Neonatal Phototherapist Course

by

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CERTIFIED NEONATAL PHOTOTHERAPIST COURSE

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INTRODUCTION

So you want to become a neonatal phototherapist. Good. The world needs more qualified phototherapists to deal with the common problem of neonatal hyperbilirubinemia. The author's intent is to present the information you need to gain a comprehensive understanding of this subject so you are comfortable functioning as a neonatal phototherapist. Although the entire body of knowledge regarding neonatal hyperbilirubinemia and its treatment cannot be presented here, it is hoped this course will serve to spur your interest to continue your learning in this area. This course begins with the assumption that you know little about hyperbilirubinemia or its treatment, but that you are familiar with medical terminology. By the end of this course you should have a solid understanding of how hyperbilirubinemia occurs, its medical importance and treatment options. Phototherapy, the most common form of treatment, is discussed in detail. Equipment options and treatment protocols are presented so you can cope with the program with which you are working, or intelligently choose the best option for you if you are developing a new program. The author admits to certain biases in regards to equipment and protocols, but has attempted to be objective in this presentation. Finally, the practicalities of developing a phototherapy service are discussed. PEP, Inc. has assisted many phototherapy services with their successful start-ups. The expertise gained from these years of experience is shared with you in this course.

This course is designed to be flexible and dynamic. You may move through the material at your own pace. A post-test is included, so you can document the learning you have achieved. You are encouraged to use this course book as an ongoing reference, and the post-test may be taken "open-book". Upon returning the post-test to PEP, Inc. and achieving a score of at least 70% correct, you will receive a certificate of completion of this course, showing you are on the cutting edge of neonatal phototherapist training.

CHAPTER I. HYPERBILIRUBINEMIA

A. Biochemistry and Physiology

Hyperbilirubinemia is the condition of having abnormally high (hyper) levels of bilirubin in the blood (emia). Bilirubin is a normal product of the breakdown of red blood cells which occurs continuously in the body. The red cells of newborns have a relatively short life span and are in a constant state of being broken down and replenished. When they are broken down in the reticuloendothelial system of the body, the hemoglobin molecules they contain are split into heme and globin. Globin recycles in the body's protein pool, and heme is further broken down by heme oxidase into biliverdin. Iron is released at this step to be reused in the formation of new hemoglobin. Biliverdin is reduced further to unconjugated bilirubin (1). This bilirubin is a waste product. Excessively high levels can lead to problems for a newborn.

Hyperbilirubinemia and Jaundice

Bilirubin binds reversibly with albumin in the blood and is thus distributed to a variety of tissues (2). In hyperbilirubinemia, the portion of bilirubin that is distributed to the subcutaneous fat may give a yellow hue to the skin, a condition called jaundice or icterus. You may notice in the medical literature that some use the terms "hyperbilirubinemia" and "jaundice" interchangeably - an understandable confusion of terms since jaundice is often the most visible indicator of hyperbilirubinemia. It is often most visible in the sclera of babies' eyes - especially in darkly pigmented infants where jaundice may be difficult to assess in the skin.

Normal bilirubin excretion

The portion of bilirubin that is unbound to albumin can diffuse across liver cell membranes where it is bound to protein. Thus, there is a net transfer of unconjugated, lipid-soluble bilirubin into liver cells where this protein-bound bilirubin is conjugated by the transfer of glucuronide from uridine diphosphoglucuronic acid (UDPGA) by the enzyme uridine diphosphoglucuronyl transferase (UDPGT). This conjugated bilirubin is water-soluble rather than lipid-soluble and is able to be excreted from the body via the bile, through the bile ducts into the small bowel, or to a lesser degree via the kidneys into the urine. Much of the conjugated bilirubin that is transferred into the bile is excreted through the bowel,while the rest is reabsorbed in the gut, back into the bloodstream, and recirculated in the enterohepatic loop or excreted in the urine (3). Most bilirubin is excreted via conjugation in the liver.

There exist two other pathways for the excretion of bilirubin that do not require conjugation by the liver. Bilirubin deposited in the skin or subcutaneous tissue may react to visible range light that hits the skin and converts the normal Z,Z isomer bilirubin into either the E, E and E, Z isomers called photobilirubin, or the E and Z isomers called lumirubin. These photoisomers are then carried to the liver and excreted into the bile without requiring conjugation.

A third pathway for excretion of bilirubin not requiring conjugation is by the conversion of bilirubin to its oxidation products which are then excreted in the urine (4).

Thus, there are a variety of dynamic biochemical and physiologic reactions that determine adequate excretion of bilirubin from the body. Any malady that either increases the load of bilirubin to be excreted beyond the body's ability to handle it, or decreases the normal excretion rate may cause a build-up of bilirubin in the blood and lead to hyperbilirubinemia.

Laboratory measurement of bilirubin

Hyperbilirubinemia is measured in the laboratory via the indirect and direct bilirubin tests. The indirect bilirubin test measures the roughly 90% of unconjugated serum bilirubin. If hyperbilirubinemia results from an excess of bilirubin production, or if the liver cells are unable to conjugate the bilirubin, one would expect to see an elevation of this indirect bilirubin level. The direct bilirubin test measures serum bilirubin in its conjugated form. Since the test only measures monoconjugated bilirubin, and since diconjugated bilirubin may account for up to 1/3 of the conjugated bilirubin, it is important to remember that the standard test for direct bilirubin may underestimate the actual amount of conjugated bilirubin by up to 34% (5).

If hyperbilirubinemia results from the inability of conjugated bilirubin to be excreted, such as in biliary atresia (the congenital absence of bile ducts), you would expect to see an elevation of the direct bilirubin level. In addition, a bilirubin fraction called delta bilirubin exists that is distinct from unconjugated bilirubin and its mono- and di- sugar conjugates. It is protein bound and behaves differently from other forms and is found in icteric sera. It is increased in hepatic and obstructive causes, and decreased in nonhepatic causes of hyperbilirubinemia, and is not found in newborns with physiologic jaundice. Its delayed clearance may confuse the accurate interpretation of conjugated bilirubin values (6, 7, 8, 9).

Normal values

Normal indirect and direct bilirubin levels in adults are commonly less than 0.7 mg/dl and less than 0.5 mg/dl respectively. Normal levels in 3-5 day old newborns are commonly less than 12 mg/dl and less than 0.5 mg/dl - higher than in adults. When these normal levels are exceeded, hyperbilirubinemia exists. A relative increase of bilirubin production as well as a relative decrease of bilirubin excretion are common among newborns (l0). Both tendencies may predispose newborns to hyperbilirubinemia.

B. Incidence and Etiology

The incidence of hyperbilirubinemia in the average newborn population is 6-10%. It typically appears 2-4 days after birth - often after the baby has been discharged from the hospital (11,12,13). There is a positive correlation between hyperbilirubinemia and numerous other factors including: birth control pills at time of conception, first trimester bleeding, pregnancy related diabetes, birth trauma, prematurity, low birth weight, small for gestational age (over twice normal rates), Oriental heritage, carboxyhemoglobin, hemolysis, asphyxia, respiratory distress, breast feeding, neonatal infections and many others (14,15,16,17,18). So you can grasp the large array of causal and etiologic factors associated with hyperbilirubinemia, they are discussed below in logical groupings.

Hyperbilirubinemia due to increased bilirubin production

There are several common events in the perinatal period that may result in an increased bilirubin production. Birth trauma including bruises and cephalhematomas (hematomas under the scalp sometimes associated with the use of vacuum extractors) will obviously increase the bilirubin load as this sequestered blood is broken down (19,20). Over twice as many babies delivered with vacuum extractors require treatment for hyperbilirubinemia than those delivered without it (21).

Hemolytic diseases (those diseases wherein red cells are lysed and destroyed) due to blood type incompatibilities between mother and baby are common in mild to severe forms. Their common denominator is that antibodies are created by the mother's immune system against the baby's blood type that is foreign to the mother's. These antibodies may cross the placenta into the baby's circulation, resulting in the breakdown of the baby's red cells and an increased bilirubin load.

Rh incompatibility (Rh negative mother with an Rh positive baby) is probably the best known of these hemolytic diseases due to its potentially devastating results. However, it is not the most common. Today, it is usually prevented with standard prenatal care, but it is still among us, and can result in severe hemolysis (22).

ABO blood type incompatibility (OO mother with an AO or BO baby) is very common, and can result in (usually) mild hemolysis (23). One study indicates that ABO testing within a few hours of birth is useful in predicting babies who are at high risk for ABO incompatibility problems (24). However, another study suggests that a positive ABO test does not increase predictive value of hyperbilirubinemia developing in ABO incompatible white newborns (25). Hyperbilirubinemia rates appear to be the same for AO as well as BO babies (26). Of the ABO incompatible babies that develop hyperbilirubinemia, 87% are female (compared to a male majority overall in hyperbilirubinemia cases) and 50% show a familial occurrence of the problem (27). Subsequent babies of the same mother are at increased risk, and 88% of subsequent at risk (same blood type) siblings will develop hemolytic disease with 62% requiring treatment (28, 29).

Maternal blood anti-Kell factor occurs in only 0.1% of pregnancies yielding a rate of 0.01% with Kell-positive newborns, half of whom have poor outcomes - a rare cause of hemolysis (30).

Other congenital diseases may result in significant hemolysis (31): G6PD deficiency is associated with high plasma ascorbic acid levels and hyperbilirubinemia (32); b-thalassemia trait apparently affords no protection against hyperbilirubinemia in this disease (33).

Umbilical cord alpha-fetoprotein levels may be useful to identify those at risk for hyperbilirubinemia (34). It was found in 4.5% of Chinese, 3.5% of Malaysian, and 1.5% of Indian babies. However, under 1% required treatment for hyperbilirubinemia and had average peak bilirubins of 12 mg/dl, not an overwhelming problem (35). Hereditary spherocytosis is another uncommon cause that should be considered once blood group incompatibilities have been ruled out (36).

Rare intrauterine hemolytic diseases have been reported: intrauterine pyknocytosis is reported as a rare cause of intrauterine hemolysis (37). Also, a rare case of anti-C hemolysis requiring aggressive treatment has been reported (38).

A case of erythrocyte glutathione S-transferase deficiency associated with hemolysis and hyperbilirubinemia has been described, but its significance in the newborn population has not been defined (39). It has been shown that the activity of enzymes that scavenge oxygen radicals, glutathione, peroxidase and superoxide dismutase are lower in infants with hyperbilirubinemia. A deficiency of factors protecting from oxygen toxicity may play a role in hemolysis and jaundice (40). There is a case report of a mother with autoimmune hemolytic disease due to Hodgkin's disease whose baby carried the same IgG antibody and required aggressive treatment for hemolytic disease (41).

Relatively excessive hemolysis occurs in cases of polycythemia wherein the baby simply has excess red cells. Of the 1.5% of newborns with polycythemia, 22-33% develop hyperbilirubinemia (42). Miscellaneous causes of hemolysis that may affect newborns include Vitamin C administered to premature infants (43) and blood heated in IV tubing (44). Phenolic cleaners were exonerated as the cause of 2 cases of Heinz body anemia and hyperbilirubinemia in one institution (45), but an unidentified oxidant in food has been postulated as a cause of this rare problem (46). Benzyl alcohol used in neonatal intensive care units has been associated with increased brain hemorrhages, but not with hyperbilirubinemia (47).

Hyperbilirubinemia due to decreased bilirubin excretion

If the liver is unable to conjugate bilirubin, its excretion is limited. Some liver-related causes of hyperbilirubinemia include pyruvate kinase deficiency (48); Type I. Crigler-Najjar Syndrome includes the absence of the hepatic conjugating enzyme, bilirubin glucuronyl transferase, activity and invariably leads to prolonged unconjugated hyperbilirubinemia, kernicterus, and death (49, 50).

Conjugated hyperbilirubinemia should make one look for a primary hepatobiliary disease, infection, or a toxic or metabolic cause that is preventing conjugated bilirubin from being transported from the liver out of the body. There are many possible causes of pediatric liver disorders that may result in hyperbilirubinemia, including genetic disorders, neoplasms, hepatitis, biliary atresia, parasites, and fatty liver (51). Such cases deserve early diagnosis because treatment may be lifesaving - such as in biliary atresia treated with surgical liver transplant (52,53). Benign recurrent intrahepatic cholestasis (BRIC) is a rare cause of such hyperbilirubinemia due to a disturbance of hepatocellular bile acid transport (54). Another rare cause is from fibrosis seen in Jeune Syndrome (55). Arteriohepatic dysplasia (Alagille's Syndrome) is described as a relatively common cause of conjugated hyperbilirubinemia (56), and a new syndrome was described in 1984 marked by renal tubular insufficiency, cholestatic jaundice, predisposition to infection, and multiple congenital abnormalities (57), with similarities to renal abnormalities associated with a paucity of interlobal bile ducts and persistent conjugated hyperbilirubinemia described in 1987 (58).

Extrahepatic causes of conjugated hyperbilirubinemia include pyloric stenosis (with or without membranous atresia of the esophagus) (59, 60) or duplication (61), and duodenal atresia(62). Hyperbilirubinemia has also been associated with open heart surgery leading to acute hepatic failure (63), and a congenital Wilm's tumor associated with a consumptive coagulopathy that resolved with surgery (64). Even distal trachea suctioning of intubated newborns has been associated with hyperbilirubinemia (65).

