Phototherapy of Hyperbilirubinemia

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Jaundice occurs in about half of all newly born infants, and is the visible expression of high concentrations of bilirubin in the circulating plasma. Bilirubin, a tetrapyrrole pigment derived from the heme moiety of hemoglobin, is carried in plasma bound primarily to albumin; small amounts may also be bound to red cell membranes. If the production of bilirubin exceeds the infant's ability to conjugate and excrete it, this pigment accumulates in the circulation, a condition called "hyperbilirubinemia," and thence is deposited in the skin and other tissues. If the amount of bilirubin in the plasma exceeds the available binding sites, it is believed to circulate in a free (unbound or loosely bound) form that can enter and damage the neural tissue of the brain, especially the basal ganglia.

Bilirubin is particularly toxic to cells of the central nervous system, and on reaching those cells, may produce irreversible brain damage known as bilirubin encephalopathy. The term kernicterus is reserved for the most severe forms of damage: deafness, cerebral palsy, or death. Strictly speaking, the presence of kernicterus can be established only at autopsy by observing the yellow staining of the basal ganglia. However, the definition given previously is often used, and will be used herein.

Severe jaundice of the newborn must be reduced promptly in order to prevent brain damage. At present, only two types of treatment are available that possess a high degree of effectiveness: exchange transfusion, in which the
infant's entire blood volume is replaced with bilirubin-free blood; and phototherapy, irradiation of the infant with visible light. Exchange transfusion has been in use since the mid-1940s, and phototherapy since late in the 1950s.

**HISTORICAL PERSPECTIVE**

One hundred years ago, when Americans were less well educated but no less gullible than now, a craze swept the country that rivaled today's diet fads (1). A mania for the use of blue light (sunlight filtered through blue glass) followed publication of studies by Augustus J. Pleasonton (2), a Civil War General and amateur scientist, who claimed that exposure to blue light would cure arthritis and a number of other afflictions, as well as increase the germination and yield of plants and the fecundity of domestic animals.

As things do, this bit of lunacy passed, except in tiny groups of color-therapy adherents who periodically have surfaced over the decades. Occasionally, a physician of some prominence might speak in its favor (3). The use of colored light had lost scientific credence by the turn of the century, when Finsen, on impeccable scientific principles, promoted natural sunlight (4) and later artificial ultraviolet (UV) radiation from carbon-arc lamps (5) for the treatment of tuberculosis of the skin. Thus, the use of colored light—phototherapy—gave way to heliotherapy, a far more respectable modality at the time.

The greater credibility granted heliotherapy was based on two factors: demonstrated effectiveness in the treatment of tuberculosis, and a somewhat mystical regard for God's natural light in the promotion of good health (an uncritical esteem which exists to some degree today).

In 1938 the German chemist, Hans Fischer, observed that bilirubin in solution, when exposed to light, decomposes and becomes colorless (6). This observation supported the later finding of Cremer and his associates (7).

The nursing sister in charge of Cremer's hospital nursery reported to him that the jaundice of infants in the sunlit part of the room faded after a short period of exposure. Cremer tested her observation in a controlled manner with intermittent exposures to sunlight and found that not only did the yellow color of exposed skin fade, but that the serum bilirubin concentrations of the infants were reduced. This was the first indication that the sera of jaundiced infants were photosensitive and that the concentration of bilirubin in these sera was reduced by photooxidation. Cremer then designed an apparatus utilizing the radiation of eight fluorescent lamps emitting blue light. These lamps were chosen because part of their emission was in the range of absorption of bilirubin (420–480 nm). Jaundiced infants were exposed to the lamps and successful reduction of visible jaundice and hyperbilirubinemia