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Hurting While Helping? The Paradox of the Neonatal Intensive Care Unit

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Comment on This Article

Abstract

Survival rates of very low birth weight infants have improved dramatically over the last few decades, primarily as a result of medical and technological advances techniques have shaped a special hospital environment for high-risk infants, the Neonatal Intensive Care Unit (NICU). The NICU's environment has been customized to maximize infant survival rates, yet concern is growing that the modern, high technology NICU environment can be detrimental to the infant's long-term physiological and social development, and may actually slow the rate of growth and recovery from illness. This article reviews some of the literature on the characteristics of the modern NICU environment and how it might be made less problematic for infant development. To illustrate the possible adverse aspects of the NICU, the article discusses the possibility of phototoxic effects from NICU lighting conditions. As a subsidiary issue, the article also discusses some of the potential benefits of adding handling and therapeutic touch to the care routines for NICU patients to illustrate how the typical NICU regimen might be improved.

Keywords: NICU, premature infants, phototoxicity, infant stimulation

Birth is one of life's certainties, but the exact circumstances surrounding a birth are subject to wide cultural and historical variations. For example, the nature of the immediate post-natal environment for our culture's full-term infant has changed markedly in the last decade. Twenty-five years ago, birth was regarded as a largely medical procedure, with mother and infant "recovering" by spending a week or more "lying in." Now healthy full-terms and their mothers are often away from their familiar home environments for only a day or two. During that time, it is probable that the infant spends at least some of the time in the hospital "rooming in" with the mother and in contact with other family members (who are no longer treated as unsanitary intruders, a potential breeding ground for harmful germs). Medically, many of the changes surrounding the process of normal, full-term delivery became possible because of changes in the level and timing of anesthetics and analgesics administered during labor. Pressure from parents for natural childbirth, as well as mounting evidence of the negative effects on perinatal mortality of early and high doses of delivery medication (Brackbill 1979) paved the way for the rather home-like conditions and short hospital stay of the healthy neonate. The majority of observers would probably applaud these changes as in both the medical and psychological best interests of the child.

Contrast the tendency to release healthy and full-term infants to their "natural" environments as soon as possible after a hospital birth with the treatment of infants born at low birth weight or before term. Over the same time interval, birth and the immediate post-natal period for premature infants has became more and more bound up with the environment of the hospital. The medical specialty of neonatology has made tremendous progress in keeping extremely low birthweight infants alive, but in the process has created an environment almost completely different from that into which infants are usually born, The most extreme case of this is found in the neonatal intensive care unit (NICU), a high technological attempt to substitute for the environment in the uterus for an infant born early.

Improved survival rates for very low birth weight (VLBW; < 1500 grams) infants have coincided with increasingly long stays in NICUs and extended exposure to potentially harmful environmental hazards at a time when the infants are normally undergoing substantial neurological development. Although there is much still to learn, there is evidence that some of the care and environmental practices characteristic of many NICUs can impede recovery from illnesses and retard development. They may be associated with long-term health and developmental problems. Other procedures and interventions attempt to emulate the environment *in utero* and can lead to increased recovery, faster weight gains, shorter stays in the NICU, and better developmental outcomes. Surprisingly, some practices which appear to be quite beneficial are not widely implemented, while others for which the evidence suggests negative effects are still in common use.

Concern about the potential negative effects of the NICU on the developing neonate has been expressed by a number of groups concerned with neonatal and infant health. For example, a joint Committee on High-Risk Infant Environment, Intervention and Follow-up has been formed, comprised of members from the American Academy of Pediatrics, the National Perinatal Association, the National

Association of Neonatal Nurses, and the Maternal and Child Health section of the American Public Health Association (1992a; b). Among this group's conclusions are that factors and practices in the NICU environment are associated with "stresses that contribute to physiologic instability and may interfere with recovery from illness, growth and development". They also suggest that we need more research on the possible adverse neurological and psychological outcomes resulting from long stays in NICUs early in life. Associated with that Committee's recommendations, a federally-funded National Resource Center on the Physical and Developmental Environment of the High-risk Infant has been established to conduct organized, systematic study and analysis of infant intensive care practices and environmental factors. The Center will review literature, survey practices, develop a National Clearinghouse for the relevant research literature, and ultimately make recommendations about how the NICU could be changed to the benefit of its young patients.

The purpose of this article is to review some of the research on NICU practices, with an eye to how the NICU environment may affect the premature infant both positively and negatively. We have chosen to concentrate on two developmental areas related to NICU experience: tactile/vestibular, relatively well developed even in VLBW infants; and visual, probably the most immature of the sensory systems for both premature and normal infants. We will survey recent evidence on the benefits of tactile/vestibular stimulation as a practice that ought probably to be more wide-spread for VLBW infants. We will also review data on possible adverse effects on an infant's visual system from the type of light environment typically found in NICUs, as another example of environmental circumstances that should be considered in planning the hospital environment of the NICU.

There is obviously much to be written on the developmental and psychological implications of the NICU experience on young infants. For example, the individual infant's level of visual development will obviously affect both cognitive and social development. Additionally, the nature of handling may have important ramifications for issues of temperament and the nature of parent-infant interactions when the infant leaves the hospital. Unfortunately, we will be unable to deal explicitly with these issues here because of space limitations. However, we hope this article will enlighten and assist those working with this population of infants, in thinking about and making changes in the NICU environment. We also hope it will generate further discussion, research, and reviews.

Description of the Typical NICU Environment

Before the introduction of NICUs in the 1960s, many VLBW infants died as a result of pulmonary complications and other sequelae of extreme prematurity. With advances in medical practice, there has been a dramatic decrease in mortality rates of very low birthweight infants, even when gestation has been shortened by as much as 30-40 percent. The 50 percent survival weight has decreased from a birth weight of 1500 g in 1970 to less than 700 g in 1990 (Glass, in press). Yet despite considerable advances, this population still has the highest rates of neonatal mortality. Those infants who survive also experience a substantially higher rate of motor and sensory deficits, cognitive impairment and other developmental problems than full-term infants (Knobloch and Pasamanick 1966; Caputo and Mandell 1970; Fitzhardinge and Ramsay 1973; Stewart et al. 1981). Preterm birth is the most common single risk factor for developmental problems during childhood, particularly visual and visual-motor problems, but also including other forms of learning disabilities (e.g., Vohr and Garcia-Coll 1985; McCormick et al. 1990; Hack et. al. 1991; Volpe 1991). In the U.S. today, more than 150,000 infants experience extended stays in the NICUs each year.