Hyperbilirubinemia due to unobvious causes

The majority of neonatal hyperbilirubinemia cases are not due to an obvious cause. The majority of hyperbilirubinemia cases are diagnosed to have "physiologic" hyperbilirubinemia - a euphemism to label the 6-10% of newborns whose bilirubin levels exceed normal within the first few days of life for which no cause is determined after a reasonable medical work-up. It has been shown that uridine diphosphate glucose phosphorylase (UDPGPP), the first enzyme in the bilirubin conjugation pathway, is at low levels in infants, and may be a contributing factor to the genesis of hyperbilirubinemia in newborns (66). It has also been observed that newborns show a decreased activity of liver enzymes involved with the metabolism of glucuronic acid and the oxidation of antipyrine (67). Thus, many clinicians refer to the "immaturity" of the liver as the cause of physiologic hyperbilirubinemia. Since the jaundice typically shows up within a few days of birth and abates several days later, the liver is understandably viewed to have "matured" in the interim to the point that it can handle the normal load of bilirubin to be excreted.

There are a host of interesting correlations with hyperbilirubinemia. Here are some of them. Remember, correlations do not causal relationships make.

Demographic parameters

Hyperbilirubinemia is more common in term infants who suffer weight loss or are male (68). It is more common in Navajo neonates (69) and Inuit babies (70). High altitude correlates with neonatal hyperbilirubinemia with 31% of newborns at 3l00 meters above sea level and 16% of newborns at 1600 meters developing

abnormally high bilirubin levels. A suggested explanation for this phenomenon is the hematologic response to hypoxia seen at altitude (71,72). A newborn with a sibling who had neonatal hyperbilirubinemia is at 3 times the normal risk to have it also (73).

Pregnancy related issues

Triplets have a 33% chance of developing hyperbilirubinemia. However, keep in mind that 75% are delivered early and their risk may have more to do with prematurity than multiplicity (74).

Likewise, survivors of threatened miscarriages have higher than normal rates of neonatal hyperbilirubinemia, but they also have a higher than normal rate of prematurity, so there may be no causal relationship between threatened miscarriage and high bilirubins (75).

Also, toxemia in the mother puts the baby at risk for hyperbilirubinemia, with 53% of such babies developing high bilirubins (76).

There are some pregnancy management issues to consider regarding the development of hyperbilirubinemia. The intraamniotic injection of methylene blue dye to diagnose ruptured membranes has been associated with hemolysis and elevated bilirubin levels (77). Likewise, oxytocin induction of labor has been associated with hemolysis and hyperbilirubinemia in the newborn, but this has been avoided by administering large volumes of sodium-free IV solutions (78). Bupivicaine epidural anesthesia during labor has been looked at and found to have no correlation with neonatal hyperbilirubinemia (79). Ritodrine used for the prevention of premature labor is associated with increased rates of hyperbilirubinemia (80). It has been observed that maternal hypocapnia correlates with neonatal hyperbilirubinemia, and proper management of maternal ventilation has been recommended (81).

Antibiotics used after primary or multiple spontaneous abortions have yielded an increased subsequent pregnancy rate and lower complications including hyperbilirubinemia (82). Dexamethasone at the common dose of 10 mg given 24 hours before delivery to help mature fetal lungs has been shown to result in bilirubin levels of three times normal at 3-4 days of age (83).

Prolonged maternal ethanol intake correlates with decreased conjugation in the liver and subsequent hyperbilirubinemia in the newborn - probably due to the decreased availability of UDP-glucuronic acid in the liver (84). Maternal liver disease with prolonged hyperbilirubinemia has resulted in hyperbilirubinemia in the baby that required exchange transfusion (85). Also, maternal liver cirrhosis can result in elevated unconjugated bilirubin levels in baby and possible kernicterus (86). On the other hand is a case report of maternal cholestatic hyperbilirubinemia wherein the baby was okay (87). It appears that liver disease in the mother puts baby at risk, but does not always cause problems.

Intrapregnancy infections can affect the baby's bilirubin level. Intrauterine measles has been associated with hyperbilirubinemia (88). Parasitic diseases in mothers tend to yield the same birth weights, rates of anemia and prematurity in their newborns as uninfected mothers, but their babies have three times the normal rate of hyperbilirubinemia (89).

Diabetes related issues

Newborns of diabetic mothers have more than their share of complications. Among them is hyperbilirubinemia (90,91). One study from India indicated the hyperbilirubinemia rate amongst newborns of diabetic mothers was only 8% (92), but most of the available data suggests an increased rate of 16-39% (93, 94, 95, 96, 97) - especially when the diabetes is diagnosed late in the pregnancy (98). A possible explanation for this increased rate is that obese diabetic mothers tend to deliver macrosomic babies with relatively increased hemolysis (99, 100, l01). Poor maternal diabetes control correlates with increased fetal morbidity (102), but on the encouraging side, aggressive treatment of pregnancy related diabetes has been shown to yield normal newborn bilirubins (103, 104, 105, 106, 107). Blood pressure in diabetic mothers does not appear to affect bilirubin levels. Both preeclamptic and chronically hypertensive diabetic moms had babies with normal rates of hyperbilirubinemia (108).

Breast feeding related issues

Breast feeding has been identified as a common factor correlated with neonatal hyperbilirubinemia (109, 110). 15-28% of breast feeding term babies develop hyperbilirubinemia (111, 112, 113)-especially after the first 3 days of life (114). Arguments in relation to the pros and cons of breast feeding sometimes sound more like religion than science, and the published data reflects this nonuniformity of opinion. One study indicates the bilirubin levels are relative to the breast feeding schedules and whether or not supplemental feedings were offered (115). One study of 200 breast feeding babies found no increased bilirubin (l16). Another suggests that early bottle feeding leads to breast refusal and inadequate intake, and this may lead to hyperbilirubinemia (117). It has also been observed that bottle fed babies have more stool, and this may account for more bilirubin excretion (118). Breast milk jaundice syndrome is late in onset

and prolonged compared to other forms of neonatal jaundice. The milk of mothers of babies with this syndrome shows an increased concentration of long-chain non-esterified fatty acids (l19, 120, 121). It remains unproven whether these fatty acids displace bilirubin and cause the observed hyperbilirubinemia (122).

Oral and parenteral nutrition related issues

Caloric intake is inversely correlated with hyperbilirubinemia in preterm infants. The mechanism is undefined (123, 124).

Bilirubin has been shown to increase with increasing amounts of IV water in the first 3 days of life, associated with decreased meconium passage. An increased enterohepatic circulation is surmised as the mechanism (125).

One study shows a low frequency of direct hyperbilirubinemia associated with total parenteral nutrition (TPN) (126), but another reports a rate of 35% (127), and another 57% (88% in the 42% subset that had infections) (128). One possible explanation of this disparity may be found in a study that demonstrated a TPN dose of 1 g/kg/15 hours yielded no increased bilirubin, whereas a dose of 2-3 gm/kg/115 hours yielded hyperbilirubinemia in premature babies (129). There appears to be a cholestasis problem associated with TPN at 2-3 months of age, possibly related to a taurine deficiency, although there is a report of clearing of unremitting cholestasis after biliary tree irrigation (130, 131, 132, 133).

Interestingly, Vitamin E deficiency has been described in neonates with hyperbilirubinemia (134, 135).

Drug related issues

Furosemide has been shown to displace bilirubin from albumin, theoretically increasing the chances of hyperbilirubinemia. Bumetanide does also, but to a lesser degree at therapeutic doses. Therefore, bumetanide may be a better diuretic to use on sick neonates (136).

Any drug that binds to albumin may compete with bilirubin and increase the toxic effects of bilirubin by displacing it. 2-hydroxy compounds are most potent. Sulfisoxazole, sulfamethozole, dicloxacillin, cefoperazone, and ceftriaxone, commonly used antibiotics, are all potent displacers.

Aztreonam, carbenicillin, mezlocillin, cefuroxime, and kanamycin have little or no displacing tendencies. Moxalactam, nafcillin, and many others have intermediate albumin binding power (137). This factor may be one to consider when choosing an antibiotic for newborns at risk.

An unusual case of accidental injection of dopamine into the right branch of the portal vein resulted in 3 1/2 weeks of direct hyperbilirubinemia (138). Be careful where you put that catheter. And, for completeness, there is a case report of hyperbilirubinemia in a newborn of a mother treated with Dapsone for leprosy (139).

Just as certain drugs can predispose to hyperbilirubinemia, hyperbilirubinemia can affect the function of certain drugs. One example is diazepam, whose distribution is poorer and elimination is faster with high bilirubin levels (140).

Infection related issues

Bilirubin inhibits serum bacteriocidal activity, so it is understandable that hyperbilirubinemia is associated with increased rates of sepsis (141). 3% of "unexplained" unconjugated hyperbilirubinemia cases were proven to have septicemia before it was clinically evident (142). Alpha hemolytic strep viridans is predominant in neonatal septicemia, and correlates with unexplained high bilirubins (143). Sepsis is something to keep in mind when you're evaluating unconjugated hyperbilirubinemia.

An interesting strong correlation has been observed between hyperbilirubinemia and endotoxemia, so that some clinicians use high bilirubin levels as a sign of endotoxemia situations where it is suspected (144,145).

Hematologic issues

Hyperbilirubinemia inhibits granulocyte migration, increases phagocytic activity, decreases antibody forming cells in the spleen, increases "activated" lymphocytes and is cytotoxic for lymphocytes and PMNs (146). Hyperbilirubinemia is associated with a significant depression of cellular immunity, but no change in humoral immunity (147). Not surprisingly, thrombocytopenia from whatever cause predisposes to bleeding episodes and hyperbilirubinemia (148).

As you can see, there are a myriad of possible causes for hyperbilirubinemia. It is not so important to memorize all these possible causes as it is to keep them in mind and keep them in perspective. Aside from the majority of cases deemed "physiologic", one series of 335 severe hyperbilirubinemics requiring aggressive treatment had 36% with ABO incompatibility, 11% with Rh incompatibility, 9% with septicemia, 6% with G6PD deficiency, and 20% with multiple causes. Of the 11% that died, 30% suffered cardiorespiratory arrest, 26%

died from septicemia, and 20% from kernicterus. In another series, 5 of 13 deaths were attributed to kernicterus (149, 150).

C. The Ill Effects of Bilirubin

Why is there all this concern about high levels of bilirubin? For years the primary reason for concern has been that hyperbilirubinemia has been associated with the neurologic disease, kernicterus. Many years ago it was observed that some of the babies who developed high bilirubins, usually in the range of 20-30 mg%, developed severe neurologic deficits, and many died. Autopsies have shown bilirubin deposits in the thalamus of these babies (151).

More recently, subtler neurologic changes have been measured. We've come to understand there exists a spectrum of brain damage associated with hyperbilirubinemia ranging from subtle decreases of cognitive function to kernicterus death (152). A consistent increase of handicap at two years of age has been observed for every 3 mg% increase of maximal total bilirubin in neonates (153). In one study of babies who received intrauterine transfusions, 1/2 of whom had hemolytic disease, 13% had abnormalities of health, hearing, and school performance in long-term follow-up (154). In a collaborative study involving 27,000 infants, those with hyperbilirubinemia had more impaired motor function at 8 & 12 months, though the difference could not be demonstrated for those over a year of age (155, 156). Children who had suffered neonatal hyperbilirubinemia, tested at six years of age, showed poor short term memory which predisposed them to listening, comprehension, and language problems later in life (157, 158). Eighteen year olds in Norway who at birth had a positive Coombs test and hyperbilirubinemia of at least 5 days had lower than average IQs (159).

Auditory brain stem response abnormalities have correlated with hyperbilirubinemia and bilirubin deposition in the brain stem, but we must remember that high risk newborns may have several possible causes for sensorineural hearing loss of which hyperbilirubinemia is but one (160, 161, 162). Deafness in newborns averages 1 per 1000 births, but in neonatal intensive care unit (NICU) survivors (73% of whom had anoxia events) the rate jumps to 1 per 52. Deafness is more common in those with low birth weights and high bilirubins. Follow-up of NICU survivors reveals a 10% rate of hearing loss at 6 1/2 years of age in those who had apnea, hypothermia and hyperbilirubinemia (163, 164, 165). Hyperbilirubinemia plays some role in the genesis of cerebral palsy. It is present in 47% of hyperkinetic and 11% of dystonic victims. Blood group incompatibility, which we know is a common cause of hemolysis and high bilirubins, is considered a "warning signal" for dyskinetic cerebral palsy (166, 167, 168, 169).

Cradle to grave follow-up studies are few; there is one showing no correlation between neonatal hyperbilirubinemia and Alzheimers disease (170).

Although the bilirubin conjugates appear to be the same for premature as well as full term newborns suffering blood incompatibilities and intrauterine hypoxia, and although brain stem evoked potentials appear to be the same for premature as well as full term newborns at high risk due to hyperbilirubinemia or perinatal hypoxemia, it has long been recognized that premature newborns are at much higher risk for developing kernicterus. All victims in one study were under 1200 grams at birth (151, 171, 172). However, in one review of 30,000 neonates, the 0.01% that died from kernicterus were all over 2200 grams, near term at 36-37 weeks gestation, and had bacterial infection as the primary cause of their hyperbilirubinemia. These, however, were from a group wherein prematurity was aggressively managed and eliminated as a primary cause of kernicterus (173).

