

Phototherapy — Traditional and Nontraditional

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An observation by an English nurse in 1956 led to the discovery that visible light could lower serum bilirubin levels in newborn infants, and subsequent research showed how photons of light energy are absorbed by the bilirubin molecule converting it into isomers that are readily excreted by the liver and the kidney. Understanding the dose–response effect and other factors that influence the way light works to lower bilirubin levels has led to the effective use of phototherapy and has eliminated the need for exchange transfusion in almost all jaundiced infants.

Journal of Perinatology 2001; 21:S93–S97.

INTRODUCTION

Exposure of newborn infants to sunlight represents the first documented use of phototherapy in the medical literature.¹ We might never have known about the benefits of phototherapy were it not for an astute observation in 1956 by Sister J. Ward, the nurse in charge of the Premature Baby Unit at the Rochford General Hospital in Essex, England.² She recognized that when jaundiced infants were exposed to the sun they became less yellow and this observation led a pediatric resident (or registrar), R. J. Cremer to conduct an experiment. He placed 13 jaundiced preterm infants, naked, in direct sunlight alternating with shade, for 15 to 20 minutes. Their initial serum bilirubin levels ranged from 10 to 25 mg/dl and, after cumulative periods of exposure for 2 to 4 hours, the average decrease in serum bilirubin level was 3.9 ± 2.93 mg/dl (range –2.0 to 12.0 mg/dl). Cremer et al.¹ then built a phototherapy apparatus with eight 24-in. blue fluorescent tubes and exposed nine preterm infants to the lights. The bilirubin level fell in all and phototherapy was born.

The Cremer et al. paper was published in 1958 and was followed by reports of no less than 19 additional studies in South America, Italy, and France between 1960 and 1967.³ Phototherapy finally arrived in the United States when Lucey et al.³ published their findings in 1968. Why did it take 10 years for this safe and effective therapy to come to the New World? Perhaps because it was quite

inexpensive, extremely simple, and almost too good to be true or, more likely, because with the exception of the Cremer et al. paper, none of the studies were published in English-language journals. I was a pediatric resident in the early 1960s at a hospital that was then delivering almost 15,000 babies per year. Hundreds of exchange transfusions were done annually yet none of my mentors ever mentioned phototherapy. (See Figures 1 and 2 for the impact phototherapy might have had.) Lucey et al.³ exposed premature infants to a light chamber consisting of ten 20-W daylight bulbs and showed that they could effectively prevent hyperbilirubinemia. Subsequently, Lucey⁴ combined his data with two other studies of prophylactic phototherapy in low birth weight newborns. In the control infants, 44% developed serum bilirubin levels >12 mg/dl compared with 8% in those treated with light. Phototherapy had arrived.

These studies and the many that followed in the ensuing three decades have confirmed the efficacy and safety of phototherapy in infants of all birth weights. More than 50 articles have been published describing controlled trials of the use of phototherapy in the newborn.⁵ Cremer et al.¹ cautiously suggested that although it was unlikely that phototherapy would “prove a substitute for

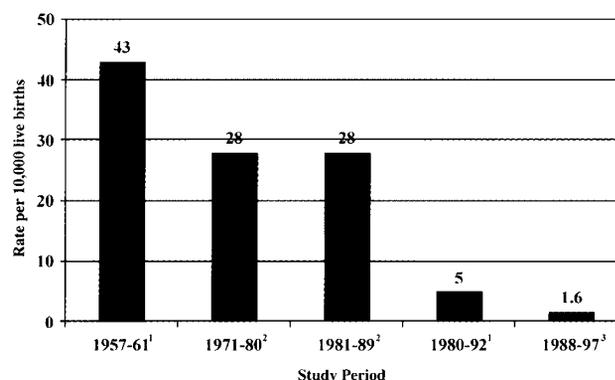


Figure 1. Number of infants in different populations who received exchange transfusions between 1957 and 1997. **1.** In Athens, Greece exchange transfusions were performed on 134 infants of 30,830 live births (birth weight ≥ 2500 g) between 1957 and 1961 and on 91 infants of 180,594 live births between 1980 and 1992 (from Valaes et al.⁸). **2.** At the University of Melbourne, Melbourne, Australia, between 1971 and 1980, exchange transfusions were performed in 114 infants of 41,057 live births and between 1981 and 1989, in 134 infants of 47,080 live births (all birth weights) (from Guarani et al.⁷). **3.** Between 1988 and 1997 exchange transfusions were performed in eight infants of 55,128 live births at William Beaumont Hospital, Royal Oak, MI (all birth weights) (from Maisels⁶).