Evidence suggests that at least some of the negative sequelae of being in an NICU are due to the unnatural circumstances of that environment itself. Originally, concern for sick prematures was spurred by studies reporting negative side effects of institutionalization particularly due to sensory/ perceptual deprivation in the institutional environment (e.g., Casler 1961; 1968). Early intervention programs for premature infants attempted to increase sensory stimulation, under the assumption that premature infants were experiencing moderate to extreme levels of sensory deprivation during their time in NICUs. Subsequent research (e.g., Cornell and Gottfried 1976; Lawson et al. 1977; Gottfried et al. 1981; Lawson, Turkewitz et al. 1985) demonstrated that, in truth, rather than sensory deprivation characterizing the NICU environment, the premature infant so-housed was actually exposed to extremely *high* levels of sensory stimulation, but in patterns uncharacteristic of those that would be experienced either prenatally or in non-hospital post-natal life. The stresses associated with this high level of stimulation, particularly given the reduced self-regulatory competence of the VLBW infants, are both potentially medically and behaviorally detrimental and can disrupt the normal development of the brain at a sensitive period of development (Als et al. 1986).

The infant in the NICU experiences a marked disruption of the rhythms or cycles of environmental stimulation experienced *in utero*, when maternal rest/activity cycles created some structure in the vestibular-proprioceptive, tactile and auditory stimulation experienced. Rather than the warm, dim, probably comfortable environment floating in amniotic fluid with significant circadian variation caused by the mother's sleep-wake cycles, the infant must contend with an environment in striking contrast to that of the uterus. After birth, the infant is likely to experience painful medical procedures, excessive handling and disruption of steep, noise, and bright lights that seldom adhere to any consistent pattern of occurrence.

Such characteristics of the NICU may actually impede the infants' medical progress while in the unit. There are a number, of reports of the physiological correlates of stress in young NICU patients; these reports include apnea/bradycardia, autonomic instability, vasoconstriction, decreased gastric constriction, and hypoxemia (Als et al. 1986; Glass, in press; Long et al. 1980). Gunnar and colleagues (Gunnar et al. 1991) have reported abnormal, stress-related activation of the hypothalamic-pituitary-adrenocortical system in newborns. High levels of these hormones may interfere with healing but they may be able to be reduced by appropriate changes in handling (see below).

Lawson et al. (1977) reported on the sound, light and handling characteristics of two NICUs. Sounds levels within the NICUs were high (69 - 88 db, comparable to traffic at a noisy street corner or on motor bus); no readings were found with sound as low as that reported for a typical office (54 db). Ambient noise came from both speech and non-speech sources. Speech sounds were more likely to vary with the diurnal light cycle, being somewhat lower at night. Non-speech sounds did not vary in amount across the day. Infants in incubators were also exposed to extremely high levels of continuous noise from fans in the incubator itself, on the order of 70-80 db (Sanders et al. 1970; Blennow et al. 1974), far exceeding levels recommended during sleep hours for adults. The constant incubator noise may also significantly mask most other sounds, including speech.

While these levels of noise may appear high, in absolute level they may not be markedly different than those experienced by the fetus *in utero*. Recent measurements of uterine sounds (primarily in sheep, but the human case should be similar) reveals that internal sounds such as maternal breathing, gastric sounds, heart beats and placental rhythms (Walker et al. 1970; Gerherdt 1989), as well as external sounds such as speech (DeCasper and Fifer 1980; DeCasper and Spence 1986) are probably experienced by the fetus. These have been recorded to be approximately 70-85 db; because of filtering by the body, most of these sounds are probably of low frequency. At the same time, while similar in intensity, the pattern and spectral characteristics of NICU noise (generated by fans and motors in equipment, personnel, telephones, pagers, trash cans, alarms, etc.) are markedly different than *in utero* (Glass, in press). Such noise is apt to be present continuously (as in fans and motors), or at least without marked diurnal cycling. While this noise may mask environmentally-relevant sounds such as speech compared to the non-NICU setting, it is possible that for some infants, the continuous noise of the incubator may stimulate sleep (Schmidt et al. 1980). Exposure to noises similar to those found in NICUs has been reported to damage cochlear hair cells in newborn guinea pigs (Douek et al. 1976), but it is not known whether exposure itself results in hearing loss in NICU patients. The problem is exacerbated by the fact that these infants are often otherwise ill; for example, some antibiotics, diuretics, and other ototoxic drugs often administered to sick premature infants have been shown to interact with noise level to cause hearing loss (Falk 1972; Carlier and Pujol 1980; Walton and Hendricks-Munoz 1991).

As will be discussed further below, NICUs are brightly lit environments, with light levels frequently exceeding by large amounts those found in brightly-lit offices. Animals exposed to similar levels of light have been reported to show clear damage to photoreceptors and other retinal structures (e.g., Lanum 1978; Williams and Baker 1980). Also, factors that have been demonstrated to increase the likelihood of phototoxic damage are common in the sick preterm population found in NICUs, namely, increased body temperature, hypoxia, ischemia, retinal disease, and exposure to constant darkness (Glass 1990).

Lawson et al. (1977) also reported that during both routine care and invasive procedures, infants were handled frequently, without regard to their level of alertness or arousal. These higher levels of stimulation typically fail to adhere to the cycles of activity characteristic of most normal environments outside of the hospital. These fluctuations are attenuated if not eliminated in many NICUs. It has been proposed that regular diurnal rhythms may be essential for normal growth and development.

Lawson et al. (1985) studied two different NICUs every 15 minutes for at least three continuous days. Infants in both NICUs were exposed to considerable amounts of stimulation, but the units differed in the periodicity of the stimulation. The diurnal rhythms in the environment influenced the infants' own state cycles (that is, when the infants were in the different types of sleep, awake or crying). The infant's ability to maintain a given state as well as to make smooth transitions among difference states, particularly in response to environmental inputs, has been used as a measure of developmental maturity and brain maturation (e.g., Brazelton 1973). Infant responsivity to different types of stimuli is state dependent. That there are differences in infant states depending on the characteristics of the particular NICU implies that the periodicity of environmental stimulation can play a role in assisting or disrupting infants' abilities to respond to environmental events. This is an influence that may have longer-term consequences for physical, cognitive and social development. In the shorter term, disturbances of sleep may interfere with normal healing processes. For example, secretion of cortisol and adrenalin is a hormonal response to stress which retards healing. This secretion is inhibited during sleep. Growth hormone, on the other hand, promotes healing by increasing protein synthesis and efficient energy use (Adam and Oswald 1984; Sassin et al. 1969). This secretion is increased during quiet sleep. Therefore, periods of quiet sleep promote healing by inhibiting the secretion of cortisol and adrenalin and by increasing the production of growth hormone.