Small babies have been observed to develop kernicterus with bilirubin levels as low as 8 mg% (174, 175). They have shown no correlation with these speculated causes: therapy, sepsis, hypothermia, asphyxia (low APGAR), hematocrit, acidosis, hypercarbia, hypoxia, hypoglycemia, or even hyperbilirubinemia (176). It has been theorized that small babies are at higher risk for brain bilirubin deposits at low bilirubin levels because they are more prone to intracranial bleeds. A study comparing infants weighing less than 1500 grams, with and without periintraventricular hemorrhages, found the two groups to have the same bilirubin levels, the same need for treatment, and the same level of handicap at 12 months of age. There was no positive relation between periintraventricular bleeds and hyperbilirubinemia and outcome (177). The picture gets somewhat more complicated when one considers that cholestatic liver disease, which is commonly associated with hyperbilirubinemia, has also been associated with vitamin K deficiency which places a baby at risk for intracranial bleeds. It's difficult to tell what is causing what (178).

A more plausible theory to explain why kernicterus develops at varying levels of hyperbilirubinemia is that for the bilirubin to enter and damage the brain there must be a breakdown of the normal blood/brain barrier (BBB). In vivo it has been shown that hyperbilirubinemia alone causes no disruption of brain energy metabolism, but hyperbilirubinemia plus an open BBB yields

disruption (179, 180). It has also been shown that the BBB permeability and brain bilirubin levels are higher at 2 days of age than at 2 weeks of age - perhaps explaining why kernicterus is primarily a disease of the first few days of life (181). Asphyxiation causes disruption of the BBB and is understandably associated with the neurologic changes that are observed with hyperbilirubinemia (182). Another bit of convincing evidence is that victims of kernicterus at low levels of serum bilirubin show bilirubin staining of the brain just as at high levels of serum bilirubin (183). As we come to understand the BBB and its disruption by a variety of pathologic processes, we may develop better strategies for the prevention of kernicterus (184). What we need is a reliable means by which to measure the integrity of the blood/brain barrier (174).

We now know that the central nervous system changes may be subtle and not evident for years after birth, or severe as in kernicterus. Sick and immature newborns are at highest risk. Brain deposits of bilirubin occur primarily with hyperbilirubinemia associated with acidosis, sepsis, hypoxia, hemolysis, hypoalbuminemia (less binding of bilirubin), or the presence of competitive albumin binders (185). It is not unreasonable to view the dynamics as a formula:

$$\frac{\text{bilirubin level}}{\text{BBB integrity}} = \text{likelihood of brain damage from bilirubin deposition}$$

As bilirubin levels rise and/or BBB integrity falls, the likelihood of brain damage or kernicterus increases.

D. Clinical Assessment

How far to go in the diagnostic evaluation of neonatal hyperbilirubinemia is a challenging question. The investigator wants to determine as precisely as possible the exact cause of the elevated bilirubin so that treatment can be most appropriately prescribed, and yet be cost-effective in the approach to a work-up. One certainly wants to find the common hemolytic and bile obstructive causes, recognizing that, after the work-up, a majority of cases will be diagnosed to have "physiologic" hyperbilirubinemia. As you have seen from the long list of possible causes above, one could do a great deal of testing to rule out all possible causes. Instead of performing an exhaustive battery of tests on every jaundiced baby, it is more appropriate to perform a basic battery that will either rule out significant causes of hyperbilirubinemia or point the clinician in the right direction toward further specific testing. Various initial test protocols have been suggested.

Serum bilirubin determinations have long been the standard for defining hyperbilirubinemia. The measurement techniques are quite straightforward and repeatable. Most hospital and clinic labs can measure direct bilirubin and total bilirubin. Indirect bilirubin levels can be calculated by subtracting the direct from the total levels. To be more accurate, a multilayer slide technique for measuring indirect bilirubin helps eliminate the up to 5-10 mg% inaccuracy of the subtraction technique (186). Knowing these levels helps determine if the pathology is occurring before the bilirubin reaches the hepatocyte or after (Is the elevated bilirubin conjugated or not?), but further testing is needed to make a diagnosis.

Screening techniques for finding those with hyperbilirubinemia have been approached from several angles. One interesting technique that is not widely practiced is the measurement of the fetal weight to placenta weight ratio at the time of birth. This technique can identify some babies previously thought to be low risk who have "outgrown" their placentas as defined by having a ratio greater than 11. This group was at risk for several problems including a 24% chance of hyperbilirubinemia (187).

Umbilical cord bilirubin levels as a predictor of subsequent hyperbilirubinemia have also been studied. In one study, those with a bilirubin under 2.0 had less than a 4% chance of needing therapy for hyperbilirubinemia, whereas those with levels over 2.0 had a 25% chance of needing treatment. In today's world of early discharges from hospitals when babies are 1 to 2 days of age, usually before hyperbilirubinemia becomes clinically evident, such a screening tool may be useful in determining who deserves follow-up monitoring (188). Other studies have indicated that cord blood bilirubin measurement is not a sufficiently accurate predictor of hyperbilirubinemia, and monitoring of serum bilirubins remains the best way to identify the important cases (189, 190).

Yet another approach hinges on the fact that carbon monoxide is produced in equal amounts to bilirubin during the breakdown of heme. Carbon monoxide can be readily measured in expired air, and since elevated levels have correlated well with hyperbilirubinemia in the first week of life, this measurement may facilitate the early recognition of bilirubin problems. However, CO levels alone have not predicted those babies that eventually needed treatment (191, 192, 193, 194, 195).

Perhaps the best screening tool developed recently is the transcutaneous bilirubinometer which provides a noninvasive way to assess bilirubin levels. Several

brands have been tested and found to be relatively accurate - claiming 80-100% sensitivity and 74- 97% specificity in identifying hyperbilirubinemia. The test varies a little with skin pigmentation, but is useful as a screening technique. One protocol suggests screening at 24 hours of age and determining the relative increase on a second reading in 24 hours as a good predictor of which babies will develop levels over 15 mg%. Correlation of this test with serum bilirubins during treatment breaks down, however, probably due to the time required for bilirubin in subcutaneous fat to equilibrate with serum. Therefore, its primary use is for screening newborn populations, not for following treatment. Combining end tidal CO level screening with this technique may yield a cost-effective, noninvasive, and accurate way to find those babies who will soon develop hyperbilirubinemia (196, 197, 198, 199, 200, 201).

Once hyperbilirubinemia has been identified, we enter the next phase of diagnostic evaluation. Who should we test, and what tests should we do? One study looked at the 6.1% of newborns in their population that developed bilirubins over 12 mg%. Of these, 45% had an identifiable cause and 55% did not. 83% of those with no cause found were breast fed compared to 47% in the control group. This finding led to the recommendation that we should investigate babies with bilirubins over 12 if they are bottle fed, and wait for levels of 15 or higher if they are breast fed (202). In a study of 2443 infants with hyperbilirubinemia, 18% met the criteria for nonphysiologic hyperbilirubinemia (9% in blacks to 31% in Asians) - those wherein you might hope to find a lab abnormality. After a $125 work-up, 48% had no identifiable cause, another 32% had a cause that was obvious from the history, exam, or initial hematocrit, and 17% had an ABO or Rh incompatibility. The lab work-up rarely yielded a finding other than ABO or Rh incompatibility, and the routine use of extensive testing is of questionable usefulness (203). Instead, a carefully organized diagnostic evaluation makes good sense (204).

Suggested routine tests include:

- bilirubin - total and direct - to identify unconjugated or conjugated hyperbilirubinemia;
- hemoglobin and hematocrit - to indicate hemolysis, polycythemia;
- ABO and Rh blood typing of mother and baby - to identify major blood type incompatibilities;
- Coombs test - to identify a red cell antibody reaction;
- albumin - to recognize those at higher risk for encephalopathy; (205)

Further specific tests may include:

1. WBC & differential count - Bilirubins over 20 mg% correlate with elevated white cell counts, increased PMNs and monocytes with Fc and C' complement receptors - possible indicators of infection (206);
2. alpha-1-antitrypsin - (207);
3. Methemoglobin elution test - to find G6PD deficiency (208, 209);
4. Liver function test battery - to better discern hepatocyte function and obstructions;
5. Liver biopsy - invasive, useful to diagnose many intrahepatic problems;
6. Ultrasound - noninvasive look at the liver, bile duct, & gall bladder. A study of 67 newborns with conjugated hyperbilirubinemia found ultrasound not to be very helpful in the diagnosis of biliary atresia, hepatitis, cystic fibrosis, metabolic liver disease, alpha-1-antitrypsin deficiency, bile duct stenosis, Alagille Syndrome, choledochal cyst, and panhypopituitarism (210);
7. Hepatobiliary scintigraphy - to image the liver and biliary tree. It has been found not to be as good as liver biopsy and should not be routinely used - especially if the procedure delays corrective surgery. With the simultaneous use of duodenal and gastric aspirate radioactivity analysis, however, this technique improves its specificity from 46% to 76% and its accuracy from 55% to 78%. This level of improvement, if achievable in your institution, may sometimes avoid an open liver biopsy and operative cholangiogram (211, 212, 213).

To monitor newborns undergoing treatment, the standard in most communities is to measure bilirubin levels at least daily. A hematofluorometer assay on heparinized blood may be useful for management in the neonatal intensive care setting (214).

Auditory brainstem response (ABR) has been used to monitor neurologic deficit in hyperbilirubinemia, which is what we're trying to prevent with all this effort.

Kernicterus has been definitely associated with increased hearing thresholds which normalized in treatment groups. Serial auditory brainstem response and middle latency response tests have been found useful in monitoring the babies' neurologic status; although

there is some suggestion that factors other than hyperbilirubinemia may be operating in the abnormals also (215, 216, 217, 218). It has been suggested that routine ABR should be performed on high risk newborns, i.e., under 2000 grams, those with hyperbilirubinemia, respiratory distress syndrome, or asphyxia (219). Since bilirubin deposits in the brain stem affect adjoining areas that control hearing and crying, the babies' increased percentage and variability of crying has also been used to monitor neurologic integrity of hyperbilirubinemia patients (220, 221).

E. Benefits of Treatment

We treat high levels of bilirubin in newborns and normal levels of bilirubin in high risk newborns as a matter of course, but are we doing any good? Several studies confirm that most auditory brain response abnormalities return to normal with treatment of the hyperbilirubinemia. One study indicated half remained abnormal if the bilirubin rose over 18 mg%. Hearing check-ups to 3 years of age are normal for those treated promptly (222, 223, 224, 225, 226, 227, 228).

The debate rages over whether or when to treat full term jaundiced babies who are otherwise healthy and have a negative work-up. Several studies indicate a low rate of problems in this large subset of hyperbilirubinemic newborns - even at high bilirubin levels in the mid-20 mg/dl range. These findings have led some to recommend no treatment for this group. There is some evidence however, that mild to moderate bilirubin elevations are associated with mild neurologic changes such as behavioral organization that may not be recognized until much later (229, 230). As we get more sophisticated in assessing subtle neurologic changes, it will be interesting to see how this group performs with and without treatment. The jury is still out on this question, but there has been a trend amongst physicians to begin treatment at higher and higher bilirubin levels in this otherwise healthy group. Twenty years ago, most newborns with bilirubins over 10 mg% got treated. That threshold has crept up to 14-18 mg % for most physicians today. A few are brave enough to not treat at all if the baby is in this low risk group. If one applies a risk/benefit analysis to these cases, one sees that even though the benefit may be small or questionable, since the risk of treatment is so very small, one can understand why so many physicians decide to treat.

F. Treatment Options

Hyperbilirubinemia treatment has been varied and creative over the years - with varying degrees of scientific basis. The *Journal of Traditional Chinese Medicine* lists Artemisia Composita as a drug for "the prevention and treatment of neonatal hemolysis integrity and hyperbilirubinemia". Results are sketchy in the Western medical literature (231). Vitamin E, which has seemingly been used to treat everything, has indeed been tried for the prevention of hyperbilirubinemia - with no effect (232).

Continuing in the homeopathic vein but with some theoretic scientific basis, riboflavin has been suggested as a treatment adjunct to phototherapy since bilirubin reacts with flavin both aerobically and anaerobically to form photosensitive compounds (233, 234). This treatment has yet to gain wide acceptance. And in the historic tradition of purging the bowels of children, suppositories have been given to newborns to hasten the evacuation of meconium. The thinking here is that meconium evacuation will decrease the enterohepatic recirculation of conjugated bilirubin. Unfortunately, the practice does not change baby bilirubin levels (235).

Drug therapy for hyperbilirubinemia has focused on phenobarbital which has clearly been shown to decrease bilirubin levels. When given in the last few weeks of pregnancy in high risk cases, it is found to be safe and effective. The babies show a higher level of conjugated bilirubin and a decreased need for other treatment. Unfortunately, effective doses are over 1 gram per day, which makes the mother and baby quite sleepy. Methylphenobarbital, which is less sedating, has been suggested as an alternative. When given to the babies, phenobarbital is not as effective as phototherapy. Its use has diminished over the years because there are better alternative treatment options (236, 237, 238, 239, 240, 241).

Another drug that may be useful in the treatment of hyperbilirubinemia is tin(Sn)-protoporphyrin, which inhibits fetal and neonatal heme oxygenase, thereby stalling the production of bilirubin. It crosses the placenta and can be used prenatally, and has been shown to suppress hyperbilirubinemia in newborns. It has suppressed jaundice in rats and Rhesus monkeys with no ill effects noted. Phototoxicity is a likely side effect, and 2 of 53 term babies with direct Coombs positive ABO incompatibility treated with Sn-protoporphyrin had transient erythema. Its suggested usefulness is when other modes of treatment are unavailable (242, 243, 244, 245, 246, 247, 248).

