus will have the most dramatic impact on maternal fetal interactions. Nevertheless, the circadian rhythm impact appears to be temporary and greatest on the most immature infants. It is well known that fetal growth and development in the prematurely born infant is influenced by a multitude of factors and clearly the environment and the intensive care unit are not a surrogate for the maternal placental unit.

We should not dismiss the potential importance of providing cycled light in the nursery environment because it is relatively easy to accomplish and at little expense. The results to date would support the importance of circadian rhythms for the fetus and the relative lack of these rhythms in preterm infants. There are few data on the effect of circadian rhythm on phys-

iologic function of the preterm infant, later growth and central nervous system development. Although an earlier onset of circadian development did not result with cycled lightening in the neonatal nursery, there may still be important biologic effects that have not been studied to date.

There are sufficient data (reviewed above) to state that there is no rationale for continuing a chaotic non circadian environmental approach in the neonatal nursery for the care of the prematurely born infant. Introducing a regular day-night cycle into the NICU and intermediate nursery has been implemented in the recent Guidelines for Perinatal Care by the American Academy of Pediatrics and The American College of Obstetricians and Gynecologists.⁵⁰ Continuing such regular day-night rhythm at home as well as maximizing the day-night differences by minimizing night time care giver intervention (including feeding) will benefit the development of preterm and term infants. Lack of circadian rhythmicity not only in light but also in the pattern of parental care may subject the infant developing circadian rhythm to conflicting temporal cues.²³

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