Infant Stimulation in the NICU

The use of stimulation programs in conjunction with medical management for premature infants has been studied intensively since the determination of the possible detrimental effects of NICUs. Different types of programs offering either enrichment or compensatory stimulation have been implemented, depending on whether the premature infant's environment has been regarded as one of sensory deprivation, sensory bombardment, or as inappropriate patterns of stimulation. In the process, infants have been provided with tactile, vestibular, kinesthetic, auditory, and visual forms of stimulation, singly or in combination. There are a number of methodological differences and notable flaws in these studies. Among those factors that have often not been controlled, and sometimes not even specified are gestational age; birth weight criteria; sample size; medical status; duration of experimental treatment; age of stimulation onset; how often and when behavioral observations were made; and type of stimulation implemented. Yet, there is overwhelming support for the effectiveness of stimulation programs (see Schaffer et al. 1980 for a review). Short-term improvements and long-term effects in weight gain, respiratory status, psychomotor and mental development, and emotional states have been the traditional outcome measures observed.

Several researchers have investigated the clinical effects of compensatory vestibular-proprioceptive stimulation (Barnard 1972; Barnard and Bee 1983; Burns et al. 1983; Edelman et al. 1982; Freedman et al. 1966; Korner et al. 1975; Kramer and Pierpont 1976; Neal 1968). These programs stimulate infants with either some form of rocking motion or by placing them on oscillating waterbeds, sometimes in conjunction with auditory stimulation. The rationale for these studies is two-fold. Firstly, it was reasoned that by nature, premature infants are deprived of the stimulation they would otherwise have received *in utero*, and therefore require some form of compensatory stimulation. Dreyfus-Brisac (1974) suggested that the deprivation of the maternal biological rhythms was the cause of preterm infants' irregular behavior and sleeping patterns. Barnard (1978) further hypothesized that the rhythmic stimulation provided *in utero* actually enhances neurological maturation, which in turn facilitates the development of state behavior organization. Secondly, it has been determined that the vestibular system is among the first of the major fiber tracts to form and function (Humphrey 1965; Langworthy 1932) such that by four months gestational age, myetination is beginning, and that by term this system is fully mature. Therefore, it has been reasoned that infants will be most receptive to stimulation of their more functionally mature systems. Further, it has been suggested that stimulation of the more mature senses will influence the development of later maturing ones (Turkewitz and Kenny 1985).

Neal (1968) found that premature infants who were rocked by hammocks suspended in their incubators exhibited significant improvements in terms of weight gain, motor maturation, auditory and visual responses, and muscle tension responses than infants not receiving this stimulation. Infants stimulated by this method have also been demonstrated to be different from unstimulated control groups in developing distinct sleep patterns earlier, showing significant increases in the amount and length of quiet sleep, and scoring higher on a general measure of motor maturation (Barnard 1973).

Oscillating waterbeds are another type of vestibutar-proprioceptive stimulation. They have been used in the belief that they imitate *in utero* stimulation and experiences, where fetuses are affected by both positional changes of the mother *and* by their own movements. By placing premature infants on this device, a similar situation is created. The frequency of the motion is typically set at 16 oscillations per minute, which approximates the frequency of the rhythm of maternal respirations found in the third trimester. Kramer and Pierpont (1976) found significantly greater weight gain and biparietal head circumference in infants who received a combination of an oscillating waterbed, recordings of a heartbeat, and a woman's voice. Burns et al. (1983) found that when an oscillating waterbed was combined with rhythmic sounds, infants showed significantly higher scores on motoric and state organization clusters derived from the Brazelton Neonatal Behavioral Assessment Scale (BNBAS). There was also a decrease in the percentage of time in quiet sleep at the time of their discharge from the hospital. Korner and her colleagues (Korner et al. 1975) found that infants with moderate or severe respiratory distress syndrome had fewer episodes of apnea when they had been stimulated on an oscillating waterbed than infants who did not receive this treatment. This type of stimulation was also found to be especially beneficial when infants were placed on the waterbeds within the first four days of postnatal life. Additionally, non-oscillating waterbeds were found to be particularly valuable for populations that were either very small; had skin problems; were recovering from abdominal surgery; or were receiving nutrition parenterally.

Bernard and Bee (1983) attempted to delineate further how variations in contingency of responding to the infant's behavior and the temporally patterning of stimuli affects behavioral outcome. They hypothesized that predictable and regular stimulation would facilitate self regulation more rapidly. This in turn should lead to a greater percentage of quiet sleep, rapid physical and neurological development, better parent-infant interaction, and improved cognitive performance. Four groups were observed which differed from one another in terms of contingency and temporal patterns of stimulation. One group, the control group, received regular NICU care. A second group, called the fixed-interval stimulation group experienced 15 minutes each hour on a rocker bed with a recording of a heartbeat (i.e., no contingency, temporally patterned). A third group, called the self-activating stimulation group experienced 15 minutes of rocking bed/heartbeat when the infant was motorically inactive for 90 seconds (i.e., contingent, but not temporally patterned). A fourth group, called the quasi-self activating stimulation group experienced 15 minutes rocking bed/heartbeat when inactive, but for only one stimulation period per hour (i.e., both contingent and temporally patterned). All three experimental groups demonstrated decreased rates of overall activity, fewer abnormal reflexes, and better orienting responses as assessed with the BNBAS. Additionally, in a follow-up study at 24 months, these infants had higher scores on the Mental Development Index scale of the Bayley Scales of Infant Development. As far as the contingency/ temporal patterning manipulation, the quasi-self activating group performed better on all assessment measures than the other two experimental groups. Barnard and Bee therefore concluded that while all variations of contingency and temporal patterns have an effect, combining both has a more powerful influence on behavior.

Tactile-kinesthetic stimulation has also proven to be an effective form of intervention. A meta-analysis conducted by Ottembacher et al. (1987) on 19 stimulation studies found that 72 percent of the infants who received some form of tactile stimulation profited from this type of intervention. As in studies employing vestibular-proprioceptive stimulation, the research methodologies and the specific effects observed in the area of tactile-kinesthetic stimulation also differed from one another. Representative of this body of work are the studies by Field and her associates (Field et al. 1986; Kuhn et al. 1991; Scafidi et al. 1986 1990). They have extensively studied the effects of body massage/stroking and passive limb manipulations on preterm infant's who were in transitional care nurseries, that is, infants who were no longer critically ill, but considered growing and stable. The basic standardized paradigm consisted of three 15-minute periods of stimulation during three consecutive hours over the course of ten days. Each session consisted of three periods. Gentle stroking of the infant's body was given during the first and third phases and passive flexion/extension movements were conducted during the second phase. In addition, within each phase, the area of the body and the amount of time it was stroked or flexed was standardized across infants. The stimulated infants averaged between 21 - 47 percent greater weight gain; spent more time awake and alert; showed better performance on the orientation, habituation, motor and state cluster items on the BNBAS; and showed better performance at a developmental assessment conducted when these infants were eight months of age. In addition, stimulated infants were discharged from the hospital five to six days sooner than non-stimulated controls. Increased levels of norepinephrine and epinephrine of stimulated babies were also found, indicating that tactile/kinesthetic stimulation may have a very specific effect on the sympathetic nervous system. They reasoned that it is quite possible that one of the mediating mechanisms for the enhanced development observed with this form of intervention is higher levels of catecholamine excretion (see Kuhn et al. 1991).