Through the 1960s and much of the 1970s, exchange transfusions were the standard treatment for hyperbilirubinemia. Although this is an invasive procedure that carries a number of risks, the benefits generally outweighed the risks, and the risks of exchanging blood were less than the risks of the hyperbilirubinemia. Still

used in extreme cases, plasma and blood exchanges can be life saving for a child who, for example, may be very premature with Rh incompatibility. The possible complications though, are many - most commonly metabolic, cardiac, and hemorrhagic. The Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) has been reported. 12% in one series developed thrombocytopenia. Retrolental fibroplasia has occurred, as well as fatal graft vs. host reactions. Intrauterine transfusions have resulted in worsening of hyperbilirubinemia from delayed absorption of intraperitoneal blood. Problems with the transfusion process include morbidity from heat-hemolyzed blood, possible lipoprotein lipase effects from heparinized blood, possible toxic effect from the presence of plasticizers in the transfused blood, and at least one case of G6PD deficient donor blood exaggerating the hyperbilirubinemia (249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264).

Technology has given us hemoperfusion as an alternative to exchange transfusion. It has effected an 80-90% removal of bilirubin from the blood without ill effects (265, 266).

Treatment for neonatal cholestatic conditions from anatomic blockage of bile drainage has been primarily the domain of surgery. In many cases hepatic function can be preserved. The success of surgery for biliary atresia depends on early diagnosis and intervention. Success rates are improving with bile drainage being established in 65% and a 5-year survival of 47% (267, 268, 269).

Based on the fact that most newborns with hyperbilirubinemia are otherwise healthy and that most of these are breast fed, one mode of treatment that has been suggested is to simply discontinue breast feeding. In a series of 87 jaundiced babies who were switched off the breast for 24-48 hours, 81 did well at home without further treatment. Another series showed that newborns that had breast feeding discontinued did as well as those receiving phototherapy (270, 271). Since this is still a debated issue, and since there are many benefits to breast feeding, quitting breast feeding has not become standard treatment - except for the relatively uncommon breast milk jaundice syndrome described in the breast feeding issues section above.

Finally, there is phototherapy. Since the purpose of this course centers on neonatal phototherapy for hyperbilirubinemia, the entire next chapter will review what is known about this most interesting modality. Compared to the treatment options discussed above, phototherapy is an attractive option. It avoids the side effects of the drugs phenobarbital and Sn-protoporphyrin, and it is as effective as exchange transfusion while avoiding many of the risks (272, 273).

CHAPTER II. PHOTOTHERAPY

A. History

Once upon a time in Essex, England, there lived a physician named R. J. Cremer. Luckily for us he worked with a bright nurse who noticed that babies placed next to the windows in the hospital nursery did not get as jaundiced as babies living on the other side of the room. Armed with this important observation, Dr. Cremer and associates demonstrated that light converts unconjugated bilirubin into colorless substances, and when he shone light on jaundiced babies, their jaundice abated (274).

Life went on apace for ten years. Phototherapy became a popular treatment modality in many countries, but not in the United States. Then, a Vermont physician named J. Lucey and his associates demonstrated that blue range visible light was the effective spectrum for preventing hyperbilirubinemia in newborns. He demonstrated that photoisomerization took place in the bilirubin, so it could be excreted without having to be conjugated (275). It soon became apparent that phototherapy was effective for treatment as well as prevention, and it appeared to be safe. Blessed with this new level of scientific legitimacy, phototherapy quickly became the treatment mode of choice.

Minimum effective doses were defined. White fluorescent lights were placed in banks over the baby in an incubator to achieve these dosages. Then more banks were added on the side or even under the baby to bathe more surface area of the baby in light and speed treatment.

First came blue fluorescent lamps that emitted a more specific spectrum and lasted 200 hours. Then came special blue fluorescent lamps that lasted 2000 hours. After that, a few white lamps were added back into the light bank so the baby wouldn't look so blue and to alleviate the nausea caused in some health workers by the scintillating blue lamps. Finally green lamps came and went rather quickly.

First, babies were all treated in incubators to control their temperatures. Then we found that most babies do just fine controlling their own temperatures, and babies could be safely treated in bassinets. Then a few brave physicians started allowing their healthier, jaundiced patients to go home with their mother and receive phototherapy at home. This move sparked a second generation of phototherapy equipment designed to be portable. Protocols were defined by responsible parties such as the American Academy of Pediatrics, and periodically updated.

Safety questions were researched. Eye damage from bright light was an early concern based on animal studies wherein retinas that were force-fed high doses of light showed damage. Putting eye patches on babies undergoing phototherapy has been standard practice since the very early days. Rashes were observed and studied, along with diarrhea, behavior, weight gain, and other parameters. In 1991, 33 years after Cremer started it all, the National Institute of Child Health and Human Development along with the National Institute of Neurologic Disorders and Stroke declared phototherapy to be safe (276).

As with many new medical procedures, phototherapy was initially practiced only by physicians in very controlled settings. As health professionals have gained experience with the relative ease and safety of phototherapy, responsibility has become naturally shared amongst nurses, home care providers, and parents.

Today there is a range of phototherapy practices. We have hospital and home locations, fixed and portable equipment, and a 5-fold range of dosages available. We can patch eyes or restrict the light to below the neck or just the trunk. We can treat continuously or intermittently. We can use a light source that is blue or white or somewhere in between. We can choose an incandescent or fluorescent light source and deliver the light directly to the skin or via fiberoptic cable. We can work individually or as a member of a treatment team.

B. Physiology of Phototherapy

Unconjugated bilirubin is normally excreted, as we have learned, by conjugating with glucuronide in the liver and passing via the bile into the gut and out. It is this process of conjugation that is the bottleneck to excretion of bilirubin in the newborn.

Unconjugated bilirubin, being lipid-soluble, is distributed to many sites in the body including the skin and subcutaneous fat. When blue range visible light in the spectrum of 480-510 nanometers strikes the skin, it readily converts bilirubin from the toxic 4Z, 15Z form to the less toxic 4Z, 15E form called photobilirubin. This form then travels to the liver where it can be excreted without glucuronide conjugation. In addition, blue light causes photoisomerization of bilirubin into its Z to E isomers called lumirubin which can also be excreted through the liver without conjugation. Photoisomers may account for up to 15% of serum bilirubin in newborns undergoing phototherapy. Thus, there are two pathways for bilirubin to bypass the conjugation requirement to get out through the liver. Also, to a lesser extent, blue light forms oxidation products of bilirubin

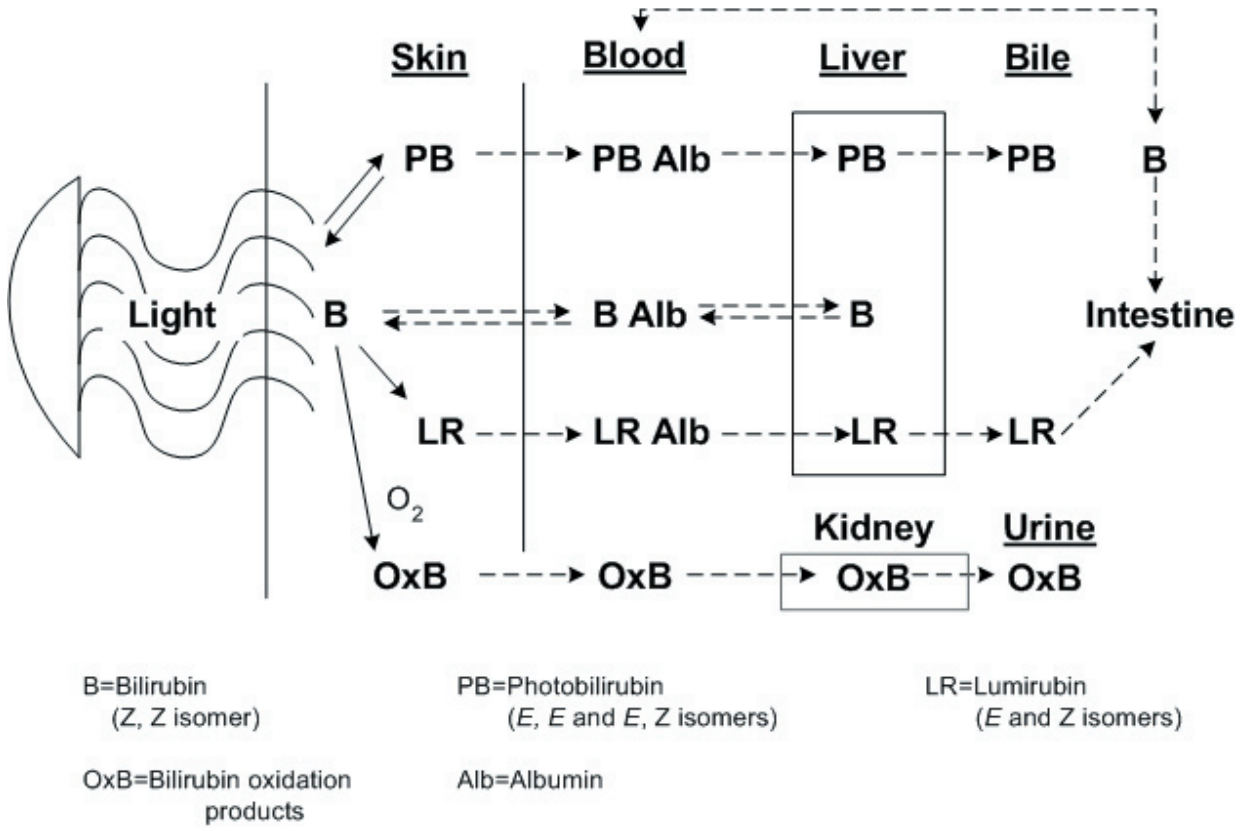


Fig. 1: General mechanism of phototherapy for neonatal jaundice. Solid arrows represent chemical reactions; broken arrows represent transport processes. Pigments may be bound to proteins in compartments other than blood. Some excretion of photoisomers in urine alos occurs.

that are excreted through the kidney, bypassing the liver altogether. Given the known mechanism of action for phototherapy, it is not surprising that phototherapy decreases the unbound bilirubin disproportionately to the total bilirubin (SEE FIGURE 1) (275, 277, 278, 279, 280, 281, 282, 283). Phototherapy has also been shown, however, to decrease conjugated cholic acid, perhaps by decreasing gut reabsorption (284). An interesting study of phototherapy delivered with and without oral agar revealed a 23% decreased duration of phototherapy in the agar group due to sequestration of excreted bilirubin in the gut agar and reduction of enterohepatic recirculation of bilirubin (285).

Another interesting bit of information on the subject of the physiology of phototherapy is that the photochemical degradation of bilirubin under anaerobic conditions is hastened by riboflavin, leading some to recommend adding riboflavin to the diet of newborns undergoing phototherapy - a practice that does not seem to have caught on well (286).

The fact that skin is where the action is in phototherapy is further supported by a study wherein newborns receiving phototherapy had their livers shielded from the light. No difference in rate of bilirubin level reduction was noted in the test and control groups (287).

The search for the ideal light spectrum yielded some interesting results. Light doses are measured in microwatts/sq cm/nm. The accuracy of Lucey's work is born out by studies that show if one delivers a narrower band of blue light at the same overall light dose, treatment courses can be shortened due to faster degradation of bilirubin.

Therefore, at 41 microwatts/sq cm/nm, special blue bulbs with the narrowest spectrum work faster than blue bulbs with an intermediate spectrum, which work faster than white bulbs with the widest spectrum (288).

Several papers have been written on the subject of green light as an alternative to blue light. Green light is less efficient than blue light in producing Z, E isomers of bilirubin, but in a few studies it appeared to reduce bilirubin levels just as fast - suggesting that structural photoisomerization is the main mechanism of phototherapy in humans. The theory is that if one turns up the intensity of green light and thereby increases the production of lumirubin, green light may prove superior to blue light in phototherapy. Other studies indicate that blue light provides faster treatment than green light, blue light

is equally or less disturbing to the health care staff, and green light was associated with severe erythema and tanning (289, 290, 29l, 292). In the real world of clinical medicine green light therapy has not caught on. One manufacturer offers green bulbs as an alternative, and has yet to receive an order for one.

C. Indications for Phototherapy

Phototherapy is indicated as a first-line treatment modality for the lowering of abnormally high bilirubin levels frequently seen in the first few days of life. It is effective for full-term infants, and even more effective for premature babies. It is effective regardless of skin pigmentation. The failure to respond rate is only 0.2%. Although phototherapy is most commonly used to treat nonobstructive hemolytic and nonhemolytic causes of hyperbilirubinemia, it is also indicated to achieve the temporary lowering of hyperbilirubinemia from biliary obstruction causes - hopefully until the obstruction can be definitively diagnosed and treated (293, 294, 295, 296).

As with any treatment modality, the indications for phototherapy to treat neonatal hyperbilirubinemia are based on an assessment of the benefits vs. the risks. As our understanding of these benefits and risks has evolved over the years, so too have the indications for the use of phototherapy.

It has been known for many years that high bilirubins in the 20 to 30 mg% range can be associated with kernicterus which often results in devastating neurologic damage. The risk of allowing bilirubin to reach these levels was perceived to be high. At the same time, phototherapy was demonstrated to be effective in lowering bilirubin levels. Therefore, the overall benefit of phototherapy - the prevention of kernicterus - was perceived to be great. Minimal problems were observed with the use of phototherapy, so the risk of phototherapy was perceived to be low. The alternative to phototherapy, exchange transfusions, were effective, but were associated with more complications than phototherapy. Therefore, phototherapy was perceived to have an attractive risk/benefit ratio, and its use became common. Twenty years ago, to avoid reaching high bilirubin ranges, many babies with bilirubins over 10 mg% were put “under the lights”. Little distinction was made of the baby’s age, size or medical condition.

