Preterm infants born at less than 31 weeks’ gestation have improved growth in cycled light compared with continuous near darkness

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Objectives: Our purpose was to evaluate the benefits of cycled light (CL) versus near darkness (ND) on health in preterm infants born at <31 weeks’ gestational age.

Study design: Randomized, interventional study comparing infants receiving (1) CL from birth, (2) CL at 32 weeks’ postconceptional age (PCA), and (3) CL at 36 weeks’ PCA in transition for discharge home. Statistical significance was assessed with segmented mixed general linear models, analysis of covariance, general estimating equations, $\chi^2$, and Fisher’s exact procedure.

Results: Infants receiving CL at birth and 32 weeks’ PCA gained weight faster than infants not receiving CL until 36 weeks’ PCA. There were no differences among the groups in length of hospitalization stay or number of ventilator days, but the power was low for these variables.

Conclusions: These findings suggest that CL has significant weight gain benefits over ND, and there are no short-term advantages of ND over cycled light for health in preterm infants. (J Pediatr 2002;140:192-9)
ficial for preterm infants. Studies have examined the effects of ND only in combination with other interventions. Preterm baboons have suprachiasmatic nuclei innervated by the retina and responsive to light at an age believed to be comparable to 25 weeks’ human gestation, but it remains unclear whether young preterm infants can develop discernible circadian rhythms. Most studies that have evaluated effects of a CL in the NICU have used continuous bright light for comparison. In convalescent preterm infants (mean gestational age >31 weeks), Mann et al found that those in CL exhibited more weight gain and sleep 2 to 3 months after discharge and spent less time feeding in the nursery than infants in constant light. Infants with a mean gestational age of 28 weeks gained more weight, were fed orally sooner, and had fewer ventilator days when they were in a CL environment. These findings are consistent with findings on the negative consequences of constant light revealed in animal studies. One study has previously evaluated the short-term effects of ND and CL. No beneficial environmental light effects on the development of circadian rhythms were observed, but the intervention may not have been early or long enough to detect group differences before discharge. The infants in this study did not receive CL until they were transferred to the intermediate nursery, and the intervention was received for a minimum of 10 days to a maximum of 6 weeks.

The purpose of this study was to evaluate the timing and short-term effects of CL (day–night) and continuous ND on the health of preterm infants born at <31 weeks’ gestation.

**Methods**

**Patients**

Infants born at <31 weeks’ gestation (n = 62) were enrolled over 14 months between May 1998 and July 1999. Infants with known anomalies associated with neurologic or visual problems (eg, congenital glaucoma, genetic disorders) were excluded from study participation. There were 4 refusals to participate and 2 study withdrawals secondary to group assignment. Infants were stratified on the basis of 2 weight categories at birth (≤1000 grams and >1000 grams) and randomly assigned with the aid of a computer-generated random list. Multiples births were included, but each set of multiples was randomly assigned to the same intervention group. A target sample size of 60 had been selected, based on a power analysis for detecting 2% differences in average weight gain with an α level of .05 and an average intervention period of 6 weeks between study groups and a minimum statistical power of 93%, using methods developed by Muller and Barton. Weight gain was chosen for the power analysis because it has the greatest impact on length of hospitalization (LOS).

**Setting**

The setting was the 24-bed intensive care (ICN) and the 12-bed transitional care nurseries (TCN) of Duke University Medical Center and the 12-bed level II special care nursery (SCN) of Durham Regional Hospital. None of the units have external windows. The same nursing staff cares for infants in the ICN and TCN. All recruitment took place in the ICN with follow-up of patients on transfer to the TCN and SCN level II units. The Institutional Review Boards of Duke University Medical Center and Durham Regional Hospital approved the study.

**Intervention Groups**

Neonates were assigned randomly to one of 3 light intervention groups: (1) CL from birth, (2) CL at 32 weeks’ postconceptual age (PCA), and (3) CL at 36 weeks’ PCA in transition for discharge home. The 3 intervention groups allowed for comparison of continuous ND and CL as well as the timing of the onset of CL. Thirty-two weeks was selected as the crossover time for group 2 because maturation of the visual system appears ready to handle light stimulation by 32 weeks’ gestation. The group receiving CL at 32 weeks’ PCA was hypothesized to have more positive health outcomes than the CL from birth or CL at 36 weeks’ gestation groups because preterm infants would be exposed to light at a developmentally appropriate time. In addition, the infants receiving CL from birth would have better health outcomes than the infants receiving CL at 36 weeks because the effects of CL on circadian rhythm development would be more beneficial than any stress.