How to measure the type of the stimulation offered is a problem inherent to tactile stimulation programs. Measurement is also an obstacle to the replication of extant results and/or to the implementation of a particular intervention program for general use. Descriptions of procedures are sometimes vague, for instance, in specifying the qualitative differences between touching, manipulating, stroking, and massaging. What are the differences between "gentle touching," "extra handling," "palm stroking," and "finger stroking"? What is the difference between the "minimal handling" used in the Als et al. (1986) study and the "planned and gentle" tactile contact used by Jay (1982)? Is the distinction one of quality or quantity? Are there differences in outcomes depending on what type of tactile stimulation was administered? Scafidi et al. (1986; 1990) note that the specific effects of stimulation and the size of the same effects have varied across studies. For instance, weight gain is an inconsistent finding, with some researchers reporting differences between a group of stimulated infants and a control group, and others reporting no differences. In fact, in two related studies, this group of researchers found that treated infants exhibited a 47 percent greater weight gain per day (Field 1986; Scafidi 1986), whereas in a replication study, they found only a 21 percent weight gain per day (Scafini 1990). They hypothesized that one reason for the discrepancies might lie in the type of tactile stimulation used in each study (for example, palm versus finger stroking). It may also be the case that the exact nature of the subject population influenced the results. The developmental status of the infant may interact with the response to tactile stimulation/handling. Very small or sick infants may actually be better off if only handled for the minimum required for routine care-giving. More stable prematures are probably more likely to benefit from therapeutic touch, although whether some classes of infants might benefit more than others remains to be studied.

In summary, studies that have administered either vestibular-proprioceptive or tactile-kinesthetic stimulation have found these programs to be beneficial to the premature infant in terms of both developmental and clinical outcomes. Yet this intervention has yet to be widely adopted as a standard NICU practice. Future studies must delineate the precise effects within and between each of the stimulation programs and also explore the mechanisms responsible for the observed improved outcomes.

Visual Effects Associated with Prematurity

Of all the sensory systems, the visual system is arguably the most immature at birth, and is the least likely to be stimulated by prenatal conditions. This immaturity is found in the structures of the eye itself (lens, cornea, pupil, etc.), and in the neural circuitry extending from the retinal photo-receptors to higher brain centers serving vision. It is thus not surprising that the visual system could be particularly susceptible to environmental effects as a result of an infant being "born too soon." Many of the sensory deficits that are reported in VLBW infants are visual (e.g., Fledelius 1976; Hoyt 1980), including myopia (near-sightedness), amblyopia (a neurally-mediated loss in acuity), strabismus (eye-turn) and retinopathy of prematurity (ROP; retinal damage causes vision losses and blindness from damage in selected parts of the visual field due to abnormal proliferation of the developing retinal vasculature).

Studies of longer-term visual outcomes of NICU "graduates" are scarce (see Abramov and Haintine 1991 for a review), but Abrarnov et al. (1985; 1986) reported functional visual losses (in acuity and spatial vision and receptor functions including color vision) measurable in four- to five-year-olds who had been in NICUs.

In part because there is no good animal model for human prematurity, we really do not know why many low-birth weight infants treated in NICUs have visual problems. There are several non-mutually exclusive possibilities, including the impact of exposure to visual stimulation at an "unnatural" time for the visual system. Such adverse effects would be due to the shortening of the intrauterine growth period and/or exposure of immature retinal structure to visual stimulation of a type not normally experienced by full-term infants or adults. The nature of the light exposure of these infants, which is central to this discussion, will be discussed further below. In addition to the unnaturalness of the timing of exposure to light, other aspects of the postnatal life of preterm infants in NICUs are abnormal in ways that might affect vision.

Infants who spend time in NICUs (often weeks and even months) present a complex clinical picture. The heterogeneity of this population demands a variety of treatments depending on the nature and severity of the disorders. These include elevated body temperatures due to infection; antibiotics for sepsis; metabolic disorders such as acidosis and hyperbilirubinemia (neonatal jaundice); high $p0_2$ levels achieved in the course of therapy for respiratory distress; low vitamin E levels; bradycardia; apnea; and hypoxia. Any or all of these might interact with light to damage visual function.

Mechanisms of phototoxicity. There are several ways in which light can damage or alter a visual system, including acoustic shock, thermal damage, photochemical damage and selective adaptation/deprivation. We will ignore the first form, which is usually associated with very brief, intense flashes of light as from a pulsed laser, a circumstance that is unlikely to be experienced by infants. Thermal damage occurs when excess energy from light raises molecular kinetic energy, heating the retina faster than it can dissipate the heat, primarily through blood flow. Such damage depends on the rate at which energy is applied to the retina, rather than total dose.

Local retinal temperature must be raised by about 10˚C to cause damage (Sliney and Wolbarsht 1980); while extreme, it is possible that such damage could occur in the NICU, through repeated exposure to very bright lights such as those associated with the use of an indirect ophthalmoscope used for too long, without enough filters or at too high a power, or tungsten light sources found in some phototherapy units (see below).

Another likely source of damage in this circumstance is photochemical damage, initiated by changes in the configurations of the absorbing molecules. Such damage depends on the absorption spectrum of the specific molecule and usually depends only on the total dose. It is possible to exchange exposure duration with the rate at which photons are being delivered, so that relatively low doses extended over a long period of time may be as damaging as one large dose. Experimental evidence suggests that more energy intensive, shorter wavelengths (towards the blue end of the spectrum) have a particular ability to damage biological tissues by this route (e.g., Sperling and Harwerth 1972). The final damage mechanism depends on the patterns of neural activity or lack of activity in the visual system, with the possibility that abnormal patterns of neural activity could lead to permanent abnormal reorganization. In the last case, two situations have been demonstrated to be problems for developing visual systems. Numerous animal experiments illustrate neural changes at the retina and in higher levels of the visual system as a result of deprivation of patterned visual stimulation, sometimes for only short periods of time early in life. Visual anomalies are particularly prevalent when the deprivation is monocular (see Movshon and Van Sluyters 1981; Boothe et al. 1985). The photoreceptors in the vertebrate retina undergo a continual process of renewal, with the cones (the photoreceptors most active in the light) replenishing their photopigments during periods of darkness and rods (more active at lower light levels) doing their metabolic housekeeping during light periods (Anderson et al. 1978; Young 1978; Hollyfield et al. 1980). Loss of cyclical light/dark cycle, as occurs in many NICUs which leave lights on continuously, may interfere with these normal metabolic renewal processes.