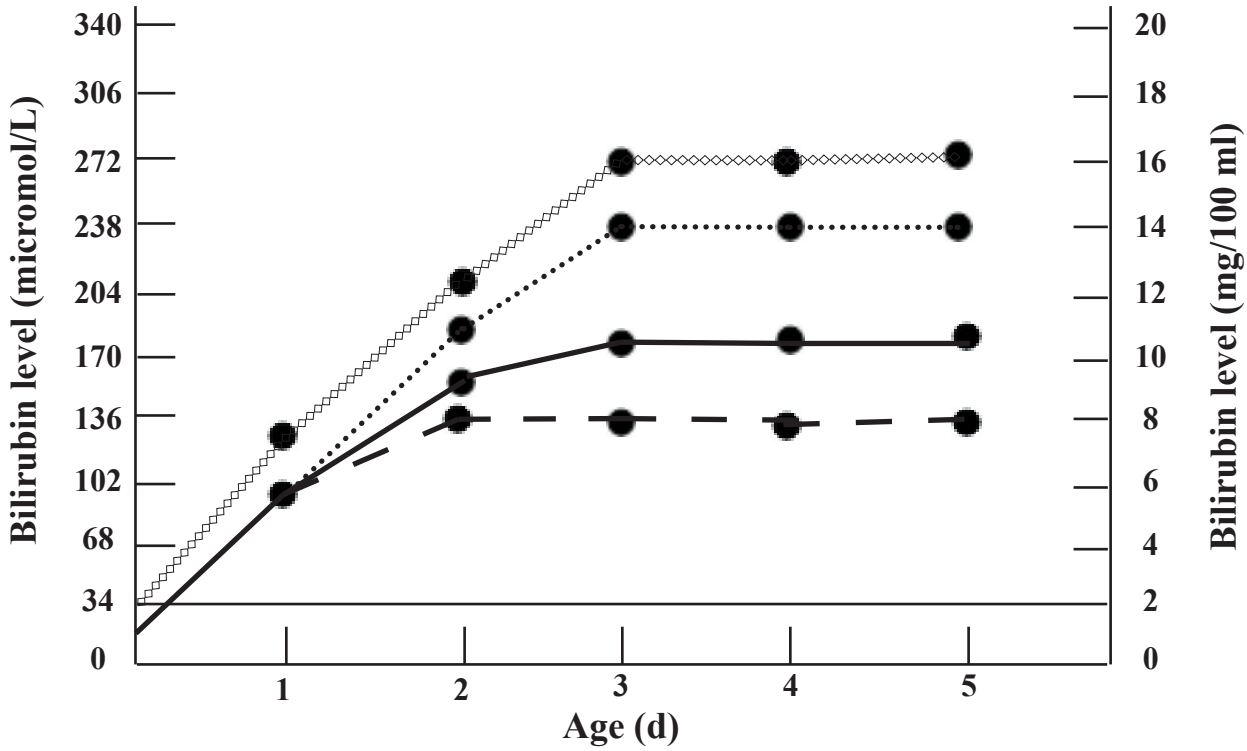


Fig. 2: Suggested guide for initiation of phototherapy in neonatal hyperbilirubinemia. Curves represent serum unconjugated bilirubin level at which phoototherapy should be considered (based on data from Cockington).
= birth weight > 2500g; = 2001 to 2500 g; = 1500 to 200 g; = < 1500 g.

Over the past two decades the indications for use of phototherapy have become somewhat more sophisticated. We have come to understand that the risk of hyperbilirubinemia for a premature, or small for dates infant is much greater than the risk for a full-size, full-term baby. We have also learned the effectiveness of phototherapy varies with different clinical conditions. Although time has demonstrated that phototherapy is a very safe treatment modality, and the perceived risk of phototherapy remains low, the perceived benefit of phototherapy - the prevention of kernicterus - has been called into question. Therefore, the perceived risk/benefit ratio has changed somewhat over the years, and the application of phototherapy has become more selective.

Controversy exists regarding the appropriate use of phototherapy in otherwise healthy, full-term babies with physiologic jaundice (easily the largest subset of hyperbilirubinemic babies).

This controversy was triggered by a study of term babies with physiologic jaundice that showed death rates with and without phototherapy were the same. Since many babies' bilirubin levels rise (perhaps into the mid-20 mg% range), then fall on their own without ever developing kernicterus is it necessary to treat all such babies? It has been shown that the risk for developing bilirubin encephalopathy is much greater the lower the birth weight. From this knowledge has evolved a nomogram to help determine when to initiate phototherapy depending on the baby's weight, age, and bilirubin level (SEE FIGURE 2). Many physicians now use such a nomogram to determine if and when to start phototherapy for a given infant. For example, an infant under l500 grams whose bilirubin exceeds 5 mg% at day one after birth qualifies for phototherapy, whereas an infant over 2500 grams must have a bilirubin over 18 mg% at day four to qualify for treatment (297, 298, 299, 300).

However, as noted in Chapter II, there is accumulating evidence regarding the subtler effects of hyperbilirubinemia at only moderate levels, and the desirability of controlling bilirubin at lower levels - short of kernicterus or death. Such evidence argues for more liberal use of phototherapy, and runs counter to the recent trends toward more restricted use. Trends, even fads, do exist in medicine, and they take time to develop and change. Perhaps, the most accurate observation to make about the indications for phototherapy is that they are in a state of flux; the precise indications are yet to be defined.

Another controversy exists regarding the use of prophylactic phototherapy. Intuitively, prophylactic phototherapy is an attractive concept. Since phototherapy is so safe, why not use it to prevent any hyperbilirubinemia - especially in those at higher risk, such as small premature babies? Babies with G6PD deficiency treated prophylactically have been shown to avoid hyperbilirubinemia. However, another study of premature babies showed no change in the clinical course with prophylactic phototherapy. It was shown that early intervention at "minimally high" levels of 5 mg% was helpful. Most studies have not clearly shown an advantage to treating before bilirubin levels elevate (301, 302, 303).

D. Risks of Phototherapy

Although there have been a number of anticipated risks of phototherapy, over many years of experience there have been surprisingly few noted problems. Most studies fail to demonstrate long term problems associated with phototherapy (304).

Ophthalmic Risk - Over 30 years ago an animal study was performed wherein newborns' eyelids were propped open and high intensity light was shone into the eyes. Retinal damage was documented under these artificial conditions. This study became the basis for the policy of protecting the baby's eyes during phototherapy. Although there is no data suggesting phototherapy in a real clinical setting with neurologically intact human newborns causes any retinal damage (except, perhaps in premature babies in bright neonatal intensive care units), eye protection continues to be the standard of care during phototherapy. Few physicians are brave enough to violate this standard (305).

Temperature Control Risk - Both hypothermia and hyperthermia have been reported with phototherapy. Hypothermia occurs in about 4% of the cases - usually seen in temperate climates and with small babies who have inherently poorer temperature control. Hyperthermia is most commonly seen in warm climates without air conditioning. Most phototherapy equipment adds a few degrees Fahrenheit to the ambient temperature, and this may create an unusually warm environment for the baby.

Dehydration Risk - This risk is primarily theoretical and has not been observed to be a significant problem. Due to the exposed skin, the usual warm environment during phototherapy, and the possible diarrhea from the excess bilirubin, dehydration might occur.

Dermatolgic Risk - A fine rash has been reported associated with the use of phototherapy, but it appears identical to the rash that has been associated with hyperbilirubinemia, and appears to be from the elevated bilirubin,

not due to the phototherapy. Rarely, a "bronze baby" is reported associated with phototherapy. The discoloration, possibly due to biliverdin, usually wanes over several weeks and is itself innocuous, but there are several possible causes of the "bronze baby syndrome". The discoloration can signal a life-threatening disease (306, 307). There is a case report of a female infant who developed cutaneous lupus lesions while undergoing phototherapy. This rash was demonstrated to be an inherited tendency (308).

Gastrointestinal Risk - Diarrhea has been sometimes associated with phototherapy, but is apparently due to the excess bilirubin, not the phototherapy per se (309, 310). Phototherapy does not appear to affect protein, fat, or energy absorption, although Vitamin B6 has been noted to be decreased in babies undergoing phototherapy (311, 312). Gut transit time appears to decrease with increasing dose of phototherapy, and lactose malabsorption is a rare complication of phototherapy (313, 314).

Carcinogenic & Mutagenic Risk - Bright light in the 350 - 450 nanometer range has been associated with carcinogenic and mutagenic changes. Blue light phototherapy is delivered in the 460 - 510 nanometer range - outside the high risk spectrum. Carcinogenic and mutagenic effects have not been observed with such phototherapy, and a study found no lymphocyte chromosome abnormalities from phototherapy (315, 316, 317).

Endocrine Risk - A study measuring growth hormone (GH), luteimzing hormone (LH), and follicle stimulating hormone (FSH) levels before and after 48 hours of phototherapy showed no impairment of the pituitary gland from phototherapy (318). White range phototherapy was associated in one study with a decreased serum calcium level related to an effect on parathyroid hormone. This effect does not appear to be a major problem (319).

Hematologic Risk - Phototherapy does not appear to affect hemoglobin concentration or oxygen dissociation (320).

E. Precautions for Phototherapy

Temperature Control - Most babies receiving phototherapy are no longer in isolettes, which provide close temperature control. They are often exposed to ambient room temperatures and do just fine. Most phototherapy devices, because of the radiant bulbs (or the occlusive truncal wraps of fiberoptic equipment) add a little heat to the baby's environment. For most babies this is ideal. As a few babies may develop hypothermia or hyperthermia, it is important to monitor the baby's temperature frequently during phototherapy. If the baby becomes abnormally cool or warm, an adjustment of room temperature, moving the treatment site away from drafts, or adding a fan is often sufficient. Occasionally, the baby may need to be placed in a temperature controlled isolette.

Hydration - Most phototherapy protocols call for monitoring of the baby's intake, output, and weight to ensure against dehydration.

Eye Protection - As noted above, it is not really known how much, if any, eye protection is desirable. There is evidence that the visual orientation response test is often compromised even at one month of age in jaundiced babies receiving phototherapy. It is unknown if this abnormality is due to the hyperbilirubinemia, the phototherapy, or the eye protection used during phototherapy which typically puts the baby's visual stimulation on hold for several days. Existing phototherapy protocols call for eye protection ranging from complete occlusion of the eyes to darkening the area around the baby's head to below ambient levels of light while allowing continued visual stimulation. Fiberoptic phototherapy equipment that delivers light to only the trunk of the baby does not require eye protection (321, 322, 323).

Protection from Radiation - Due to the known risk of ultraviolet radiation causing skin burning and possible carcinogenic changes, the FDA requires phototherapy equipment to have a means to shield out UV light from the light source from reaching the baby. This is usually accomplished with a special plastic shield that transmits visual spectrum light, but does not transmit UV spectrum radiation. Due to the theoretical risk of visual range radiation up to 450 nanometers, some protocols suggest covering the baby's genitals with an opaque minidiaper. It is unknown if this is necessary in the clinical setting. Large studies have failed to demonstrate any genetic changes from phototherapy (317).

Cardiovascular Effect - Cardiac output is reduced about 6% during phototherapy, possibly due to the decreased activity of the infant. Also, limb and skin blood flow increases about 40%. These effects should be considered when using phototherapy for a sick infant who may already have compromised tissue perfusion (324).

Neuromuscular Effect - Phototherapy has been associated with a temporary decrease in muscle tone and pull-to-sit response. It is speculated that these effects may be due to separation of the baby from normal neuromuscular stimulation during phototherapy and might be controlled with intermittent stimulation during phototherapy (323).

