Phototherapy
Research Study Tool

Lübeck, April 2017
This tool will continue to grow and change with new material. We hope you find it to be helpful.

We have compiled studies that are referenced in multiple PowerPoints and webinars into one template to make it easier to find the reference you are looking for.

The next slide is the table of contents where we have identified major topics within jaundice management then grouped the research studies into these categories.

The numbers next to each category are hyperlinked to bring you directly to the article slide. For example, there are 6 studies within the tool that talk about the first category “Accuracy”. The “back” hyperlink on the study slide will take you back to the table of contents.

Each study slide includes short information on the research conducted: Objective, result, and conclusions plus a link to read more or purchase the full study.
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## Categories

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Objective: To investigate the association between neonatal phototherapy use and childhood cancer.

Result: Although phototherapy use was associated with increased cancer rates (particularly nonlymphocytic leukemia), control for confounding variables eliminated or attenuated the associations.

Conclusion: Nonetheless, the possibility of even partial causality suggests that avoiding unnecessary phototherapy may be prudent.


https://www.ncbi.nlm.nih.gov/pubmed/?term=Retrospective+Cohort+Study+of+Phototherapy+and+Childhood+Cancer+in+Northern+California
**Objective:** This article reviews the parameters that determine the efficacy of phototherapy, briefly discusses current devices and methods used to deliver phototherapy, and speculates on future directions and studies that are still needed to complement our presently incomplete knowledge of the facets of this common mode of therapy.

**Result:** The therapeutic efficacy of phototherapy is dependent primarily on the following factors: the spectral qualities (wavelength range and peak), intensity of light (irradiance), exposed body surface area (BSA), skin thickness and pigmentation, the total bilirubin at clinical presentation, and duration of exposure.

**Conclusion:** Phototherapy is one of the most common medical interventions for most term and preterm infants with neonatal hyperbilirubinemia. Furthermore a better understanding of the photobiology, characteristics of the devices employed for phototherapy, the efficacy and safety of phototherapy applications, and improvements in spectroradiometers and phototherapy devices are all necessary for more predictable and improved clinical practices and outcomes.
Objective: The objective of this study was to search for a “saturation point” (ie, an irradiation level above which there is no further decrease in total serum bilirubin [TsB]). This was a prospective randomized study performed in the NICU of Aalborg Hospital, Denmark.

Result: A highly significant linear relation was seen between light irradiance and Δ TsB0–24 (%).

Conclusion: During phototherapy with LED, we recommend that the distance from the light source to the infant should be reduced as much as possible to obtain an optimal light irradiance, when intensive phototherapy is needed in late preterm and term infants. With neoBLUE LED, this is the distance from the light source to infant of ~12 cm, or an irradiance up to 55 mW/cm²/nm. The small positive effect of formula supplementation is relevant if a maximal TsB fall is essential and may be used with due support of breastfeeding.
Objective: To see whether commercially available phototherapy systems produce sufficient irradiance over the surface area of the neonate. They are tested: Hill-Rom Microlite, Draeger Phototherapie 800, Medestime Duo, Natus neoBLUE, Bilicrystal IV2 (top unit), Bilicrystal IV2 (under unit), Medela Bilibed, LED Bilibed

Result: A 10-fold difference in peak central irradiances was found between the systems tested, with a fourfold to fivelfold difference in effective irradiance to the baby surfaces. Although work published over 20 years ago showed that levels of irradiance should reach 2 mW/cm² to achieve optimal effectiveness, some of the commercial systems tested do not appear to achieve this level.

Conclusion: Purchasers of neonatal phototherapy systems need to take into account whether the systems will produce sufficient irradiance over the area to ensure maximal effect, to keep the treatment time to a minimum.
Managing the jaundiced newborn: a persistent challenge

Summary: Pediatrists and family physicians deal regularly with jaundiced newborn infants who emerge unscathed from their transient exposure to an elevated serum bilirubin level. Yet, despite published guidelines for the management of neonatal jaundice, there are rare infants in whom bilirubin encephalopathy develops. The aim is to help clinicians identify and manage jaundice in the newborn, intervene when appropriate and, when possible, prevent bilirubin-induced brain damage. It would be ideal if the published guidelines for the management of hyperbilirubinemia, including treatment with phototherapy and exchange transfusion, were based on estimates of when the benefit of these interventions exceeded their risks and costs.