In the animal research on phototoxicity (see Lanum 1978 for a review), a number of secondary variables affect the severity of damage, some of which may be relevant in the case of the young NICU patient. At least for primates, age is a factor; young monkeys appear to be more susceptible to damage from light than older animals (Messner et al. 1978). Elevation of body temperature, even by a small amount (1-3˚ C) increases phototoxic effects (Friedman and Kuwabara 1968), potentially a problem with neonates whose body temperatures are often locally elevated by sepsis and/or warming lamps (Fielder et al. 1986). Reductions in oxygen tension (Crockett and Lawwill 1983) can also increase damage; premature infants often require supplemental oxygen which may increase their susceptibility to light damage. As already alluded to, the presence of a diurnal cycle (light/dark) appears to limit damage, even after controlling for dose (Lanum 1978), probably because the dark cycle allows for some recovery by the visual system, a likely consideration in NICUs with 24-hour illumination.

The Visual Environment of the NICU

There is wide variability in the levels of illumination found in NICUs, and the situation is dynamic. A comprehensive survey of NICU light levels has long been needed, but still remains undone (Fulton et al. 1986); it is on the agenda for the National Resource Center mentioned above. Concern about possible adverse effects of high levels of illumination maintained with abnormal light/dark cycle has caused some hospitals to lower light levels overall and to lower lights at night. However, it is still the case in many hospitals that lights are on 24 hours a day, and are often within the range reported to cause retinal damage in experimental animals. The lights are both from ambient illumination and from devices designed to assist various medical conditions. The most common sources are radiant warmers to maintain temperature, banks of fluorescent lights for a treatment called phototherapy for hyperbilirubinemia, and lights from various ophthalmic instruments such as the indirect ophthalmoscope (used to inspect the retina).

Ambient illumination. To talk about the potentially-damaging effects of NICU lighting requires some technical information. The first issue in assessing the potential damage to the visual system of environmental light is the issue of measuring light. Light measurement is a rather arcane subject, and is easy to do incorrectly. For any wavelength, measures of light intensity are divided into two distinct systems: radiometric and photometric. In radiometry, light is treated simply as a form of energy and its radiant power (Watts) is measured. In photometry, the ability of the light to stimulate the visual system is factored in. The visual system is not equally sensitive to all wavelengths; in the visible part of the spectrum, sensitivity peaks in the region normally described as yellow and green and declines for shorter wavelengths (towards blue and the ultraviolet) and longer wavelengths (towards red and the infrared). In photometry, the power of light at each wavelength is weighted by a standard sensitivity curve, derived from a small group of adult observers (the CIE photopic luminous efficiency function; see Wyszecki and Stiles 1982). The most common metric unit of illuminance (a photometric measure of light falling on a surface) is "lux."

Unfortunately, most studies of visual phototoxicity state their intensities in photometric terms. Because these are based on a standard version of an adult human photopic function, the measurements probably do not apply to all ages or all species. A particular problem is that photometric measurements will grossly underestimate the power at the two ends of the visible spectrum, where the photometric weights are small; in particular, the especially hazardous short wave-lengths are underestimated in photometric measurements. Another range of problems concerns whether the most appropriate measurements are for light failing on the eye or for light actually entering the eye and falling on the retina, which is probably most relevant for many forms of light damage. Intensity of light actually reaching the retina will be affected by a number of anatomical factors (eyeball length, the transmission of the ocular media, pupil size, transmission of the eyelid, etc.), only some of which have been determined for VLBW infants.

These measurement difficulties not withstanding, most studies have reported high levels of illumination in NICUs. To give some point of comparison, illumination in an average living room at night will be 100 - 200 lux, while out of doors, the diffuse illumination on a bright but cloudy day can be as high as 10,000 lux. The recommended level for a business office has risen from around 200 lux in the 1950s to more than 500 lux today (despite medical concern that even for adults, more light may not necessarily be better; Cogan 1968).

Table 1 summarizes some of the published data on NICU light levels. Generally levels are high: the more recent values across NICUs in the United States (Hamer et al. 1984; Glass et al. 1985; Landry et al. 1985) and England (Moseley and Fielder 1988; Robinson et al. 1990) have average illuminance during the day of somewhere between 400 and 1000 lux, which may reduce at night to about 100-400 lux. However, there is a great deal of variability both across (see Table 1) and within NICUs (McCloud and Stern 1972). The one study that attempted radiometric measures at different wavelengths in NICUs (Landry et al. 1985) reported data which implies that photometric measurements may be underestimating total dosage by as much as 30 percent, particularly at short wavelengths which have been demonstrated to cause damage in animal studies.

Table 1. NICU illumination

Ambient illuminance measured at level of infant's eyes. Sources: usually white fluorescent lights, but often with some added daylight. Measurements converted to lux, where necessary.

Mean	Range	Conditions	Study
970			Giunta & Rath (1969)
5400	540 – 26 900	Day, sunny[1]	MacLeod & Stern (1972)
1000	750 – 1500	Day, overcast	(same unit)
190	160 – 210	Night	
680	320 – 900		Lawson et al. (1977)
170			(2 different units)
530	340 – 1400		Gottfried et al. (1981)
508	240 – 1400		(2 different units)
1300	30 – 12 000	Day, sunny[1]	Hamer et al. (1984)
50	10 – 100	Night	(same unit)
750[2]	590 – 1100		Glass et al. (1985)
970	380 – 2000		(2 different units)
732[3]	258 – 1485		Landry et al. (1985) (8 different units)
417[3]	236 – 752	Day, sunny[1]	Robinson et al. (1990)
524[3]	246 – 905	Day, rainy	(7 different units)
348[3]	192 – 690	Night	

Notes: [1]Various times of day; includes areas receiving direct sunlight.
[2]Median for infants <1000 g at birth. No shielding.
[3]Mean and range of mean values from individual NICUs.

It is clear that there is no "typical" light dose in an NICU. As Figure 1 (Hamer et al. 1984) shows, within a single nursery, there are wide variations in illumination depending on time of day and outside conditions (if there are outside windows). However, in many cases, the light levels are in a range that have been demonstrated to cause damage in animals. Within a given unit, infants are often moved to different locations, and so may have different levels of exposure depending on how close they are to windows and other sources of light, for instance, the incubators of neighboring infants who may be exposed to radiant warming lights or banks of phototherapy lights (see below; also Robinson et al. 1990).

