lid, threaded into the retention plate, and passed through the cornea into the globe. The result of this technique has been remarkable, since these patients, who have been blind for years without any hope of recovering sight, have been able to read and have useful vision. The behavior of skin surrounding a plastic implant is quite different from that of corneal tissue surrounding the same implant. Even though follow-up of this group of patients is rather short, the absence of extrusions makes this unusual technique most promising.

Certainly, this type of clinical research which, by necessity, is limited to a few medical centers, has shown dramatic results in many cases; in others, the results have been discouraging. It is probably the most expensive type of experimental and clinical investigation; however, restoration of sight to any hopelessly blind person, even for a few months, is worth the expense and frustration of repeated surgery.

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Phototherapy and retinal damage

In recent years, it has become common in many neonatal intensive-care units to use phototherapy to lower the bilirubin level in low-birth-weight infants who suffer from hyperbilirubinemia. Typically, phototherapy units consist of a bank of eight to ten fluorescent tubes placed over the incubator, 40 to 100 cm. from the infant, producing 300 to 500 ft.-c. of illumination. Duration of exposure to the lights can range from a few hours to 6 or more days of continuous or intermittent (e.g., 6 hours on, 2 hours off) exposure.

Since phototherapy is a relatively new procedure, especially in the United States, there is concern about possible deleterious side-effects of the treatment. One hazard which has concerned investigators is the possibility of retinal damage to infants exposed to phototherapy continuously for several days. The basis for concern about retinal damage lies in several studies in the animal literature which have shown structural and functional changes in the retinal photoreceptors following extended periods of exposure to illumination, even at levels considerably lower than those used in phototherapy.

Both light microscopy and electron microscopy have been used to assess structural changes in the retinas of exposed animals. Light microscopy reveals that the retinas of rats exposed to low-level (18 ft.-c.) continuous illumination for as little as 4 days exhibit fragmenting or absent terminal segments of receptor cells and pyknotic receptor cell nuclei.1 (A pyknotic nucleus is one which is shrunken and contains chromatin condensed into a solid structureless mass.) Longer exposure durations (14 to 30 days) produce further fragmentation of the receptor cells and, even-
ually, complete destruction and disappearance of both the inner and outer photoreceptor segments. If the animal’s body temperature is elevated, e.g., through the use of tungsten rather than fluorescent lights, or the illuminance of the lights is increased, as during phototherapy, the time course of destruction will be accelerated considerably. In addition, elevated body temperature will result in extensive damage to the pigment epithelium. Electron microscopy has revealed more detail concerning structural changes in the photoreceptor layer subsequent to light exposure in the rat. Initially, after short exposure durations, there appears a loss of the regularity of the lamellar arrangement of the photoreceptor (rod) outer segment, with microvilli of the pigment epithelium extending between the damaged outer segments. Following longer exposure, the outer segments are reduced to large, pear-shaped structures filled with a tubular, rather than a lamellar, arrangement of membranes, and they become separated from the receptor inner segments. Finally, if exposure is continued, both the inner and outer segments disappear and microvilli from the retinal Müller cells grow to join with microvilli from the basement membrane of the pigment epithelium. There is evidence that some morphological and physiological recovery can occur with relatively short exposure durations, but once destruction of the photoreceptors and bonding of the microvilli occur, damage is irreversible.

Changes in the retina in intact animals have been investigated ophthalmoscopically and through electroretinographic measurement of dark adaptation. With the ophthalmoscope, it is difficult or impossible to detect damage due to light exposure, even when later histological examination reveals extensive photoreceptor damage. However, the electroretinogram (ERG) indicates a slower rate of dark adaptation and a reduced ERG amplitude for continuously exposed rats as compared with rats maintained under the normal cyclic pattern of light exposure. Furthermore, the a-wave portion of the ERG, which originates in the photoreceptor layer, is abolished, thus changing the over-all shape of the ERG. The ERG has also been used to monitor recovery following light exposure. When damage is moderate, i.e., the photoreceptors have not been destroyed, the length of time required for the ERG to regain its normal shape and magnitude depends upon the duration of exposure. However, when photoreceptor cells have degenerated and Müller cells have bonded with the basement membrane of the pigment epithelium, the ERG never regains its normal shape. Estimates of the minimum light exposure required to produce irreversible damage in rats range from 2 hours' exposure to fluorescent light of approximately 150 ft.-c. to exposure for 1 week to fluorescent lamps of 750 to 1,000 ft.-c.

In light of the clear evidence in the animal literature that continuous exposure to relatively low levels of illumination can produce extensive retinal damage, physicians have become concerned that phototherapy might be harmful to infants' eyes. Their concern is emphasized by the finding that piglets, whose retinas are similar to the retinas of newborn infants, exhibited extensive retinal damage after as little as 12 hours of exposure to lights in a commercially produced infant phototherapy unit. Furthermore, the short wavelengths of light which are most effective in producing retinal damage are also the wavelengths that are the most efficient in lowering bilirubin levels. Therefore, in recent years considerable emphasis has been placed on protecting the eyes during phototherapy. Follow-up testing of ocular functioning has also been recommended.