Conclusion: The management of jaundice in the newborn is a challenge because of the desire to avoid the devastating outcome of kernicterus while minimizing testing and treatment in the majority of newborns, who will do perfectly well with no interventions for jaundice. By simply combining the gestational age with the predischarge, hour-specific bilirubin level (transcutaneous or total serum level), one can, with considerable confidence, quantify the risk of severe hyperbilirubinemia in most newborns.
Conclusion:
Kernicterus is devastating and completely preventable condition when severe hyperbilirubinemia is recognized early and treated aggressively. Because prevention is the key, clinicians need a systematic approach to identify the infant who may develop severe hyperbilirubinemia, acute bilirubin toxicity, and kernicterus. A simple start to prevention of kernicterus should include use of the “JAUNDICE” mnemonic to identify infant risk factors, promotion of successful breastfeeding in both the hospital and in the home, and more rigorous use of the hour-specific bilirubin nomogram. Making a 2- to 3-day follow-up appointment is essential for all infants prior to discharge from the hospital. Recognition of mild prematurity with lengthened hospital stay is prudent. Further research is required regarding the cost-effectiveness and generalizability of universal TSB screening and use of the hourspecific nomogram in all healthy term and near-term infants. Hopefully, we can truly make kernicterus a “never event.”
Summary:
A newborn male infant is brought to the pediatrician's office with pronounced jaundice and a total serum bilirubin level of 19.5 mg per deciliter. Phototherapy is considered. In term and late-preterm infants, phototherapy is typically used according to guidelines that take into account the total serum bilirubin level, gestational age, postpartum age, and the presence or absence of specific risk factors.
Objective: This paper considered the accuracy of the devices used to monitor the output of phototherapy sources used to treat neonatal hyperbilirubinemia.

Result: Specific meters investigated included a GE Biliblanket Light Meter II, a NeoBLUE radiometer and a Bio-TEK radiometer 74345 device.

Conclusion: The paper highlights the need for accurate measures of spectral irradiance from phototherapy devices in order to ensure the light levels to which the neonate is exposed are safe and effective.

Gartner LM


Objective: This article report about the context between breastfed infants and the late-onset, prolonged neonatal jaundice

Conclusion: Of even greater concern is that 50 years have now passed and there has been very little further study of the association between human milk feeding and prolonged neonatal jaundice, despite continued clinical concern
The natural history of jaundice in predominantly breastfed infants.

Objective: Breastfed newborns are more likely to develop prolonged hyperbilirubinemia than those fed formula, but the prevalence of prolonged hyperbilirubinemia in a largely white, North American breastfed population is unknown. In this population, we documented the natural history of jaundice and the prevalence of prolonged hyperbilirubinemia, and we evaluated the utility of assessing the cephalocaudal progression of jaundice in office-based practices.

Result: There was a strong correlation between the TcB level and the jaundice zone score, but there was a wide range of TcB levels associated with each score.

Conclusion: Practitioners can be reassured that it is normal for 20% to 30% of predominantly breastfed newborns to be jaundiced at age 3 to 4 weeks and for 30% to 40% of these infants to have bilirubin levels ≥5 mg/dL. The jaundice zone score does not provide an accurate assessment of the bilirubin level, but a score of zero (complete absence of jaundice) suggests that the level is unlikely to be >12.9 mg/dL, whereas a score of ≥4 usually predicts a level of ≥10 mg/dL.
Treatment of jaundice in low birthweight infants

Objective: Exchange transfusion and phototherapy remain the staples of intervention for the jaundiced newborn. Clinical management of the jaundiced low birthweight infant is discussed.

Result: “No prospect can be entertained that this light treatment will prove a substitute for exchange transfusion in the erythroblastotic infant with active haemolysis, but the method may be turned to clinical advantage in controlling the level of serum-bilirubin in cases of jaundice of prematurity.” It would be no exaggeration to say that phototherapy has succeeded beyond their wildest dreams. Just how effective it has been can be gauged from the impact it has had on the number of exchange transfusions performed for hyperbilirubinaemia10,11 (fig 1), and nowhere has this difference been more dramatic than in infants weighing < 1500 g.
Is the light-emitting diode a better light source than fluorescent tube for phototherapy of neonatal jaundice in preterm infants?

Mohammadizadeh, Eliadarani, Badiei Z.

Objective: Light-emitting diodes (LEDs) are light sources recently used for phototherapy in neonatal jaundice. We compared the efficacy and safety of LEDs with fluorescent phototherapy in the treatment of indirect hyperbilirubinemia.

Methods: This controlled trial was conducted on preterm infants hospitalized in neonatal intensive care unit of Shahid Beheshti Hospital in Isfahan (Iran) who needed conventional phototherapy for uncomplicated indirect hyperbilirubinemia. Neonates received phototherapy through devices with LEDs or special blue fluorescent tubes. Primary outcomes included the rate of fall of total serum bilirubin (TSB, mg/dL/hour) and duration of phototherapy (hours). Secondary outcomes were treatment failure and side effects.