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Journal of Perinatology 2001; 21:S93–S97

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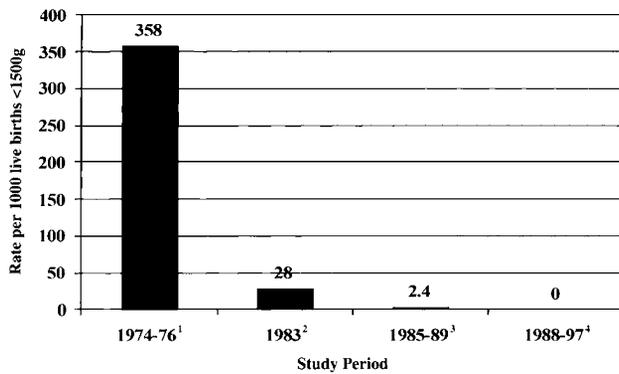


Figure 2. Number of infants in different populations with birth weight < 1500 g who received exchange transfusions between 1974 and 1997. **1.** A total of 215 newborns < 1500 g in the NICHD Cooperative Phototherapy Trial were assigned to the control group (did not receive phototherapy). Seventy-seven of 215 infants (35.8%) received a total of 161 exchange transfusions. In the phototherapy group, 17 of 196 (8.7%) infants received exchange transfusions. These data are included to illustrate the frequency of exchange transfusion before the introduction of phototherapy (from Keenan et al.⁹). **2.** Of a total of 1338 live births < 1500 g in the Netherlands, 1983, 37 infants (2.8%) required at least one exchange transfusion (from van de Bor, et al.¹⁰). **3.** Of 833 live births (500 to 1500 g) in a 17-county region in Northwest Carolina, two infants required an exchange transfusion (0.24%) (from O’Shea et al.¹¹). **4.** No exchange transfusions were performed in 1213 live births < 1500 g at the William Beaumont Hospital, Royal Oak, MI between 1988 and 1997 (from Maisels⁶).

exchange transfusion in the erythroblastotic infant with active hemolysis . . . the method may be turned to clinical advantage in controlling the level of serum bilirubin in cases of jaundice of prematurity.” It would be no exaggeration to say that phototherapy has succeeded beyond their wildest dreams. Just how effective phototherapy has been can be gauged by the dramatic impact that it has had on the number of exchange transfusions performed for hyperbilirubinemia. Although Rh immune globulin (RhoGam, WinRho) has dramatically reduced the risk of erythroblastosis fetalis, the use of phototherapy for all causes of hyperbilirubinemia has rendered exchange transfusion almost extinct.⁶ Figures 1 and 2 show the remarkable decline in the number of infants who received exchange transfusions at different institutions from the 1970s to the 1990s.⁶⁻⁸ Newer phototherapy techniques (see later) and pharmacologic interventions are likely to reduce these numbers even further. Under the circumstances, it is no longer possible to train a pediatric resident to perform an exchange transfusion and it will soon be difficult even for neonatal fellows to receive appropriate training in this technique. With decreasing experience, the likelihood of complications with each procedure will surely increase.

THE NEW PHOTOTHERAPY

Until recently, most of the phototherapy used in full-term infants and almost all used in low birth weight infants has been prophylactic

— to prevent the serum bilirubin level from reaching dangerous levels — and a relatively low dose of phototherapy is usually sufficient for this purpose. Although phototherapy is still used prophylactically in the neonatal intensive care unit and the well-baby nursery, most full-term infants in the United States who receive phototherapy today are those who have left the hospital and are readmitted for the treatment of serum bilirubin levels of 20 mg/dl or higher. These infants need a therapeutic, rather than a prophylactic, dose of phototherapy, the objective being to get the bilirubin down as soon as possible. Although most of the information needed to deliver this intensive form of phototherapy has been available for many years, most full-term infants still receive phototherapy in a dose that is well below the optimum therapeutic range.¹²

This “new phototherapy” has arisen out of the recognition that phototherapy requires the same sort of approach that is applied to drug therapy — an understanding both of the dose–response effect and the influence of other factors on the way light works to lower the serum bilirubin level (just as absorption and volume of distribution affect the efficacy of a drug). When a phototherapy light is turned on, the infant receives an infusion of discreet photons of energy similar to the molecules of a drug in a medication. These photons are absorbed by the bilirubin molecules in the skin producing a therapeutic effect, just as binding of drug molecules to a receptor has the desired effect.