Light was provided with Philips Cool White fluorescent lamps (Philips, Somerset, NJ) measured as illuminance. Each lamp emits 5.5% as UVA light and 94.5% as visible light. Filters over the lamps filtered out UVA light, so only visible light reached the infant. ND (5-10 lux) was provided by using protective devices during the daytime and either dimming the room light or using protective devices at nighttime. Infants receiving ND were exposed to 5 to 10 lux light throughout the day except during 6:30 to 7:30 AM and 6:30 to 7:30 PM, when lighting levels varied based on change of shift nursing care needs. These transition hours were applied to all groups. CL was provided in an 11-hour-on, 11-hour-off pattern with one transition hour at the change of shifts. The incubator cover was folded on top of the incubator or the bassinet cover was off to achieve daylight at 200 to 225 lux between 7:30 AM and 6:30 PM.

Group status was maintained during lighting for medical procedures by protecting the eyes with eye pads. All infants were exposed to unavoidable retinal light stimulation through routinely scheduled ophthalmologic examinations at 4 to 6 weeks of age and every 1 to 2 weeks thereafter. The standard of care in the study nursery is to place preterm infants in an incubator as soon as possible after admission; therefore, all study infants were in incubators within 24 hours of age. Infants remain in incubators regardless of severity of
illness or ventilator modality. Compliance with the intervention for each group was evaluated through documentation on the nursing flow sheets and bi-weekly spot checks by the investigator. Compliance with the protocol ranged from 92% to 94% in all nurseries. Light and ND measures were taken weekly at each study infant’s bedside to monitor any unknown environmental differences that may have occurred during the study period. The day of the week sampled rotated weekly such that each day was sampled over a 7-week period. The mean lux measures remained in the ranges established for ND (5-10 lux) and light (200-225 lux) throughout the study for all infants.

Measures

**Growth.** Infants were weighed daily on calibrated scales. The weights were summed and averaged to determine weekly weight gain for each week of the infant’s hospitalization.

**Number of Ventilator Days and Length of Stay.** Lung maturation and disease, reflected by total number of ventilator days, and physiologic health, measured by total hospital days, were determined to evaluate the intervention potential to decrease hospital cost. Because days of mechanical ventilation and length of stay (LOS) were highly skewed, the natural logarithm of each patient’s score was used in analyses.

**Hearing (Brainstem Auditory Evoked Response).** The nursery audiologist conducted the brainstem auditory evoked response (BAER) as close to discharge as possible so that infants were no longer requiring antibiotic therapy or at risk for other conditions that might affect hearing. All infants were tested with the use of the Algo 2 brainstem auditory evoked instrument (Natus Medical, San Carlos, Calif). Results were categorized as pass (35 dB or no more than a mild hearing loss) or fail (a hearing loss cannot be ruled out, and further audiologic testing was conducted after discharge). Passing results are at the 99.8% confidence level.17

**Retinopathy of Prematurity.** Ophthalmologic examinations were conducted weekly, biweekly, or monthly, beginning at 1 month of age (6 weeks of age for infants born at <25 weeks’ gestation) until the infant had mature retina or retinopathy of prematurity (ROP) disease had resolved. The International Classification of ROP was used to categorize disease.

**Covariates.** Baseline descriptive and illness specific data were obtained from the medical record. With the exception of intraventricular hemorrhage (IVH) (which differed among the groups), the covariates were added to analyses to be conservative and attempt to rule out other explanatory variables. Birth weight and average weekly caloric intake were used in analysis of weight gain, birth weight, severity of neurologic insults (Neurobiologic Risk Scale [NBRS]),18 and length of time to reach growing calories without regression were used in the analysis of ventilator days and LOS, and birth weight, NBRS, IVH, and number of ventilator days were used in the analysis of ROP. IVH was coded grades I through IV (I, isolated germinal matrix hemorrhage; II, hemorrhage involving part of the germinal matrix; III, hemorrhage involving all of the germinal matrix; IV, hemorrhage involving germinal matrix and periventricular white matter).