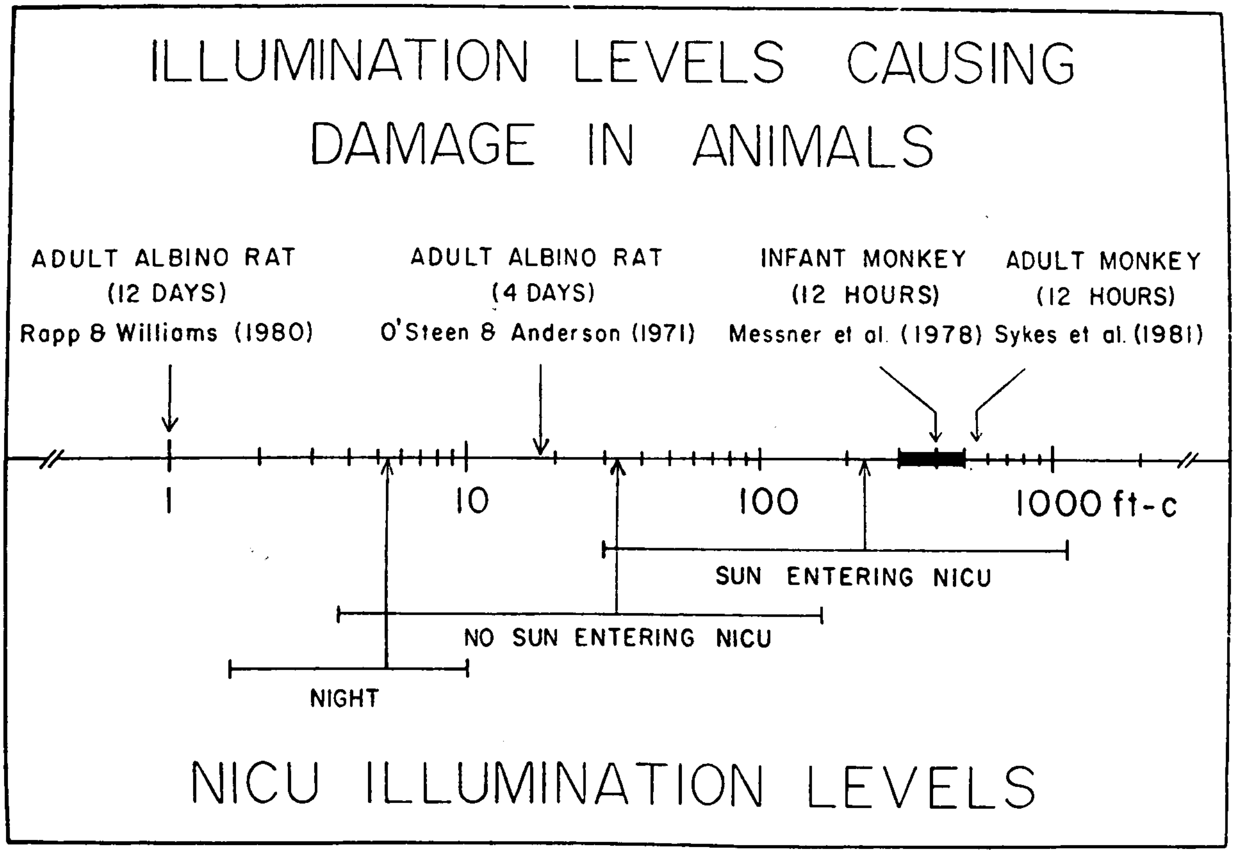

Figure 1. Levels of illumination in NICUs vary across the day, and are in ranges associated with visual system damage in animal studies. This figure illustrates this variation for one NICU. Units on the logarithmic axis are in foot candles (multiply ft.cd by 10.76 to convert to lux). The horizontal bars associated with each upward pointing arrow indicate the range of illuminations measured in each case. The thickened portion of the axis represents measured light levels in typical phototherapy units. For the animal studies, the number in parentheses represents the shortest duration of exposure found to cause damage for each study's level of illumination (downward arrows). Figure reprinted from Hamer et al. (1984) with permission of Association for Research in Vision and Ophthalmology.

In most NICUs, ambient illumination is by means of ceiling fluorescent fixtures, which will serve as an extended source, thus reducing retinal illuminance. If such units are covered with plastic diffusers, they will also generally have low UV transmission, but newer units that are fitted with open waffle-like plastic grids do not attenuate UV. (Long-term UV exposure is associated with the development of cataracts, so is probably more of a problem for staff than for infants.) Not all hospitals use ceiling fluorescents. One large NICU we observed used intense tungsten lights recessed into the ceiling without diffusers; for upright adults, ambient illumination was pleasingly diffuse, but an infant on its back would have a sharply focused image of light on the retina. Infants in incubators and on ventilation or other respiratory assist are typically maintained on their backs, without much ability to change body position. The head is generally turned to one side so that the two eyes are not equally illuminated. The eye closer to the mattress is more likely to be closed (Moseley, et al. 1988), and on average a third less light reaches it (Robinson et al. 1990). One might then expect that phototoxic damage might be asymmetrical for the two eyes. This prediction is consistent with the damage reported by Abramov et al. (1985; 1986).

There are other aspects of the premature infant that influence the total light exposure. The structures in the infant's eyeball are more transparent, particularly, to short wavelengths (Weale 1982). Eyelids of newborns are also more transparent than those of adults (Robinson et al. 1991), but even so, they are especially effective filters for wavelengths most likely to be hazardous. This effect could serve to protect the retina, although for prolonged exposures, even small quantities of light may be important for a photochemical process that depends only on total dose. Also, somewhat surprisingly, infants do not always keep their eyelids closed, even in brightly lit nurseries. A careful 24 hour monitoring of eyelid opening reported a curvilinear trend with age in amount of eyelid opening (Robinson et al. 1989). Infants less than 24 weeks' gestation kept their eyelids closed about 55 percent of the time. This rose to over 90 percent at 24 weeks, but declined again to around 60 percent closure time after 30 weeks. Infants in brighter and continually lit NICUs spent more time with eyelids closed than in units with less total illumination (Robinson et al. 1989; Lawson and Turkewitz 1986). While this may be protective, Lawson and Turkewitz also reported that in brighter units, there was an apparent decoupling of eye opening and variation in lighting across the day, implying that infants were not learning to relate their behaviors to environmental characteristics appropriately.

The characteristics of environmental light have been shown to interfere with the development of sleep/wake cycles (Glass and Sostek 1984), possibly because constant bright lights are stressful.