To date, only three studies have reported follow-up testing of the eyes of infants exposed to phototherapy shortly after birth. Infants in all three studies had been afforded eye protection either with gauze bandages or with opaque masks. Two of the studies examined exposed in-
fants within the first 2 years of life. Hodgman and Teberg found that light-treated infants examined at 31 to 68 weeks of age gave normal responses to "gross visual... tests." Kalina and Forrest examined 30 5-month-old infants ophthalmoscopically and found no evidence of damage subsequent to phototherapy at birth. It must be remembered, however, that ophthalmoscopic examination of piglets with extensive receptor damage revealed no evidence of abnormality. In the third follow-up study, a more specific examination of photoreceptor (rod) function was carried out; the ERG was used to follow the course of dark adaptation in 4-year-old children who had been exposed to phototherapy at birth. The results of this study gave no evidence for differences in rate of dark adaptation or in absolute ERG amplitude between light-exposed and control subjects. In addition, all children in the light-treated group had a visual acuity of 20/30 or better, indicating a lack of extensive cone damage. While this study strongly suggests that infants whose eyes are patched during phototherapy do not receive permanent large-scale retinal damage, it is, nonetheless, a negative result. As such, it does not rule out the possibility that damage might occur with different infants under slightly different conditions, e.g., in the infant whose eye patch slips off, or in the infant in the incubator adjacent to the infant receiving phototherapy. Furthermore, since the intensity values of phototherapy lights are not reported in terms of retinal illuminance, it is impossible to know exactly what proportion of the retina was exposed to continuous illumination. Therefore, it is possible that damage might be localized on the retinas of phototherapy-treated infants and not be revealed in ERG tests, since the ERG is a mass response of the whole retina.

Finally, three other potential ocular hazards related to light therapy in newborn infants must be pointed out. First, there is a danger of excessive exposure to ultraviolet radiation from the phototherapy lights. Both the Food and Drug Administration and the Committee on Phototherapy in the Newborn Infant have recommended that some form of ultraviolet-absorbing material be placed between the infant and the bulbs, both to protect the infant from ultraviolet radiation and to prevent injury resulting from bulb breakage.

A second potential hazard is that of damage to the eyes of infants left for days or weeks under the bright room lights of the nursery for 24 hours a day. While the output of the room lights is less than that of the phototherapy units, the animal studies have indicated that continuous exposure to even very low levels of illumination can result in extensive damage. Therefore, establishment of cyclical eye patching or cyclical exposure to lights should be considered for infants who will remain for extended periods of time in the hospital nursery. Follow-up testing of infants exposed to continuous light would also be advisable. Only one such follow-up has been reported to date. The study used ERG recording to assess rod function in 4-year-old children who were exposed as infants to 6 days of continuous room lights in the premature nursery. No differences were found in rates of dark adaptation or ERG amplitudes between the light-exposed group and a group of 4-year-old children born in the same hospital but kept in a dimly illuminated nursery. Obviously, further follow-up testing is required to assess the possibility of localized damage and to assess photoreceptor function in infants exposed to even longer periods of continuous illumination in the nursery.

Finally, there is a potential hazard which is related not to the excess of illumination provided by phototherapy lamps, but rather to the infant's lack of exposure to an illuminated world while its eyes are patched during phototherapy. That is, both animal and human studies have suggested that there is a critical period early in life during which a lack of visual stimulation...
may hinder the development of the visual system. If this critical period were to occur during eye patching for phototherapy, abnormal visual development might occur. Fortunately, however, the critical period seems to occur well after the first week of life, which is the time when phototherapy is usually given to infants. Nonetheless, it would be advisable to remove the infant from phototherapy occasionally, e.g., when it is being fed, and allow it to view the visual world around it. Alternatively, a set of dark filters could be alternated with the opaque eye patches to produce a day/night cycle in the visual stimulation received by the infant.

In summary, studies of rats and piglets have indicated that continuous exposure to levels of illumination similar to those used to treat hyperbilirubinemia in newborn infants can result in severe photoreceptor damage. Furthermore, severe damage to the photoreceptors of animals has been found subsequent to several weeks of exposure to room lights 24 hours a day. These results indicate that care must be taken to protect both the eyes of infants exposed to phototherapy and the eyes of infants who are lying adjacent to a phototherapy unit or who must remain for a number of days under nursery lights 24 hours a day. In addition to eye protection, the possibility of intermittent exposure to the phototherapy units (e.g., 6 hours on, 2 hours off), which has been used in several hospitals, should be considered.

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REFERENCES