### Table I

<table>
<thead>
<tr>
<th>Variable</th>
<th>Near darkness/cycled light (n = 19)</th>
<th>Cycled light (n = 22)</th>
<th>Near darkness (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen days</td>
<td>Mean ± SD 40.8 ± 46.5</td>
<td>Mean ± SD 42.0 ± 53.1</td>
<td>Mean ± SD 58.4 ± 49.2</td>
</tr>
<tr>
<td>Phototherapy days</td>
<td>Mean ± SD 7.3 ± 2.5</td>
<td>Mean ± SD 7.2 ± 4.5</td>
<td>Mean ± SD 9.4 ± 4.6</td>
</tr>
<tr>
<td>Day of life start feeds</td>
<td>Mean ± SD 5.5 ± 5.8</td>
<td>Mean ± SD 9.0 ± 18.9</td>
<td>Mean ± SD 7.0 ± 8.2</td>
</tr>
<tr>
<td>Day of life to full feeds</td>
<td>Mean ± SD 35.3 ± 51.2</td>
<td>Mean ± SD 42.8 ± 45.1</td>
<td>Mean ± SD 42.0 ± 28.0</td>
</tr>
<tr>
<td>Calories/kg/d*</td>
<td>Mean ± SD 108.5 ± 27.5</td>
<td>Mean ± SD 116.0 ± 55.8</td>
<td>Mean ± SD 108.5 ± 30.2</td>
</tr>
<tr>
<td>NBRS†</td>
<td>Mean ± SD 4.2 ± 3.8</td>
<td>Mean ± SD 3.5 ± 2.8</td>
<td>Mean ± SD 4.1 ± 3.5</td>
</tr>
<tr>
<td>RDS</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>R/O Sepsis and sepsis</td>
<td>Mean ± SD 9 (47.4)</td>
<td>Mean ± SD 11 (50.0)</td>
<td>Mean ± SD 15 (71.4)</td>
</tr>
<tr>
<td>IVH (all grades)†‡§</td>
<td>Mean ± SD 7 (37.8)</td>
<td>Mean ± SD 6 (27.3)</td>
<td>Mean ± SD 4 (19.1)</td>
</tr>
<tr>
<td>PDA</td>
<td>Mean ± SD 9 (47.4)</td>
<td>Mean ± SD 7 (31.8)</td>
<td>Mean ± SD 11 (52.4)</td>
</tr>
<tr>
<td>NEC</td>
<td>Mean ± SD 3 (15.8)</td>
<td>Mean ± SD 3 (15.6)</td>
<td>Mean ± SD 4 (19.1)</td>
</tr>
<tr>
<td>Transferred to SCN</td>
<td>Mean ± SD 9 (47.4)</td>
<td>Mean ± SD 8 (36.4)</td>
<td>Mean ± SD 7 (33.3)</td>
</tr>
</tbody>
</table>

*RDS, respiratory distress syndrome; PDA, patent ductus arteriosus; NEC, necrotizing enterocolitis; SCN, special care nursery.

*Average calories/kg per day over all postconceptional age weeks.
†<5 = low-risk, ≥5 = high-risk.18
‡Papile classification.
§Statistically significant differences between groups, Fisher’s exact test (P < .0001).

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II, IVH with normal ventricular size; III, IVH with acute ventricular dilation; IV, IVH with parenchymal hemorrhage), according to Papile's classification.19 The length of time to reach growing calories without regression was defined as the number of days until the infant was taking growing caloric enteral feedings (100 mL/kg/day) and continued taking growing calories until discharge. Because days of mechanical ventilation were highly skewed, the natural logarithm of each patient’s score was used in analyses.