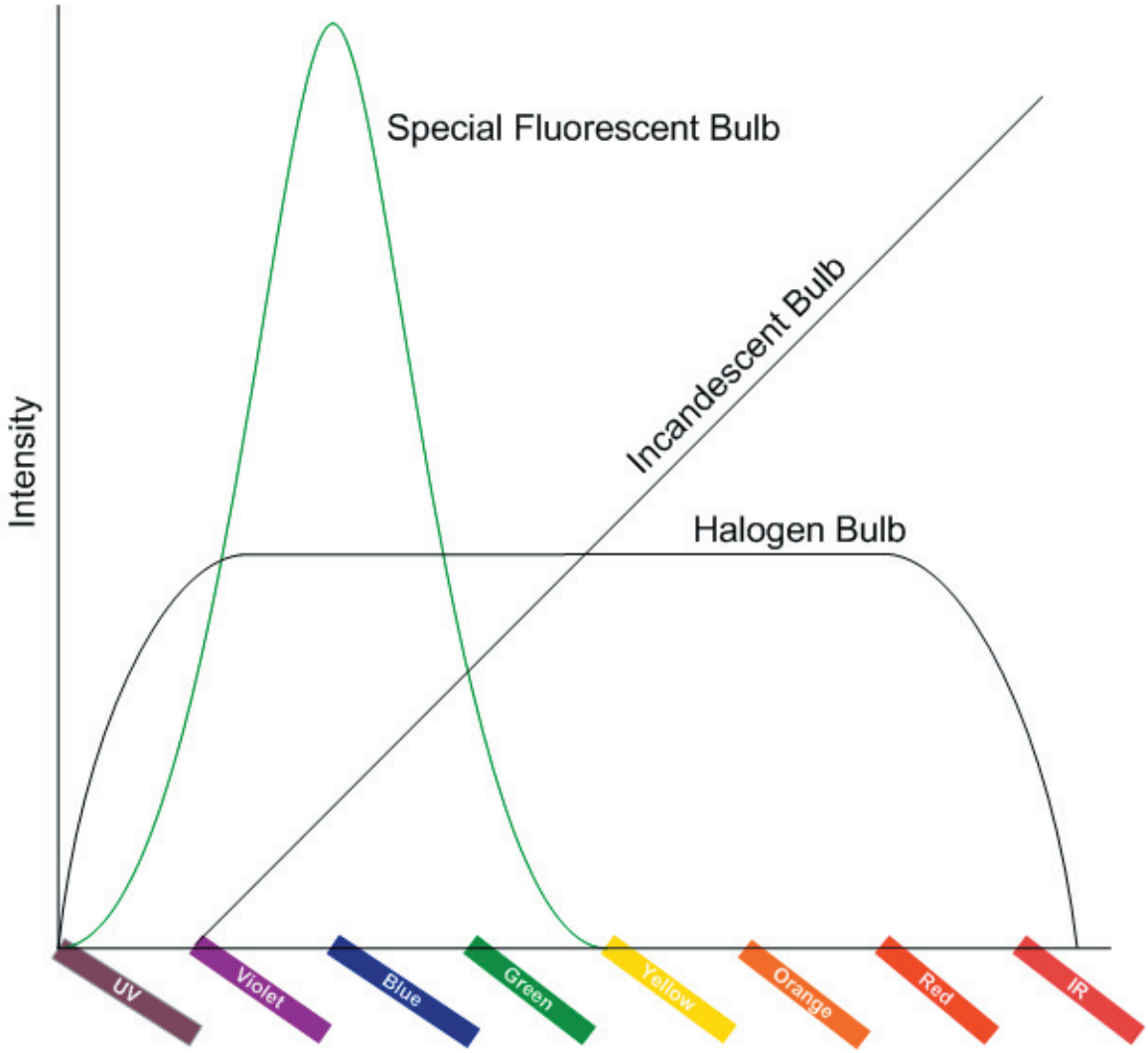


Fig. 3: Light Source Spectrum Output

Behavioral Effect - Phototherapy has been associated with decreased cuddliness, poorer self-quieting, and tremulousness. Separation from the mother has been speculated as a cause of these changes. Intermittent phototherapy allowing time for contact with the mother and home phototherapy have been offered as possible solutions (323).

F. Contraindications

Contraindications to the use of phototherapy are few. Rapid and severe elevation of bilirubin, such as seen in rapid hemolysis, may overwhelm the ability of phototherapy alone to control the bilirubin level. This condition is not a contraindication to using phototherapy, but another treatment modality such as exchange transfusion may be needed as well.

Jaundice may be the first sign of biliary obstruction. Phototherapy will not cure the underlying cause of the hyperbilirubinemia and is contraindicated as the primary treatment. However, phototherapy may be useful for temporarily controlling bilirubin levels until definitive diagnosis and treatment can be carried out.

The rare development of the “bronze baby syndrome” may be a contraindication to continued phototherapy.

The use of phototherapy to prophylactically prevent hyperbilirubinemia has not been shown to be helpful (325).

Since phototherapy yields no measurable change of the immune response, its use is not contraindicated with sepsis (326).

G. Light Source & Dosage

Light Source - Various sources have been used to provide visual range light for phototherapy. Incandescent bulbs have high output in the red range and relatively little output in the blue range; they are relatively ineffective. Halogen bulbs provide a fuller spectrum of light (more blue than incandescents), and have been suggested for use where space is at a premium, such as with incubators or radiant warmers or as the light source in fiberoptic phototherapy devices. The main source of phototherapy light over the years, however, has been fluorescent bulbs. Initially, white fluorescent bulbs, whose light output spans the visual spectrum were found to be effective. Then, blue fluorescent bulbs were developed that deliver a more specific range of light that coincides with the range found to be effective for phototherapy. By using blue bulbs, a doubling of the dose could be delivered. Then, special blue fluorescent bulbs were developed which have twice the blue light output of regular blue fluorescent bulbs. They also last ten times longer (SEE FIGURE 3) (327, 328).

Most modern phototherapy devices use blue or special blue bulbs to deliver the bulk of the phototherapy. They often also use one or more white fluorescent bulbs for two reasons. White light helps to assess the baby's true skin color; they look cyanotic under all blue lights. White light helps prevent the nauseating effect a few health workers suffer with all blue lights (328).

For a period in the mid- 1980s there were several articles advocating the use of green light rather than blue light for phototherapy. This recommendation was based on the theoretic advantage of green range light in the photodecomposition of bilirubin and that green range light is further from the spectrum close to blue light that has been associated with changes in mammalian cell genetics. Subsequent studies indicate that blue light is more effective than green and has fewer side effects. Therefore, green lights never became a popular light source for phototherapy. From 1987 to 1990, one equipment manufacturer offered green bulbs as an option, but received no orders for such bulbs (329, 330, 331, 332).

Light Dosage - In the 1960s the minimum effective dose of phototherapy was found to be 4 microwatts/sq cm/nm fluorescent light bulbs were banked in groups and placed a standard 18 inches from the baby (to clear the isolette) to achieve this dose. One study suggested that increasing the dose could shorten the course of treatment, but that "saturation" was achieved at about 8 - 12 microwatts/sq cm/nm. Subsequently, multi-bulb banks and double banking (lights above & on one side of the baby) were employed to achieve these higher dosages. More studies demonstrated that "saturation" does not really exist, and the higher the dose of light, the more rapid the bilirubin breakdown. Phototherapy equipment has evolved in recent years so that 20 or even 35 microwatts/sq cm/nm can be achieved. Under experimental conditions doses up to 90 microwatts/sq cm/nm have been used with no apparent ill effects (333, 334, 335, 336, 337, 338).

Fluorescent bulbs, the most common source for phototherapy, decay slowly over time. Blue bulbs lose about 20% of their output after 200 hours. Special blue bulbs lose about 20% after 2000 hours. Some equipment manufacturers recommend using a dosimeter after each use to ensure the bulb output is still adequate. Others employ a simple bulb change schedule after so many hours of use as the decay rate is quite predictable (339).

Another evolution of equipment that affects light dose is the surface area of skin that is treated. Traditional phototherapy was delivered with 2 foot long fluorescent bulbs placed over a baby that wore only a minidiaper and eye patches. In this configuration, about 45% of the baby's surface area could be treated with one bank of lights. If the baby's head is shielded from the light to avoid having to use eye patches, the surface area treated falls to about 40%. Fiberoptic devices treat only 10% to 25% of the surface area. Therefore, when calculating the light dose, it is no longer adequate to just measure the light intensity output of the phototherapy device. A more useful measurement is phototherapy treatment units (PTUs), which can be calculated by multiplying the intensity of light provided by the device by the surface area being treated.

One manufacturer of a small surface area device maintains that it matters little how muc skin area is treated as the bilirubin circulates in the blood and will come to the area of skin being treated. In actuality, bilirubin is dynamically distributed in the blood and many tissues. Specifically, it is held in subcutaneous fat where the greater the surface area exposed to phototherapy, the faster will be the treatment. This theory is supported by two pieces of evidence. One comes from the same manufacturer who believes the opposite, and who also points out that the skin area under treatment with their fiberoptic patch returns to a normal, non-jaundiced color as evidence of the effectiveness of their device. What is not mentioned is that the remaining majority of skin surface remains jaundiced as it is not being treated. The other evidence is from a clinical trial comparing a 40% surface area device with a 25% surface area device. Treatment time using the larger surface area device was about half as long as the treatment time required with the small surface area device (340, 341, 342).

Continuous vs. intermittent phototherapy is another variable to consider. Originally, most phototherapy was delivered continuously; theoretically to maximize treatment and minimize the length of treatment needed. It soon became obvious that feeding and nurturing needs must be accommodated during each day, so even the strictest of "continuous" regimens was never truly continuous. As the perceived importance of bonding and visual stimulation increased, and as home phototherapy gained acceptance, the concept of intermittent phototherapy became more popular. Studies have demonstrated that much of the photodecomposition of bilirubin takes place within the first minutes of exposure of light to a skin area. Clinical trials have clearly shown that intermittent phototherapy is as effective as continuous - and far more convenient. Light regimens of 15 minutes on and 15 minutes off, 15 on and 30 off, 15 on and 60 off, and 1 hour on and 4 hours off have all been shown to be as effective as continuous phototherapy (343, 344). Now, most physicians want to see the baby "under the lights" a good portion of the day, but parents are encouraged to intermittently remove their baby from treatment for feeding, cuddling, etc. In home phototherapy, parents are often instructed to turn the phototherapy equipment off at night so everyone can get a good night's sleep.

CHAPTER III. EQUIPMENT

Disclaimer: The authors are associated with the development of phototherapy equipment. Although this involvement gives them a unique expertise in this field, they have also developed equipment design biases, and may not be truly objective when comparing different phototherapy devices.

A. Phototherapy Devices

There are several types of phototherapy equipment from which to choose. They vary by design, light source and portability.

The most common type of hospital phototherapy equipment uses a bank of fluorescent blue and white bulbs (usually from 4 to 8 bulbs) arrayed over the baby. Hospital devices commonly have one overhead bank or an overhead and a side bank of lights mounted in rectangular, metal boxes. These may be attached to a vertical frame that has a wide floor base or may be ceiling mounted. This configuration works well where space is not at a premium. They can be placed over a baby in a bassinet or isolette, and they typically deliver 8 - 12 microwatts/sq cm/nm of illuminance. They are fused and have special plexiglas bulb covers to screen out ultraviolet light. They are often equipped with clocks to measure treatment time delivered, and some have built-in or add-on dosimeters to measure bulb output. Eye protection is required. For many years this type was the primary equipment available and continues in common use today. Manufacturers include Physician Engineered Products, Inc., AirShield, Inc., Olympic, Inc.

A variation on the floor-mounted design that is somewhat less bulky is the single halogen bulb device manufactured by Healthdyne, Inc. Output of this single bulb is low so the treatment rate is lower than with multi-bulb banks. Portable phototherapy equipment came on the scene in 1985 and has become increasingly popular. It was initially intended for use in the home, but has also been found useful in-hospital where rooming-in with the baby's mother is desirable, or where space considerations prevail, or because of the advanced features available only on portable equipment. The features of each model are discussed below.

First generation portable devices have mostly come and gone. The Rocky Mountain Medical Co. was first on the scene with a portable device. Treatment is delivered at 12 - 15 microwatts/sq cm/nm. The unit is quite heavy at 40 lbs, and often requires two people to deploy and set up, but it is portable. Eye protection is required and a dosimeter is recommended. This company has gone out of the business.

Likewise, second generation portable devices have seen their day, but you may encounter one in the field. One was made by Aequitron, Inc. It was smaller and lighter than the Rocky Mountain device. Treatment doses are also in the 12 - 15 microwatts/sq cm/nm range. Eye protection is required; a dosimeter is recommended. This company has also stopped production of its home phototherapy device. E & B Medical Co. also produced a portable device similar in size to the Aequitron model, and it is also no longer in production, treatment doses are similar. Eye protection is required; a dosimeter is recommended.

Physician Engineered Products, Inc. initially produced a portable device similar in size and weight to other second generation devices, but with several design improvements. First, its suitcase style design makes it easy to set up. The unit deploys from a hinged back into a triangular configuration that is more stable. It sets up in 20 seconds, and there are no loose parts to lose. Ballasts are in the bottom, so no tip-over switch is needed. Second, this Home BiliLight utilizes a unique eye protection face screen that avoids having to use eye patches that may slip off. A semi-darkened head chamber is created that allows continued visual stimulation and eye contact. Third, this is the only device with a built-in temperature control system. If the baby chamber temperature is less than 75 degrees F, a warming unit in the device activates until the temperature exceeds 75 degrees F. If the chamber temperature exceeds 98 degrees F, the lights (which add 6-7 degrees) will flash, and then turn off to warn the caretakers that the environment is too warm. Fourth, the treatment dose is increased by about 50% to 20 microwatts/sq cm/nm. Although the surface area treated falls from 45% to 40% because of the face screen, the markedly increased light dose yields an overall increase of phototherapy treatment units from about 600 PTUs with other portable fluorescent units to 800 PTUs with this device.