Light Spectrum

The spectrum of light delivered by a phototherapy unit is determined by the type of light source and the filters used. The most effective lights are those with wave lengths that are predominately in the blue-green spectrum because of the optical properties of bilirubin and skin. At these wave lengths light penetrates skin well and is absorbed maximally by bilirubin, which then undergoes photochemical reactions to form excretable isomers and break down products.

Measuring Phototherapy Doses

Drug dosages are measured in units of weight whereas photon dosages are measured in the quantities listed in Table 1.¹³ “Spectral

Quantity	Dimensions	Usual units of measure
Irradiance (radiant power incident on a surface per unit area of the surface)	W/m ²	W/cm ²
Spectral irradiance (irradiance in a certain wavelength band)	W/m ² per nanometer (or W/m ²)	μW/cm ² per nanometer
Spectral power (average spectral irradiance across a surface area)	W/m	mW/nm

From Maisels.¹⁴

Table 2 Factors That Determine the Dose of Phototherapy

Spectrum of light emitted
Irradiance of light source
Design of phototherapy unit
Surface area of infant exposed to the light
Distance of infant from light source
From Maisels. ¹⁴

irradiance,” usually expressed as microwatts per square centimeter per nanometer, can be measured with a precision instrument known as a spectroradiometer, but clinicians have generally used simple and much less expensive radiometers to measure spectral irradiance. Unfortunately, unlike spectroradiometers, these radiometers take only a single measurement across a band of wavelengths — typically 425 to 475 or 400 to 480 nm. In addition, there is no standardized method for reporting phototherapy dosages in the clinical literature — investigators have used different instruments with varying spectral responses, different filters and different units for expressing the results. Thus, it is difficult to compare published studies on the efficacy of phototherapy.

Clinical studies¹⁴ have shown that five major factors influence the dose and, therefore, the efficacy of phototherapy (Table 2). Table 1 defines the radiometric quantities used in assessing the dose. Tan¹² has demonstrated the direct relationship between the irradiance used and the efficacy of phototherapy (Figure 3).

Effect on Irradiance of the Light Spectrum and the Distance Between the Infant and the Light Source

Figure 4 shows that the light intensity (measured as spectral irradiance) is inversely related to the distance from the source. The relationship between intensity and distance is almost (but not quite)

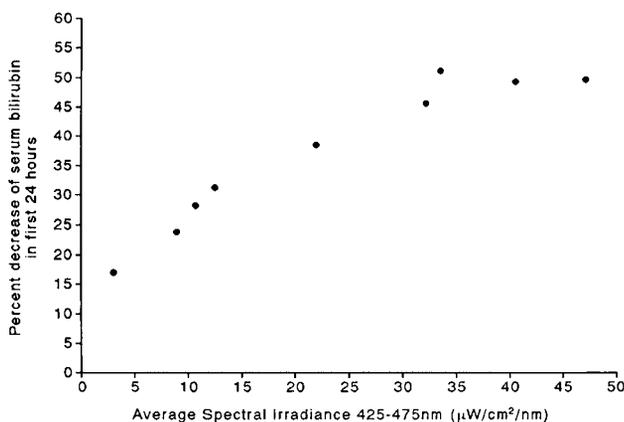


Figure 3. Relationship between average spectral irradiance and decrease in serum bilirubin concentration. Full-term infants with nonhemolytic hyperbilirubinemia were exposed to special blue light (Phillips TL52/20W) of different intensities. Spectral irradiance was measured as the average of readings at the head, trunk, and knees. Drawn from the data of Tan.¹²