Infants in intermediate care nurseries showed faster weight gains, better feeding, and improved sleep patterns in a nursery in which light, noise and handling were reduced during the night (Fajardo et at. 1990; Mann et al. 1986). Such data point to the importance of normal diurnal rhythms in a number of modalities for proper development (Mirmiran and Kok 1991; Glotzbach et al. 1991). The problems may last longer than the hospital stay. Mann et al. (1986), for example, suggest that NICUs are not good "training" for developing appropriate sleep patterns after leaving the hospital. Parents often report poor sleep patterns after discharge from the NICU, possibly because of infants' exposure there to nearly constant light and noise. They report anecdotally that some parents find the only way to get their former-NICU infant to sleep at night is to mimic the environment of the hospital, namely to turn on the bedroom lights and play music. Sleep problems after discharge may be among the milder consequences of a neonatal intensive care experience, for as Gottfried and Hodgeman (1984) state, the NICU may have become too intense.

Even more striking are data on pupillary response to light at different ages. When the eyelids are open, the pupillary reflex (constriction of the pupil caused by illumination of one or both eyes) become important because retinal illumination is proportional to pupil area. Even in adults, some of the initial constriction in response to light is transient and followed by a dilation (relaxation) to a steady-state size associated with a given level of light intensity (Lowenstein and Loewenfeld 1962). In monkeys, this relaxation occurs even at very high intensities and is actually most rapid for intensities producing visible retinal lesions, suggesting some sort of "overload" of the pupillary system (Clarke and Behrendt 1972). The pupillary light reflex seems to be present in most infants by 31-34 weeks' gestation (Robinson 1966; Isenberg et al. 1989; Isenberg et al. 1990; Robinson and Fielder 1990). However, the retina responds to illumination well before 26 weeks. Under the illumination of a typical NICU (around 600 lux), the average area of a preterm infant's pupil is 35 percent larger than it will be at 35 weeks, by which time nearly all infants demonstrate a pupillary response (Robinson and Fielder 1990). Thus, the smallest and youngest infants, those most likely to have the longest stays in the NICU, may not be as well protected for light exposure than older infants or adults would be.

Phototherapy. Premature infants often have a condition known as neonatal hyperbilirubinemia, a type of physiological jaundice. The level of bilirubin in the blood of many prematures is much higher than in normals. High levels of bilirubin are neurotoxic to the developing nervous system. When the level become too high, the capacity of the blood to bind the bilirubin is exceeded and significant amounts can enter the central nervous system leading to brain damage and even death (Behrman et al. 1974; Scheidt et al. 1977). It was accidentally noticed some years ago (Cremer et al. 1958) that infants positioned near a window had less jaundice than those whose incubators were in other parts of the room. Transcutaneous exposure of bilirubin to short wavelength light permanently changes its chemical structure into a form that is not neurotoxic. Since that discovery, phototherapy for hyperbilirubinemia has become widely accepted around the world. In the most widely used forms, the infant, wearing only a diaper, is placed in an isolette above which are positioned one or more banks of fluorescent lamps. Even though it is only short wavelengths that are effective in reducing serum bitirubin (McDonagh 1985), medical staff often object that the blue lights interfere with their ability to gauge cyanosis by skin color, and so in most cases, cool white tubes are used, despite the extra light exposure that this entails.

Light intensities inside phototherapy units greatly exceed NICU ambient levels. We estimate them to be at least 10,000 lux, and even higher in some of the newer units with tungsten sources. Because much of the energy is at short wavelengths, we should be particularly cautious about measuring only illuminances - there may be sufficient intensity in the short wavelengths for photo-chemical damage to the retina. This is particularly true in the units that use only blue fluorescent lights.

Infants receiving phototherapy typically have their eyes covered with protective shields. When properly fitted, the commercially available occluders are quite effective in blocking light, especially when coupled with closed eyelids (Chin et al.

1987). However, mere use of occluders does not necessarily protect the retina. Staff sometimes use makeshift occluders made from, for example, stacks of gauze pads, which may not attenuate sufficiently, and even the best occluders may not stay in place well. In a minute-by-minute study of infants in an NICU, it was observed that for those receiving phototherapy, the occluders slipped and no longer fully covered the eyes more than 50 percent of the time (Robinson et al. 1989). This observation is easy to confirm anecdotally in conversation with NICU staff. Often the slippage exposed only one eye, another factor that predicts the possibility of monocular damage.

There are some animal data on exposure to phototherapy units. Piglets and infant macaque monkeys raised in human phototherapy units without occluders but with the ability to close their eyes suffered considerable histological damage to their retinas (Sisson et al. 1970; Messner et al. 1978). In the latter study, newborn macaques were exposed to illuminance of about 4300 lux for periods from 12 hours to four days. Even after 12 hours, there was some immediate damage to photoreceptors. Ten months later, all exposed eyes showed some recovery, but many eyes were histologically abnormal, particularly if exposed for three or four days. Thus, there is reason to be concerned for infants receiving phototherapy. What is less obvious is that there might be even greater risk for infants in NICUs who are the neighbors of infants receiving phototherapy. It is not generally the practice to shield the eyes of infants next to those being photo-treated, yet there can be a significant increase in total light exposure for such patients, as our data on control infants demonstrates (Abramov et al. 1985 1986).

Retinopathy of prematurity. It is also likely that visual effects of prematurity interact with many of the medical problems of the early postnatal period. This population often contains very sick infants, although we have little information about the specific visual effects of their illnesses. A condition of special interest, because it is specifi- cally retinal, is ROP, formerly called “retrolental fibroplasia.” With increased survival rate of VLBW infants, there has been a concomitant increase in ROP. In the most extreme cases, ROP results in retinal detachment and blindness (e.g., Flynn 1987). It was once thought that ROP was caused by the administration of high doses of oxygen, but it now seems that ROP is more associated with prematurity itself than with oxygen *per se.* The current view links ROP to incomplete vascularization of the retina before term, which in the premature infant continues postnatally but abnormally, leading to fragile capillaries which rupture and hemorrhage. In some but not all cases, ROP damage regresses. Because of the severity of damage when regression does not occur, infants are often treated with cryotherapy, which has proven effective in pre- serving visual function (Cryotherapy for Retinopathy of Prematurity Group 1990).

There are somewhat controversial data that excessive light exposure may exacerbate ROP, possibly by increasing the demand for oxygen by increasing retinal activity, thus encouraging proliferation of blood vessels. It has been noted (Glass et al. 1985), that the increase in incidence of ROP is also correlated with a 5 - 10 fold increase in intensities of light in NICUs over the last 30 years. To test the possibility that high light levels in the NICUs exacerbate ROP, sheets of light-filtering material were placed over some incubators, reducing illuminance by about half (Glass et al. 1985). Under-1000-gram infants so protected had a significantly lower incidence of ROP than unprotected VLBW infants. The study has been criticized methodologically (e.g., Stopie 1986) for running the experimental and control groups sequentially rather than concurrently. Avery and Glass (1986) have acknowledged that the control group in Glass et al. (1985) may have been inadequate. A similar effect has been reported by Hommura et al. (1988), but not by Ackerman et al. (1989). Given the potential importance of this finding, the study clearly awaits consistent replication.