A more recent development in phototherapy equipment is the fiberoptic devices. These use a single halogen bulb light source that is directed through a fiberoptic cable to a patch that applies to the baby's skin. These devices have the advantage of not having to use eye protection as the light is enclosed behind opaque coverings. They are also the lightest weight devices and are quite portable. The manufacturers advertise the advantage of providing continuous phototherapy, but as noted above, this is no advantage over intermittent phototherapy and is a relative inconvenience. One disadvantage is that the baby is continuously tethered to the light source by the fiberoptic cable, restricting where the

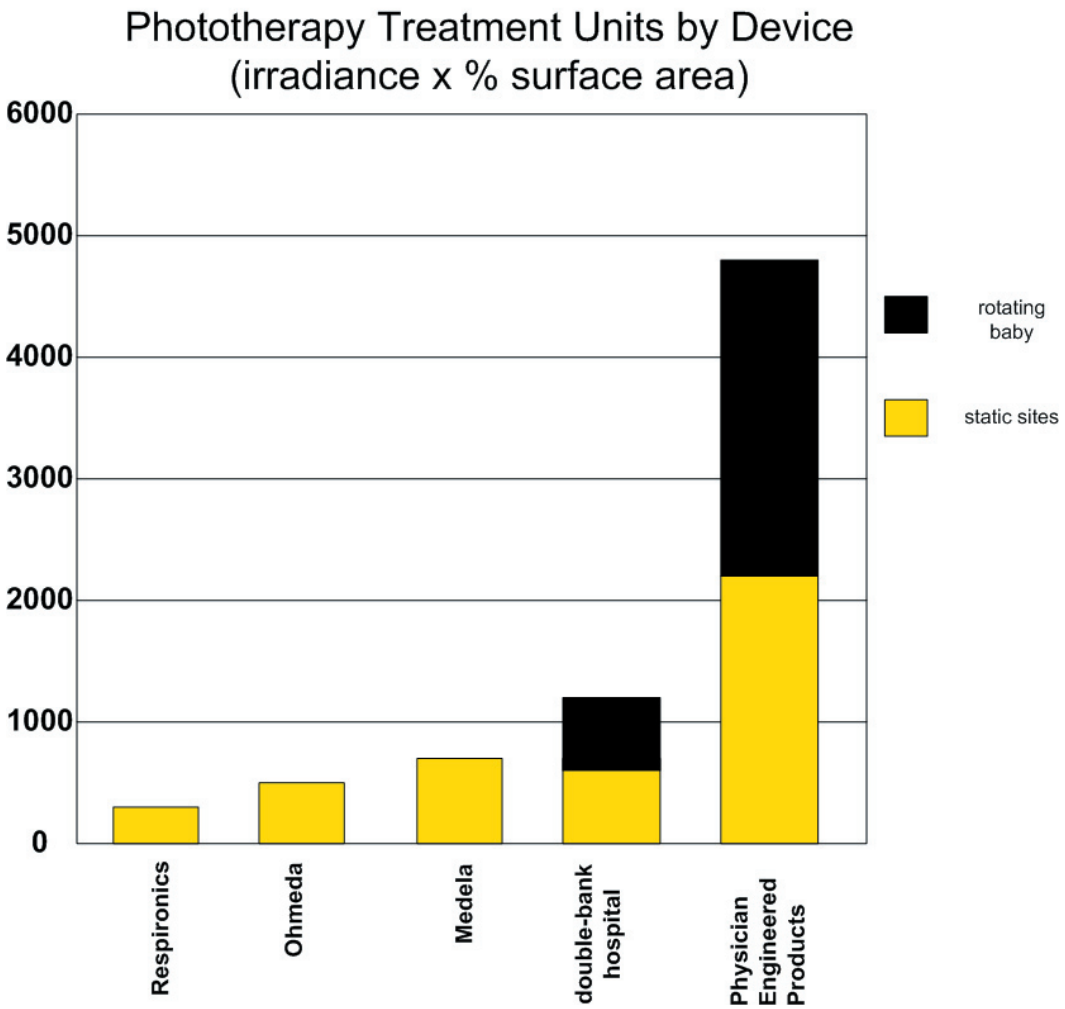
baby can be held, fed, and cuddled. The biggest drawback to fiberoptic devices is the low treatment level provided. The original Wallaby (now Respironics) device provides only 7 - 10 microwatts/sq cm/nm to 25% of baby's skin surface - yielding only 175 -250 PTUs. The Ohmeda device contains a rheostat that provides up to 35 microwatts/sq cm/nm, but to only 10% of the baby's skin surface - yielding 350 PTUs. In the early 1990s, most other devices provided 2 to 3 times as many PTUs as these fiberoptic devices, and the treatment delivered by one device was up to 4.6 times greater (SEE FIGURE 4). When a home care provider studied length of treatment they found that while using the most popular devices, the suitcase fluorescent style took about half as many days to bring the bilirubin levels down to desired levels as the fiberoptic style (SEE FIGURE 5) (360). In recent years, the fiberoptic device manufacturers, have increased the irradiance, but generally at the expense of less body surface area covered, so the PTUs remain little changed and much lower than other devices.

In the most recent advances in portable phototherapy, Physician Engineered Products began producing the Ultra BiliLight – a third generation device. It has several attractive features: 1) double the irradiance to 2400 PTUs (4 to 8 times the fiberoptic devices and at least twice the irradiance of double-banked hospital units); 2) shorter treatment times; 3) half the weight (14 lbs.).

B. Photodosimeters

Photodosimeters come in a variety of styles. Some are designed to only measure in the blue range specific to phototherapy. Accuracy varies also, with good quality devices costing about $500. Originally, phototherapy devices recommended using a photodosimeter on a regular basis to guard against bulb output drop-off. More recently, the increase in irradiance in newer models eliminates the need for a dosimeter. Instead, the Physician Engineered Products device uses a protocol of keeping track of the hours burned for each set of bulbs. Since the rate of bulb output decay is known, a simple schedule of bulb replacement after 2000 hours of use eliminates the need for an expensive dosimeter (345).

Fig. 4: PTUs provided by different devices.



Type of Light	Number of Patients	Beginning Bilirubin Level	Average Age (hours)	Average Treatment Time (days)
Older PEP Model	1,047	16.7 mg/dl	70	2.5
fiberoptic light	10	13.8 mg/dl	72	4.4

Fig. 5: Treatment times.

C. Bilirubinometers

A bilirubinometer is a piece of equipment needed to monitor the rise and fall of the baby's bilirubin level. Standard hospital lab bilirubinometers provide the standard of accuracy needed in this environment. Spectrometric devices are as accurate as the diazo method, are simpler to run and require a smaller blood sample. Several brands of transcutaneous bilirubinometers are now on the market which do not require drawing a blood sample. They are considered accurate enough for screening purposes, but not for day-to-day monitoring of a baby with hyperbilirubinemia. To date, although this may change as technology develops, the standard of care is to monitor hyperbilirubinemic babies with serum bilirubin or whole blood bilirubin measurements (346, 347, 348).

CHAPTER IV. PUTTING IT ALL TOGETHER

A. Typical Scenario

Most commonly, hyperbilirubinemia is recognized on the second or third day of life as the baby's skin and sclera appear jaundiced. A few hospitals routinely check bilirubin levels at this time, but most do not. Bilirubin levels are often checked only if there is suspicion of hyperbilirubinemia. If the baby is premature or has other medical problems, the physician may wish to monitor the baby's bilirubin before it appears jaundiced, and begin treatment at an earlier point than if the baby is normal size and has no other medical problems.

Since many newborns are discharged from the hospital on the first or second day of life, the jaundice that occurs in about 8% of them may not be recognized until they are at home. Because of this timing, some physicians like to see their babies during the first week of life in the clinic or at a home visit. Some jaundice is first recognized by the parents who may call it to the attention of their baby's doctor. Clearly, some jaundiced babies are now going unrecognized as they are not being seen by a health professional during the critical time frame that they are jaundiced. Presumably, as most babies are otherwise healthy and seem to tolerate the rise and eventual fall of their bilirubin levels without treatment, there are no reports that this nonrecognition has been a clinically significant problem. It is somewhat worrisome, however, that subtle neurologic changes may be occurring due to unrecognized and untreated hyperbilirubinemia.

As noted above, the point at which hyperbilirubinemia becomes clinically significant varies with the baby's size. If a baby's bilirubin level is approaching or at clinically significant levels, the attending physician is likely to launch a diagnostic evaluation to look for a systemic, hematologic, or hepatic cause of the hyperbilirubinemia. This evaluation typically includes:

1. Obtain a history to assess for maternal diabetes, family history of neonatal jaundice, known blood incompatibility: Rh negative or type O mother, toxemia of pregnancy, rubella-susceptible mother, premature delivery, perinatal stress or hypoxia at delivery, or a mother with a positive serology.

2. Perform a physical exam to evaluate jaundice, infant size, hydration level, signs of a hemorrhagic disorder, plethora, hematomas, liver abnormalities, congenital abnormalities, respiratory distress, central nervous system depression, cataracts or chorioretinitis.

3. Sick appearing infants are assessed for possible infection with cultures.

4. ABO and Rh typing and Coombs' test are done. Testing for rare blood type incompatibilities is done if the Coombs' test is positive indicating a hemolytic disease, but there is no ABO or Rh incompatibility. Only a type O mother will make antibodies against the blood of a type A or B infant, and only an Rh negative mother will make antibodies against the blood of an Rh positive baby.

5. Conjugated and unconjugated bilirubin levels as well as other liver function tests are done to assess for liver or biliary obstruction diseases.

6. Other hemolytic causes are evaluated by performing a complete blood count, platelets, reticulocyte count, and red blood cell morphology smear.

7. Bilirubin binding capacity is assessed with a serum albumin level.

8. Optionally, antenatal infections such as toxoplasmosis, rubella, cytomegalic disease, herpes, and syphilis (TORCH diseases) can be screened for with an IgM antibody test.

If the diagnosis is made of a rare biliary obstruction, the physician may initiate phototherapy until definitive correction of the obstruction can be carried out. If hemolysis is diagnosed, the first-line treatment is likely to be phototherapy. If the hemolysis is too severe or rapid, exchange transfusions or hemoperfusion may be carried out in addition to phototherapy.

The majority of jaundiced babies will have no obvious cause for their hyperbilirubinemia and will be diagnosed to have physiologic jaundice. Under these conditions, and if the baby has no other risk factors, the physician is likely to tolerate a higher bilirubin level before initiating treatment with phototherapy. It is not uncommon for the bilirubin to be over 15 mg/dl in a baby over 2500 grams, or over 10 mg/dl in a baby in the 2000-2500 gram range before phototherapy is started.

The physician then decides whether to treat the baby in-hospital or at home. This decision hinges on several factors: present location of the baby and mother, presence or absence of coexisting medical problems, desires and reliability of parents, availability and reliability of a home program, cost and insurance coverage, and physician and/or hospital income considerations. Studies indicate that in most communities 80% of jaundiced babies can be treated at home. For a variety of reasons (**see The Phototherapy Team**), in many communities most babies are still treated in-hospital.

If the baby is treated in-hospital, it may be treated while rooming-in with the mother, or it may be treated in the nursery under supervision of the nursing staff. If the baby is treated at home, the equipment and training of the parents may be provided by home care dealers, home nursing services, or clinic outreach services. Commonly, a home care dealer will supply the phototherapy equipment and have one or more nurses or respiratory therapists cross-trained as phototherapists. Another common scenario is to have the local home nursing service provide the in-home training and subcontract with a home care dealer to provide the equipment.

Typically, the home phototherapy provider receives a call from a clinic or hospital nurse or discharge planner requesting phototherapy service be started the same day. Hopefully, the parents' desires and abilities will have been assessed by this point. The phototherapist arranges to meet and train the parents to use a standard protocol for overseeing the phototherapy. An informed consent form is signed. A location is chosen for the equipment, and it is set up on the first visit, and treatment is begun.

The protocol to be followed by the parents (often provided by the equipment manufacturer or the attending physician) usually calls for monitoring of the baby's temperature, weight, intake, and output at regular intervals throughout the day. Eye protection is monitored. Treatment may be interrupted for feeding, cuddling, sleeping, etc.

The parents bring the baby to the clinic each day for a clinical assessment and a bilirubin (and possibly a hematocrit) check, or these may be done in the home by a visiting nurse/phototherapist.

When the bilirubin level drops to below 7-10 mg/dl, treatment is often discontinued. Depending on the baby and the equipment used, it may take 2 to 6 days to achieve this level. Average treatment time is 3 days (349, 350).

The phototherapy equipment is cleaned between uses. Some devices require a dosimeter check between each treatment. Generally, phototherapy equipment requires little maintenance.

B. The Phototherapy Team

A primary objective of the conscientious phototherapist is to satisfy the needs of the members of the phototherapy team: the baby, the parents, the physicians, the nurses, the lab techs, and you, the phototherapist.

The baby: depends for several days of its new life on other team members; requires adequate nutrition, temperature control, sleep, bonding, and nurturing; deserves to be in a safe and loving environment.

The parents: need comfort and reassurance that the phototherapy is safe and effective; deserve to have their new life with their baby disrupted as little as possible; need to have time to be with their baby; have a right to influence (but probably not control) how the phototherapy is carried out; may have a need to participate or avoid participation in their baby's treatment; deserve to have their financial needs considered.

The physicians: are ultimately responsible for the outcome of the phototherapy decisions; ultimately decide what phototherapy program to use; need to have confidence in the team members; need to have confidence in the phototherapy service being provided; usually wish to be "in the loop" as much as possible; may need to be educated to the pros and cons of home vs. hospital programs; deserve up-to-date information about equipment options; may have unspoken personal, clinic, or hospital financial considerations that influence which phototherapy program they prefer.

The nurses: if responsible for hospital discharge planning or clinic or hospital patient care, need a reliable phototherapy service with a quick response and after-hours availability; need to coordinate screening/teaching/monitoring duties with the service provider; if responsible for home care, need all of the above plus usually a contractual relationship with the phototherapy service.

The lab techs: need coordination with the phototherapy service to provide lab results to the physician in a timely manner; may need a financial agreement to simplify billing.

You, the phototherapist: work under physicians' orders as an extension of their physicians' legal authority; deserve the satisfaction of being associated with a high-quality phototherapy service; have a duty to provide your service with competence and professionalism; should expect adequate compensation for your service.

C. Pitfalls - Recognition, Avoidance, & Cures

Problems with the Baby:

1. Problem:
Bilirubin level goes up instead of down with treatment.

Recognition:
Daily bilirubin checks climb. Early in treatment this

sometimes happens as bilirubin is being created faster than the phototherapy is breaking it down. The physician will decide when it is climbing to a risky level.