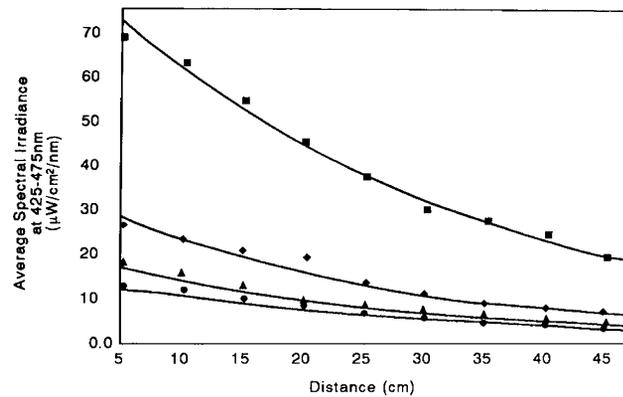


Figure 4. Effect of light source and distance from the light source to the infant on average spectral irradiance. Measurements were made across the 425- to 475-nm band using a commercial radiometer (Olympic Medical, Seattle, WA). The phototherapy unit was fitted with eight 24-in. fluorescent tubes: (■) indicates special blue, General Electric 20-W F20T12/BB tube (General Electric, Milwaukee, WI); (◆) blue, General Electric 20-W F20T12/B tube; (▲) daylight blue, four General Electric 20-W F20T12/B blue tubes and four Sylvania 20-W F20T12/D daylight tubes (Sylvania, Danvers, MA); and (●) daylight, Sylvania 20-W F20T12/D daylight tube. Curves were plotted using linear curve fitting (True Epistat; Epistat Services, Richardson, TX). The best fit is described by the equation $y = Ae^{-Bx}$. From Maisels.¹³

linear, indicating that these data do not obey the law of inverse squares, which states that the light intensity will decrease with the square of the distance. This law applies only to a point source of light, and phototherapy units do not provide a point source of light; the light source has some features of both a cylindrical and a planar source. Thus, the light intensity is a function of the distance but does not vary with the square of the distance. Figure 4 also shows the important effect of the light spectrum (determined by the type of light used) on irradiance.

Spectral Power

The “spectral power” is a product of the skin surface irradiance and the spectral irradiance across the surface area.¹⁵ Because irradiance and surface area are key elements in determining the efficacy of phototherapy, one can compare phototherapy doses only by expressing the dose in terms of the spectral power delivered to the infant. For example a fiberoptic pad has a surface area of 134 cm² and a maximum spectral irradiance of 22 μW/cm² per nanometer. The spectral power is 134 × 22 = 2948 μW/nm or 2.9 mW/nm. A standard overhead bank of fluorescent phototherapy tubes deliver light to about one-fourth of the total surface area of a newborn. The term newborn has a surface area of approximately 0.22 m² or 2200 cm² and one-fourth is 550 cm². Special blue tubes 15 cm above the infant provide an average spectral irradiance of 54 μW/cm² per nanometer and, therefore, a spectral power of 550 × 54 = 29700 μW/nm or 29.7 mW/nm (10 times that of a fiberoptic pad). But infants are not flat so all of these calculations are approximations at best.

USING PHOTOTHERAPY EFFECTIVELY

Light Source

The most effective light source currently commercially available for phototherapy is that provided by special blue fluorescent tubes. These are labeled F20 T12/BB (General Electric, Westinghouse) or TL52/20W (Phillips, Eindhoven, The Netherlands). It is important to note that these are different from regular blue tubes (labeled F20T12/B) (Figure 4).

Distance from the Lights to the Infant

The special blue fluorescent tubes should be brought as close to the infant as possible to take advantage of the dramatic effect that the distance from the light source to the infant has on the spectral irradiance (Figure 4). Thus, the infant should be in a bassinet, not an incubator, because the top of the incubator prevents the light from being brought sufficiently close to the infant. When intensive phototherapy is necessary in low birth weight infants, we place our special blue fluorescent lights between the radiant warmer and the warmer bed. In a bassinet it is possible to bring the fluorescent lights within about 10 cm of the infant. At this distance, special blue tubes provide an average spectral irradiance of more than 50 $\mu\text{W}/\text{cm}^2$ per nanometer (Figure 4). Naked full-term infants do not become overheated under these lights. It is important to note, however, that the halogen, spot phototherapy lamps cannot be positioned closer to the infant than recommended by the manufacturers without incurring the risk of a burn.

Surface Area

Because the surface area of the infant exposed to phototherapy is a critical element in determining the efficacy of phototherapy, a number of systems have been developed to accomplish this.

Garg¹⁶ and Tan¹⁷ have devised systems that provide phototherapy both above and below the infant and a similar system has been commercially produced in the United States.* The availability of fiberoptic pads has made it easy to increase the surface area of the infant exposed to phototherapy and in preterm infants this type of “double phototherapy” is approximately twice as effective as single phototherapy.^{18,19} In term infants we routinely use special blue lights above and fiberoptic pads below the infant. In a small trial we found this system to be as effective as the Olympic BiliBed. Even greater surface area exposure can be achieved with our system by lining the sides of the bassinet with aluminum foil.