The NBRS18 was used as an overall severity of neurologic insult score. It summarizes 7 neurologic insults received by an infant throughout hospitalization on a 0 to 4 scale, with a total score possible range of 0 to 28. The 7 medical indicators (duration of mechanical ventilation, acidosis, infection, seizures, IVH, periventricular leukomalacia, hypoglycemia) used to calculate the NBRS were collected as part of the illness-specific data. Data were obtained weekly from the medical record. The NBRS has a correlation of 0.60 with neurologic examinations at 6 and 15 months of age.18 Because the scale is based on the entire hospitalization, data at discharge were used. A score of ≤5 is an indicator of low risk, and ≥5 is an indicator of high risk.18

**Table II.** Mixed model results with 95% confidence intervals

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter estimate</th>
<th>SE</th>
<th>DF</th>
<th>t value</th>
<th>P value</th>
<th>Lower 95% confidence interval</th>
<th>Upper 95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept*</td>
<td>103.89</td>
<td>12.06</td>
<td>569</td>
<td>8.61</td>
<td>&lt; .0001</td>
<td>80.19</td>
<td>127.58</td>
</tr>
<tr>
<td>CL from birth†</td>
<td>7.10</td>
<td>11.09</td>
<td>569</td>
<td>0.64</td>
<td>.5224</td>
<td>–14.69</td>
<td>28.89</td>
</tr>
<tr>
<td>CL at 32 wk†</td>
<td>18.79</td>
<td>11.55</td>
<td>569</td>
<td>1.66</td>
<td>.0984</td>
<td>–3.51</td>
<td>41.09</td>
</tr>
<tr>
<td>PCA‡</td>
<td>27.75</td>
<td>5.09</td>
<td>59</td>
<td>5.45</td>
<td>&lt; .0001</td>
<td>17.55</td>
<td>37.92</td>
</tr>
<tr>
<td>PCA§</td>
<td>0.77</td>
<td>0.47</td>
<td>569</td>
<td>1.64</td>
<td>.1011</td>
<td>–0.15</td>
<td>1.69</td>
</tr>
<tr>
<td>32-wk effect¶</td>
<td>37.53</td>
<td>17.09</td>
<td>569</td>
<td>2.20</td>
<td>.0285</td>
<td>3.96</td>
<td>71.10</td>
</tr>
<tr>
<td>PCA CL at 32 wk¶</td>
<td>11.59</td>
<td>4.46</td>
<td>569</td>
<td>2.55</td>
<td>.0110</td>
<td>2.62</td>
<td>20.15</td>
</tr>
<tr>
<td>PCA CL from birth¶</td>
<td>8.51</td>
<td>4.17</td>
<td>569</td>
<td>2.04</td>
<td>.0415</td>
<td>0.33</td>
<td>16.69</td>
</tr>
</tbody>
</table>

*Intercept equals standard score at 32 weeks.
†Parameter estimate difference for cycled light (CL) at birth and CL at 32 weeks when compared with CL at 36 weeks group.
‡PCA effects equal the linear slope.
§PCA effects equal curvilinear slope.
¶Modeled 2 slopes for each group, one before and after 32 weeks’ PCA.
¶Interaction effects between PCA and CL at 32 weeks and CL at birth groups when compared with CL at 36 weeks group.
#Interaction effect between PCA and t32.

**Weight Gain**

The cumulative average weekly weight gain was 117 ± 138 g for infants receiving CL from birth, 122 ± 149 g for infants receiving CL at 32 weeks, and 95 ± 112 g for infants receiving CL from 36 weeks.

A segmented, mixed general linear model was used to analyze the pattern of weekly weight gain.20,21 The analysis examined changes in weight gain over time by group before and after 32 weeks’ PCA and whether the groups differed in the amounts and developmental pattern of change.20,21 This technique was essential because two of the intervention groups (2 and 3) were receiving the same intervention (ND) before 32 weeks’ PCA and two of the intervention groups (1 and 2) were receiving the same intervention (CL) after 32 weeks’ PCA and whether the groups differed in the amounts and developmental pattern of change.20,21 This technique was essential because two of the intervention groups (2 and 3) were receiving the same intervention (ND) before 32 weeks’ PCA and whether the groups differed in the amounts and developmental pattern of change.20,21

**RESULTS**

**Characteristics of Study Infants**

Infants were similar with respect to gestational age (27.1 ± 2.0 weeks) and birth weight (1000 ± 223 g) across the 3 intervention groups. Most infants were nonwhite (75%), and approximately half were female. The only variable differing among the groups was the incidence of IVH (grades I through IV) (Table I). The group receiving CL at 36 weeks had the least IVH, and the group receiving CL at 32 weeks had the most IVH. However, between birth and 7 days of age, when most IVH occurs, infants in both of these groups had the same intervention, ND.