Avoidance:
Your best insurance is to use high-dose equipment and ensure the baby is undergoing treatment a significant part of each day. Adequate hydration also helps.

Cures:
Increasing light intensity may help. Some babies still require exchange transfusion in addition to phototherapy. A cause of hyperbilirubinemia that is not cured with phototherapy may need to be reconsidered. In rare cases, breast feeding may need to be discontinued, particularly in delayed hyperbilirubinemia.

2. Problem:
The baby gets hypothermia.

Recognition:
Temperature checks every several hours while undergoing phototherapy; temperatures under 96 degrees F.

Avoidance:
Choose a treatment site that is warm enough (70 degrees F is usually good) and away from drafts. Be wary of tiny babies. Use equipment that provides warming for the baby.

Cures:
Increase the ambient temperature by raising the room temperature or moving to a warmer location. A few babies may require an isolette.

3. Problem:
The baby gets hyperthermia.

Recognition:
Temperature checks every several hours while undergoing phototherapy; temperatures over 100 degrees F.

Avoidance:
Avoid unusually warm treatment sites. Be wary of large babies. Use equipment that controls for excessive warmth.

Cures:
Decrease the room temperature or move to a cooler location. Place a fan near the baby. Leave the baby out of treatment for periods of time. A few babies may need an isolette.

4. Problem:
The baby loses weight.

Recognition:
Intake, output, and weight monitoring every day. Some weight loss is common during the first few days of life. The physician will decide when the weight loss is significant and abnormal.

Avoidance:
Provide adequate feeding opportunities during treatment; observe for diarrhea.

Cures:
Increase feedings; supplement breast feeding; consider a lactose-free formula if having diarrhea.

Problems with Parents:

1. Problem:
Fear, unhappiness or anger about phototherapy.

Recognition:
Parents make overt statements or appear anxious or hostile to caregiver for no apparent reason.

Avoidance:
Demonstrate at the outset that you are sympathetic to the unexpected disruption in their lives at a time when first contacts with their new baby are so important to them. Reassure the parents about the usually benign nature of hyperbilirubinemia and phototherapy. Indicate a desire to make the treatment course as easy and convenient as possible.

Cures:
Gently confront their emotions by giving them permission to feel the way they do. Explain that it is normal. Do not take their response personally. Demonstrate a calm confidence that will serve to reassure them.

2. Problem:
The parents are unable to cope with home phototherapy.

Recognition:
The parents are not following prescribed protocol; their questions indicate poor understanding of the protocol and their duties; their attitude indicates inappropriate concern or discontent; they barrage you with phone calls.

Avoidance:
The parents should be well screened before phototherapy is begun. About 90% of parents can succeed very well with home phototherapy; those who cannot are usually easily recognized by the physician. Some populations are at high risk for failure - e.g., drug abusers. Occasionally, you may need to consult the physician if your visit(s) with the parents raises concerns for them or you.

Cures:
Careful reinstruction may be successful. Keep the physician informed. The occasional baby will need to be readmitted to the hospital to receive phototherapy if it cannot be safely performed at home.

Problems with Equipment:

1. Problem: Phototherapy bulbs burn out during treatment.

Recognition:
Staff or parents call you.

Avoidance:
Regular bulb replacement at recommended intervals usually avoids this problem. Fiber-optic devices were prone to unexpected burn out, but this problem is being addressed.

Cures:
With most fluorescent bulb devices, suboptimal but adequate treatment is delivered with two bulbs out. Bulb replacement is usually not an emergency.

2. Problem:
Fiberoptic cable breakage.

Recognition:
Light intensity falls off when measured with dosimeter.

Avoidance:
Minimizing cable motion during treatment prolongs the life of the rather expensive cables.

Cures:
Replace cable.

3. Problem:
Eye patches come off.

Recognition:
Protocols call for frequent care giver observation to ensure eye protection.

Avoidance:
Some brands stay on better than others. Those with adhesive work well, but may cause a rash.

Cures:
Replace patches as needed. Use a face shield instead of eye patches.

4. Problem:
The baby scoots out from under face shield.

Recognition:
Frequent observation of the baby is required.

Avoidance:
Blocking the baby's feet with a towel usually prevents backwards scooting.

Cures:
Reposition the baby. Adding eye patches is rarely needed.

5. Problem:
Chafing or rash from fiberoptic device skin patch.

Recognition:
Rash develops under patch site.

Avoidance:
It is hard to predict which babies will develop this infrequent problem.

Cures:
Change patch position if possible.

CHAPTER V. DEVELOPING A HOME PHOTOTHERAPY SERVICE

A. Hospital & Home Programs

Phototherapy for neonatal hyperbilirubinemia was for many years only delivered in-hospital. In many areas of the U.S. today it still is the most common reason for prolonged hospitalization in term neonates. As the relative ease and safety of phototherapy became established, it began in the mid-1980s to move into the home care setting. The theoretical disadvantage of this trend is that the baby is now being treated in a less controlled environment -less controlled temperature, uncontrolled caretaker oversight, and diminished professional clinical observation. In a well-run home phototherapy program about 4% of the babies will have to be readmitted to the hospital for a variety of reasons ranging from a coincidental illness to hypothermia to parental inability to succeed with a home program.

The advantages of home phototherapy, however, are being increasingly appreciated:

1. Parents generally much prefer having the baby at home - especially if treatment in-hospital means a readmission after an early discharge as is so often the case today. Their schedules are less disrupted. Breast feeding is facilitated. They have more time with their baby. They have the satisfaction of participating in their baby's treatment.

2. Costs are much less - usually one half to one third the cost of hospital treatment.

3. Clinical results are similar to hospital treatment. Although one study indicated the duration of treatment was longer at home, most studies indicate similar treatment times. With the newer, high dose home equipment, treatment at home is actually shorter than standard hospital treatment times. Complications have been very few.

4. Babies who are treated at home breast feed longer and have lower cortisol levels even up to 3 months of age than those treated in the hospital (351, 352, 353, 354, 355, 356, 357, 358).

Medical and pediatric societies have selection protocols for home phototherapy. The suggestions are that home therapy is appropriate for babies who are:

1. Full-term & over 24-48 hours old;

2. Over 5 lbs (2270 grams);

3. Otherwise healthy with a negative diagnostic evaluation for significant disease;

4. Moderately hyperbilirubinemic in the 14 - 18 mg/dl range;

5. Blessed with competent parents (353, 359).

B. Personnel Needs

Personnel requirements are very much dependent on the type of program you develop. Another factor is that the programs sometimes evolve as time goes along and physician confidence builds. The two most popular types of programs are the "full nursing" and the "clinic visit" scenarios. With the initial program, successes come most easily with the clinic visit style.

The typical first day of in-service treatment involves receiving a call from the physician's nurse that the mother and the baby need to be seen at 3 p.m. this Monday afternoon. The phototherapist then travels to the home and spends approximately 45 minutes educating the mother on the dynamics of jaundice. The phototherapist and the mother set up the equipment and begin treatment, paying special attention to the details of the mother's role in the baby's treatment.

Most device manufacturers provide a record sheet that helps guide the parents through the treatment. This record sheet serves to discipline the mother into paying continued close attention to the details of the baby's treatment. It also provides a written record of the amount of treatment, the baby's temperature, food intake, bowel output, etc. In the vast majority of situations the home is the perfect place to treat the baby. However, the role of the phototherapist is to view the home situation carefully and reaffirm that this is a stable home and suitable for the baby's treatment.

The "clinic visit" scenario involves the phototherapist going to the home on that Monday and doing the in-service-education with the mother as described above. On Tuesday, the mother and the baby take the completed record sheet and travel to the doctor's clinic. The physician then is able to stay in the clinic loop and has a chance to examine the baby and interact with the mother. If the phototherapist has done their job effectively, the mother can now communicate intellectually about infant jaundice and the physician is positively impressed with the program.

The physician can review the record sheet and can feel confident that the mother is being attentive and the therapy is proceeding as planned. Additionally while in the doctor's clinic the doctor's nurse does the blood

draw and the doctor's lab does the blood work to determine the bili level.

This clinic visit scenario has elements that should be recognized. First the physician can continue to participate and have contact clinically with the patient. The physician can be involved financially. That is by receiving clinic visit fees and lab charges. It should be pointed out that this reimbursement is deserved because the ultimate responsibility for the care of the patient lies with the physician.

During subsequent days of therapy, the mother and the baby continue to see the physician daily. The phototherapist maintains close telephone contact with the mother and will perhaps stop in if they happen to be "in the neighborhood." When beginning a home phototherapy program this scenario tends to be more successful. The physician has a chance to review their decision to treat the baby at home the very next day during the clinic visit. If this visit goes well and the baby's bili level is responding to the therapy, you are off and running.

The "Full Nursing" scenario involves the phototherapist, in this case a nurse. The nurse does the first day setup of the equipment, begins the therapy, educates the parents on infant jaundice and observes the home conditions. Then daily visits thereafter to the home to check with the mother and baby. During the visit, the nurse does the heel-stick blood test on the baby and brings the sample to a lab per the physician's request. Utilization of this style of program tends to separate the physician from their patient, but it does enable the mother to avoid travel involved with either the clinic visit scenario or leaving the baby in-hospital for treatment. A new mother, especially a breast-feeding mother, would travel 3 to 4 times a day to be with the baby if it were being treated for hyperbilirubinemia in the hospital.

It also should be said that programs that start with the "Clinic Visit" scenario tend to become hybrid programs. That is to say that as the physician refers and has good results, babies will be referred on Friday and the clinic is closed on Saturday and Sunday. At this point the physician will ask the phototherapist to see the baby at home on Saturday and Sunday, but will want to see the baby in the clinic on Monday. On Saturday and Sunday the mother can either take the baby to a lab or the nurse phototherapist may do the blood draw.

While initially the "Clinic Visit" tends to be handled by health care providers that are trained as phototherapists, these health care professionals have been involved with home phototherapy from the beginning. This is a result of equipment being handled by home health care companies and durable medical equipment suppliers. These types of organizations have always had strong involvement in home care and respiratory therapy. Therefore, most have health care professionals on staff.

Many organizations begin using existing RT staff for providing the home phototherapy service to the community and as the program develops they add a part-time nurse to handle the blood draw and the expanded program.

C. Equipment Needs

Researching and choosing the equipment you will use in your program should take place soon after your decision to start a program. Becoming aware of the styles and types of phototherapy units can typically take 2 to 3 months. The best source for finding the names of the manufacturers is by looking in one of the many buyers guides. A call to the manufacturers will bring the typical flow of the product information.

Additionally, many manufacturers will provide clinical information to support features of their particular unit. Another good opportunity to evaluate equipment is at one of the many national medical trade shows held every year. This enables one stop, same day comparisons.

During the equipment selection the most important thing to look at is the device's ability to provide a stable temperature environment for the baby, the need for, and the type of, eye protection, the ease of use for the mother and most importantly, one that provides the best therapy.

The costs of a home phototherapy program can be as little as $1900, including disposables and printed material costs.

Most often organizations begin with 2 units. This raises the capital investment to between $3800 and $5500. Operating a program with just one unit runs the risk that after you've done your marketing and you get the first referral, then the second referral comes and you must turn it down. Having to turn down the first referral a doctor gives you is not a desirable way to start a relationship with a referring physician.

There are formulas available that provide a guide for the number of units required for your program. This formula works only if you know approximately how many referrals you will receive in the first year. A good example is an HMO contract. HMOs know how many births will occur within their population so it can

remove much of the guess work. In real life, programs tend to start with a minimum of 2 units per location and add units as needed.

D. Reimbursement

Reimbursement varies greatly from state to state and from insurance company to insurance company. For the "Clinic Visit" scenario, the average national charge for equipment rental is $100 per day, and this includes the disposables.

A new trend is charging $170 for the first day and $100 for every day thereafter. The "up" charge on the first day covers the implied "set up/in-service" the first day. Insurance companies are used to this and respond to this type of billing quite well. Another innovative technique is to bill a one time, flat rate whether it takes one day or five days of treatment. Billing a third party for the "Full Nursing" scenario is essentially the same except for charges being higher to cover the nursing visits.

E. Marketing

Many different marketing approaches have been taken when setting up or expanding a home phototherapy program.

Marketing to natural childbirth class teachers provides another opportunity for referrals. Take the instructors to lunch to build an awareness of your program. Perhaps they will give 15 minutes of class time to describe infant jaundice, phototherapy and the options available. Don't forget to develop a handout summarizing your service.

In smaller markets, offering a 'new' medical service such as home phototherapy may land you an article in the local newspaper. Be sure that the medical reporter is aware of your organization's programs and new offerings.

Home phototherapy programs have been successfully started after initial rejection by the physician community. By using radio and television advertising it is possible to build an awareness of the home treatment alternative. With mothers asking about home treatment it is difficult for physicians to avoid the issue.

If there are HMO groups active in your area, be sure to contact them. They tend to be tough negotiators but they can be a steady source of referrals.

Successful programs all begin with a strong clinical base. Building a strong relationship with a referral source is only possible after a certain comfort level is achieved. A course such as this may be a clinical refresher or a crash course on hyperbilirubinemia to prepare the Phototherapist, but it ultimately may be used as a marketing tool. It shows professionalism in an individual that has shown the effort to become certified. For an organization to have its in-service people certified reveals a real commitment to the program. Professionalism is the thing that we all strive for; hopefully this course can make a contribution towards attaining that goal.

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