What Decline in the Serum Bilirubin Can You Expect?

The rate at which the bilirubin declines depends on the factors listed in Tables 2 and 3 and different responses can be expected depending on the clinical circumstances. In exceptional circumstances, when bilirubin levels are >30 mg/dl a decline of 10 to 11 mg/dl may

Table 3 Clinical Factors Influencing the Efficacy of Phototherapy

Postnatal age of the baby
Gestational age of the baby
Birth weight
Cause of the jaundice
Bilirubin value at start of treatment
Light dosage and spectral emission
From Tan. ¹⁷

occur within 2 hours.²⁰ On average in nonhemolyzing infants, we have achieved a decrement of 32% of the initial bilirubin level in the 18 hours after the initiation of phototherapy. Using a combination of a standard phototherapy unit above and four special blue tubes directly underneath the bassinet, Garg et al.¹⁶ were able to produce an average decline of 43% in hyperbilirubinemic infants in the first 24 hours. Tan¹² exposed infants to an irradiance of 34 $\mu\text{W}/\text{cm}^2$ per nanometer in the 425- to 475-nm range and achieved declines in serum bilirubin levels of approximately 50% in the first 24 hours in nonhemolyzing infants. With standard phototherapy systems, decreases of 6% to 20% of the initial bilirubin level can be expected in the first 24 hours.^{16,19,21}

Although Tan’s data¹² suggest that there is a saturation point beyond which an increase in the irradiance produces no added efficacy we do not know for a certain that a saturation point exists. Given that the conversion of bilirubin to excretable photoproducts is partly irreversible and follows first-order kinetics, there may not be a saturation point. Certainly, with existing equipment there is no such thing as an overdose of phototherapy.

NEWER LIGHT SOURCES

Fiberoptic Phototherapy

Fiberoptic phototherapy systems were introduced in the late 1980s and consist of a light that is delivered from a tungsten–halogen bulb through a fiberoptic cable and emitted from the sides and ends of the fibers inside a plastic pad. These systems have some advantages over conventional phototherapy: Eye patches are unnecessary and an infant can be held and nursed while receiving phototherapy. Fiberoptic systems also provide a convenient way to deliver double phototherapy when it is necessary to expose more of the infant’s surface area, and this type of double phototherapy in preterm infants is about twice as effective as single phototherapy.^{18,19} Their main disadvantage, particularly in the term infant, is that they cover only a small surface area. This significantly decreases the spectral power of fiberoptic systems (see previously). For a given light source, enlarging the pad means that the light must be distributed over a greater area, thus reducing the irradiance (when compared with a smaller pad and the same light source). In a meta-analysis of the randomized and quasi-randomized controlled trials that have compared the efficacy of fiberoptic therapy with

*BiliBed, Olympic Medical, Seattle, WA.

conventional phototherapy, Mills and Tudehope²² found that fiberoptic phototherapy was generally less effective than conventional phototherapy; but, in preterm infants, when two fiberoptic devices were used simultaneously, fiberoptic phototherapy was as effective as conventional phototherapy. A combination of fiberoptic and conventional phototherapy was more effective than conventional phototherapy alone.

Most recently it was shown that conventional phototherapy blunts the expected postprandial increase in mesenteric blood flow; this does not occur in infants receiving fiberoptic phototherapy.²³ Nevertheless, there are no clinical data to suggest that conventional phototherapy is associated with an increase in gastrointestinal problems.

Light-Emitting Diodes

Seidman et al.²⁴ have used high-intensity gallium nitride light-emitting diodes (LEDs) to deliver phototherapy. LEDs deliver high-intensity narrow-band light in the spectrum of choice (blue, blue-green) with minimal heat generation. LED devices can be low-weight, low-voltage, low-power, and portable and can be used in light mattresses or jackets that provide intensive phototherapy in the hospital or at home. A recent clinical trial of a blue gallium nitride LED²⁴ showed that LED phototherapy when used at a low irradiance of 5 to 8 $\mu\text{W}/\text{cm}^2$ per nanometer was as effective as conventional phototherapy. The potential benefits and versatility of this type of phototherapy are substantial, and we await additional trials with interest.

CONCLUSION

Phototherapy is a simple, safe, and inexpensive technique for preventing and treating neonatal hyperbilirubinemia. Understanding how to use phototherapy effectively will further decrease the need for exchange transfusions and new phototherapy techniques should increase the utility, versatility, and portability of this widely used treatment for newborn infants.

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