**PROCEDURE.** Parents were approached for consent after delivery, or as soon as the mother had recovered from delivery and the study procedures could be explained. Infants were enrolled within 48 hours of admission into the intensive care nursery. The intervention was initiated after group assignment and continued until the infants were discharged from the hospital.
The fixed effects and random error are similar to the usual multiple regression parameters. The random effects are the difference between the patient’s regression line and the population regression line. Mixed models accommodate repeated observations within individuals by modeling the covariance structure within patients. In these models, individual differences over time are captured by random coefficients. The advantage of this technique over traditional approaches, such as repeated-measures analysis of variance, is that it can describe group changes over time, does not have restricted and unrealistic assumptions, can easily handle missing data and nonuniform time intervals, and allows time-varying covariates.21,22

In a preliminary mixed model, weight gain was regressed over PCA as both linear and quadratic trends and segmented change at 32 weeks. Segmenting the groups at 32 weeks modeled 2 slopes for each group, one before and one after 32 weeks’ PCA. The interactions between the PCA trends and group were also included in the initial model. Birth weight and caloric intake (calories/kg/day), although not significantly different among the groups, were initially included as covariates to control for their potential influence on weight gain. The intercept, PCA, and intervention group were included in the random effect component to allow each infant to have an individual developmental trajectory. A second screening analysis was conducted with intercept, PCA, and all variables that reached \( P < .10 \) in the preliminary analysis. Variables remaining after this screening procedure were used in a final model analysis if they reached significance at \( P < .05 \). This procedure simplified the model until only the linear and quadratic trends of PCA, the 32-week effect, intervention groups, and the interaction between intervention group and linear PCA were left as explanatory variables (Table II).

There was a significant linear trend \( (P = .0001) \) for all groups (Figure). In addition, there were significant differences in the trajectory of weight gain among the 5 groups over time (PCA). The patterns of weight gain before and after 32 weeks’ PCA were significantly different \( (P = .03) \), and there was a significant interaction effect between the change at 32 weeks and the linear trend \( (P = .001) \). The CL at 32 weeks and CL from birth groups’ growth accelerated significantly earlier than the group receiving CL at 36 weeks’ PCA \( (P = .01 \) and \( P = .04 \), respectively) (Figure).

Ventilator Days and Length of Stay

Ventilation days and LOS were each dependent variables in an analysis of covariance, between-groups design controlling for birth weight, NBRS, and time to reach growing enteral calories. Ventilator days (CL from birth, \( 17 \pm 23 \) days; CL at 32 weeks, \( 23 \pm 26 \) days; CL at 36 weeks, \( 26 \pm 27 \) days) and LOS (CL from birth, \( 78 \pm 43 \) days; CL at 32 weeks, \( 74 \pm 41 \) days; CL at 36 weeks, \( 86 \pm 40 \) days), group means, trended in the direction of the hypotheses that the CL groups would perform better, but there were no statistically significant differences among treatment groups. The covariates birth weight \( F (1, 54) = 21.20; P < .0001 \), severity of neurologic insult \( F (1, 54) = 4.07; P < .05 \), and time to reach growing enteral calories \( F (1, 55) = 27.23; P < .0001 \), best predicted LOS and the covariates birth weight \( F (1, 55) = 4.06; P < .05 \), and severity of neurologic insult \( F (1, 55) = 9.47; P < .0001 \), best predicted number of ventilator days.

Auditory Functioning

Auditory functioning (BAER) was analyzed by means of \( \chi^2 \) and Fisher’s exact procedure. There were no statistically significant differences among groups in the failure of each ear analyzed separately, but the infants receiving CL at 32 weeks had significantly more failures \( (n = 7) \) in one or both ears than the infants receiving CL at 36 weeks \( (n = 1) \). However, there were no significant differences between the infants receiving CL from birth and the infants receiving CL at 36 weeks. BAER examinations repeated after dis-
charge revealed subsequent passing scores that resulted in no significant differences between the infants receiving CL at 32 and 36 weeks.