If it is true that light increases the incidence of ROP and that in the average NICU light intensities are already very close to the threshold for doing so, the procedures for diagnosing and monitoring ROP may themselves add to the problem. All preterms have retinal examinations, almost always with an indirect ophthalmoscope. If ROP is diagnosed, it must be carefully followed, which means regular examinations of the fundus (the back of the eye). The diagnostic instrument is itself a very intense source (Ts'o et al. 1972). A 15-minute exposure of monkeys to an indirect ophthalmoscope produces evidence of retinal damage (Friedman and Kuwabara 1968). Guidelines for use of such instruments with adult patients (e.g., Kirkness 1986) advise that the examination should not exceed 23 seconds at highest power and 80 seconds at the lowest. Dawson and Herron (1970) estimated at that a two minute exposure at maximum power is equivalent to exposure at 20,000 lux for three hours. Infant examinations typically take about three to five minutes, and these examinations are likely to be repeated a number of times, although practitioners do not always use full power. There are also informal reports that protective filters are sometimes omitted for a "clearer" look at the fundus, and that care is not always given to using the lowest possible intensities during the examination. Additionally, the procedure requires dilation of the pupils which takes time to wear off, thus increasing the retina to appreciably more of the ambient nursery illumination. That indirect ophthalmoscopic procedures themselves may be stressful to neonates is supported by a report by Hermansen and Sullivan (1985) who observed feeding intolerance after indirect ophthalmoscopy in newborns.

Suggestions for Change in NICU Environment

Concerted efforts by neonatologists and perinatologists have strikingly reduced neonatal mortality over the last three decades. The improved survival rate of VLBW infants is a credit to the medical, scientific and engineering personnel who have created a highly specialized NICU environment. In part this environment has unwittingly evolved to serve those concerned with the survival of the sick, VLBW infant (physicians, nurses, technicians and parents). Yet by its very characteristics (crisis atmosphere, bustle, noise and high illumination) it may be causing unintended damage to the patients, damage that may be avoidable. As Glass (in press) points out, the aversive conditions found in the NICU would not be conducive to the development of even the healthiest full-term. Glass argues that more research is not needed to determine whether excessive handling, noise and lights should be reduced. Rather than devoting our efforts to showing that the NICU does no harm, we should attempt to establish limits for the safety of various features of the NICU environment.

While the methodologies, paradigms, and effects reported in infant stimulation studies are diverse, we can unequivocally conclude from the positive patterns of outcome measures that early stimulation of preterm infants is beneficial and should be common practice in NICUs. There are however some general considerations that need to be taken into account and also some specific areas that need to be investigated to potentially optimize the effects of these types of programs. Intervention programs need to be closely tied to not only the severity of the premature infant's immediate medical condition, but also to the developmental status of the individual infant. Support for this approach can be found in a study conducted by Als and her associates (Als et al. 1986), on a group of premature infants who were at risk for respiratory complications. After assessing each infant on several behavioral and physiological measures, they, along with the assistance of an infant's primary nurse, made modifications in the care of the infants. They found that infants benefited both medically and developmentally from this individualized care; that is, the time they spent on a respirator was briefer and their feeding patterns normalized sooner. In following these infants longitudinally, they found that these babies had better regulation scores at one-month post-estimated dates of confinement (post-EDC) and had significantly better scores on the Bayley Scales of Infant Development at three, six, and nine months post-EDC.

Korner (1987) asserted that whatever type of stimulation program is used, it should exploit the sensory systems that are already functioning. Again, this is important because systems that have already matured set the stage for and influence development in the less mature systems. Further research is needed to determine the optimal levels, amounts, and duration required to affect positive outcomes. Also importantly, researchers need to explore and delineate the mechanisms that are responsible for the observed positive outcomes in the various populations studied. The goal of future stimulation programs should be to strike a balance between standardizing some of the procedures in their investigations and designing individualized programs based on an infant's status.

With respect to light, the bulk of the animal literature, and scattered research on hazards of visible light in infants support the argument that as long as it is consistent with overall good medical care, we should modify the lighting in NICUs. As a first step, we need better, radiometric measurements in relevant wave bands of current levels of light in NICUs (cf. Fulton et al. 1986), preparatory to establishing safety standards for such environments. At present, light is one of the few environmental factors not monitored in NICUs. Efforts should be continued to develop simple and effective light measurement devices to measure both light sources and dosages delivered at the infant. We need better information about light exposure near and in the vicinity of warming lights and phototherapy units, near windows at different times of day, and from ambient artificial illumination at different times of day. We also should survey the various instruments used for examination. Light levels from such instruments should be kept as low as possible until safe levels have been determined. Duration and cyclicity of lighting also needs to be specified.

Even in the absence of such a survey of current practice, the design of lighting in NICUs should be made much more flexible. It is necessary, for example, to have sufficient light on an individual infant to detect subtle cyanosis, changes in skin color that communicate respiratory problems. However, it is not necessary to light up the entire nursery to monitor infants at risk for such problems. Some medical procedures undoubtedly require more than safe-ambient levels of light from time to time. Yet if such lighting can be regulated and individually-controlled at each incubator, this extra light can be applied only when needed, and at the same time, spare neighboring infants from unnecessarily high light levels. Specific procedures involving very high intensity instruments, such as indirect ophthalmoscopy used to evaluate ROP status should be practiced so as to use the minimum light needed, with appropriate filters in place.

Infants receiving treatments such as phototherapy could be either segregated or efforts made to shield the neighbors of infants receiving such treatment from extra, high light dosages. Attention should be paid to designing better fitting eye shields for tiny infants. General room illumination should be monitored routinely, with some attempt to keep the total light levels relatively constant at some reasonable level (compensating for changes in outside illumination on a sunny versus a rainy day, for example, in units with outside windows). Ambient lighting could be automatically or manually cycled to lower levels during the night. Many of these changes could be imposed without undue expenditure in existing NICUs, but especially should be part of the plans for new construction or renovation of existing NICUs, in consultation with lighting engineers and visual professionals.

Medical necessity prevents us from being able to duplicate the uterine environment for the premature infant. In any event, it is far from clear that this would be optimal for the preterm infant's development after its early introduction to the world. There is a need for a certain amount of patterned stimulation for proper post-natal development once the infant is born. Yet with moderate efforts at revision of procedures, equipment and setting, potentially harmful aspects of the NICU could be eliminated or significantly improved.

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