**ROP Development**

The general estimating equation procedure (GEE)\(^{22}\) was used to evaluate differences in the development of ROP. The GEE can be thought of as ordinal logistic regression for correlated outcomes. It has the same advantages of the mixed model analysis discussed previously. ROP was coded as immature retina = 0, and the stages of disease = 1 through 4. To determine if the intervention groups were predictive of ROP, a general estimating equation was calculated for ROP with the intercept, intervention group, PCA as both a linear and quadratic trend, and the interactions between the PCA trends and intervention group. A model reduction procedure with each variable was entered into a preliminary GEE analysis. Birth weight, number of ventilator days (log), NBRS, and IVH were initially included as covariates in the model because of their potential to be predictive of ROP. A second GEE analysis was conducted with intercept, PCA linear and quadratic trends, intervention group, the interactions between PCA trends and intervention group, and all variables that reached \( P < .10 \) in the preliminary analysis. The variables remaining after this screening procedure were used in a final mixed model analysis, which included only those variables with a value of \( P < .05 \). One infant died at 35 weeks’ PCA and 6 infants were transferred or discharged without ROP data; therefore, only 55 infants are included in this analysis.

The maximum severity of ROP throughout hospitalization assessed with Fisher’s exact test was not significantly different among the 3 groups (Table III) \( (P = .63) \). However, in the GEE analysis, ROP demonstrated a significant linear increase in severity over time for each of the intervention groups (parameter = 0.20; \( P = .0001 \)) and was best predicted by birth weight (parameter = –0.002; \( P = .0001 \)). The ND group appeared to have more severe ROP earlier (parameter = 0.32; \( P = .09 \)).

### DISCUSSION

The findings of this study suggest that CL has short-term advantages over continuous ND for the health of preterm infants. Like other CL studies,\(^{6,11}\) infants receiving CL from birth or beginning at 32 weeks’ PCA gained weight significantly faster than infants that were in ND until 36 weeks’ PCA. There were no group differences in LOS and ventilator days; however, they were not the primary outcomes on which sample size was calculated. The study was not sufficiently powered to detect LOS and ventilator day differences, given the variability among the groups. However, the trend toward decreased LOS and ventilator days in the CL groups supports the significant weight gain differences among the groups.

Although previous findings have suggested that continuous bright light is detrimental to the health of preterm infants,\(^{6,10,11}\) findings of this study would suggest that CL does not have the same deleterious effects. Negative effects previously associated with continuous bright light, including increased activity, decreased sleep, and more apnea and bradycardia, were observed at higher illumination levels than in this study.\(^{1,2,5,6}\) The standard nursery light levels in this study were low (200-225 lux) compared with previous research (400-900 lux).\(^4\) Lower illumination levels may be less stressful to the preterm infant, as evidenced by the finding that the infants receiving CL at 32 weeks and from birth had similar mean weekly weight gains before and after 32 weeks. Additionally, any stress associated with light exposure before 32 weeks may have been outweighed by the benefits of CL. Causal mechanisms contributing to the group differences in weight gain could include differences in sleep-wake activity cycles, gastrointestinal hormone secretion, or endocrine functioning.

Auditory outcomes were evaluated to ensure the safety of CL because premature stimulation of one sensory system is known to influence the development of other sensory systems.\(^{23,24}\) The finding of a higher BAER failure rate in the

### Table III. Number of patients with maximum ROP stage by intervention group at hospital discharge

<table>
<thead>
<tr>
<th></th>
<th>Near darkness/cycled light</th>
<th>Cycled light</th>
<th>Near darkness</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=19)</td>
<td>(n=22)</td>
<td>(n=21)</td>
<td></td>
</tr>
<tr>
<td>Normal retina</td>
<td>4</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Immature retina</td>
<td>4</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>ROP stage 1</td>
<td>4</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>ROP stage 2</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>ROP stage 3</td>
<td>2</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>ROP stage 4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infants requiring laser surgery</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

No significant differences among groups. Fisher’s exact procedure, \( P = .63 \).
Infants receiving CL at 32 weeks versus 36 weeks was unexpected. Because infants receiving CL from birth and at 36 weeks did not differ in BAER failure rates and there were no significant differences on later testing between the infants receiving CL at 32 weeks and CL at 36 weeks, these failure differences may be related to false-positives or problems with testing rather than a true maturational difference in auditory development.

Since ND has become the standard of care in nurseries using the developmentally recommended methods by Als et al., ROP incidence was evaluated to ensure the safety of CL. As expected, each intervention group had similar maximum severity of ROP disease, but the trend that the ND group developed more severe ROP earlier in gestation was unexpected. There have been conflicting reports about the effect of light on the development of ROP. Glass et al. found a higher incidence of ROP in preterm infants exposed to continuous bright light, especially infants with birth weight <1000 g, and they hypothesized that light may cause alterations in retinal metabolism and cellular damage. Other studies found no differences in the incidence of ROP when infants were shielded from light by blankets or eye patches for all or part of the day. The period of ND provided by the CL may have enabled retinal photoreceptors to recover or light may have promoted retinal maturation. Appropriate visual stimulation is known to be necessary for visual development, and excessive light exposure is known to damage the retina. However, whether appropriately timed moderate light exposure may facilitate retinal development is unknown. Light exposure earlier than normal for an organism can facilitate some aspects of intersensory development. It is also possible that ND is harmful to the retina. In healthy adults, retinal oxygen consumption is increased in darkness, with a concurrent increase in retinal blood flow to increase oxygen delivery. If retinal oxygen consumption is also increased in darkness in preterm infants, the immaturity of the autonomic nervous system and cerebral blood flow regulation mechanisms may not preserve retinal perfusion during episodes of low blood pressure. It is unclear whether the rate at which ROP develops is related to long-term visual outcomes and should be evaluated further.

Future research should evaluate further the best time to introduce CL to preterm infants to maximize physical growth and visual and auditory development. In addition, the development of circadian rhythmicity in preterm infants exposed to prolonged CL environments in the hospital should be evaluated. The presence of significant circadian rhythms provided by maternal and rest-activity cycles in the intrauterine environment suggests that they are important for human development. Implementation of CL at the most appropriate time for the preterm infant may help promote the development of circadian rhythms and growth and development before and after hospital discharge.

**REFERENCES**


50 Years Ago in The Journal of Pediatrics

APLASTIC ANEMIA IN SIBLINGS WITH MULTIPLE CONGENITAL ANOMALIES (THE FANCONI TYPE)


Five decades ago, Levy reported his observations concerning the clinical course of 2 brothers with Fanconi’s anemia. He painstakingly detailed the physical anomalies and hematologic decline in the boys, after their symptom presentation at 6 years old, as the 29th and 30th published cases of Fanconi’s anemia. Treatment with oral iron, diluted hydrochloric acid, thyroid extract, subcutaneous injections of liver extract, a diet adequate in vitamins, and discharge to a resort for convalescent care were, not surprisingly to modern readers, ineffective. Both boys died within 10 to 15 months after the development of marrow aplasia, not unexpected in an era when transfusion support was limited to whole blood.

The author interpreted the cases in terms of the prevailing hematologic wisdom of the era. He suggested that the development of aplastic anemia at the same age in the siblings was because of a “maternal factor” or “imperfections in the germ plasm responsible for the production of the hematopoietic system leading to its exhaustion.” The congenital malformations associated with Fanconi’s anemia were ascribed to “defective germ plasm” or consanguinity.

Our modern understanding of the multisystem manifestations of Fanconi’s anemia draws extensively on the publication of detailed clinical descriptions such as this. Although hematologists today have characteristic chromosomal breakage studies after clastogenic stress to confirm a clinical diagnosis of Fanconi’s anemia, and the genes responsible have been cloned for many kindreds, we still do not understand why bone marrow failure commonly occurs in early childhood or develops in a specific patient. Levy observed his patients briefly, yet detailed their cases so carefully that by reading his report, we feel we know them. With modern supportive care, including androgen therapy, blood component transfusion, and the potential for cure with bone marrow transplantation, clinicians today may potentially observe their patients for decades. Yet, can we say that we will know our patients any better or detail their courses any more clearly than Levy?

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