Conclusions: LED light source is as effective as fluorescent tubes for phototherapy of preterm infants with indirect hyperbilirubinemia. Considering less frequent side effects, less energy consumption, longer life span, and lower costs, LED phototherapy seems to be a better option than current conventional phototherapy.


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3544129/
Objective: Quantify any association between neonatal phototherapy and DM-1 in a northern California integrated health care system.

Methods: This retrospective cohort study included 499,642 children born at ≥35 weeks'. We ascertained phototherapy, bilirubin levels, and other covariates from electronic records. We identified DM-1 cases using a diabetes registry and inpatient and outpatient diagnoses. We used traditional and propensity-adjusted Cox models to quantify associations.

Result: There was no evidence of increasing diabetes incidence. We found no association between phototherapy and DM-1 in either unadjusted analyses or analyses adjusted for hyperbilirubinemia and other covariates. DM-1 incidence was most strongly associated with race and ethnicity, with whites at highest risk and Asians at lowest risk.
LED versus daylight phototherapy at low irradiance in newborns ≥35 weeks of gestation

**Objective:** To compare the decline in TSB after 24 h of LED or fluorescent phototherapy from below in breastfed neonates ≥35 weeks of gestation.

**Methods:** Seventy-four neonates treated with a 17-bulb blue LED were compared with 76 neonates treated with a 7-bulb daylight device in a rooming-in unit. Spectral irradiance was measured at 5 points on a 30 × 60 cm rectangle on the gel transparent mattress.

**Conclusion:** LED with heterogeneous irradiance was as effective as daylight phototherapy with homogeneous irradiance; however there is a greater need for rigorous control of the room temperature.

Brandão, Draque, Sañudo, de Gusmão Filho, de Almeida


https://www.ncbi.nlm.nih.gov/pubmed/?term=LED+versus+daylight+phototherapy+at+low+irradiance+in+newborns+%E2%89%A535+weeks+of+gestation+%3A+randomized+controlled+trial
Neonatal hyperbilirubinemia and the risk of febrile seizures and childhood epilepsy.

Objective: The aim of the study was to estimate the association between newborn children treated with phototherapy for hyperbilirubinemia and the subsequent risk of febrile seizures or epilepsy in early childhood.

Result: Newborns treated with phototherapy for hyperbilirubinemia had a higher risk of developing epilepsy in early childhood but not febrile seizures. The increases risk of epilepsy were only present for boys not for girls.

Conclusion: Phototherapy for hyperbilirubinemia in newborns was associated with an increased risk of epilepsy for males in early childhood. No excess risk was seen with febrile seizures.
Randomized controlled trial of light-emitting diode phototherapy.

M J Maisels, E A Kring and J DeRidder


http://www.nature.com/jp/journal/v27/n9/full/7211789a.html

**Objective:** We wished to compare the efficacy of light-emitting diode (LED) phototherapy with special blue fluorescent (BB) tube phototherapy in the treatment of neonatal hyperbilirubinemia.

**Result:** After 155 h of phototherapy, the rate of decline in the total serum bilirubin (TSB) was 0.350±0.25 mg/dl/h in the LED group vs 0.270±0.25 mg/dl/h in the BB group (P=0.20).

**Conclusion:** LED phototherapy is as effective as BB phototherapy in lowering serum bilirubin levels in term and near-term newborns.
Is phototherapy in neonates a risk factor for malignant melanoma development?


**Objective:** To determine whether phototherapy of the newborn's sensitive skin could be a risk factor for **malignant melanoma**.

**Result:** None of the patients with childhood malignant melanoma had received phototherapy, in comparison with 11 of the controls. This difference was not significant.

**Conclusion:** This preliminary report shows **no significant risk of developing childhood malignant melanoma after phototherapy** of the skin in neonates with hyperbilirubinemia. However, the median follow-up time was only 18 years.
**Light-Emitting Diodes: A Novel Light Source for Phototherapy**

**Summary:** High intensity light-emitting diodes (LEDs) are being studied as possible light sources for the phototherapy of hyperbilirubinemic neonates. These power-efficient, low heat-producing light sources have the potential to deliver high intensity light of narrow wavelength band in the blue-green portion of the visible light spectrum, which overlaps the absorption spectrum of bilirubin (BR). We compared the efficacy between single LEDs of different color and then constructed a prototype phototherapy device using 300 blue LEDs. The efficacy of this device was compared with that of conventional phototherapy devices by measuring the *in vitro* photo degradation of BR in human serum albumin. The LEDs were purchased from Nichia Chemical Industries.

**Result:** In summary, because of their small size, high luminous intensity, and their narrow wavelength band light, LEDs may be an attractive light source for phototherapy not only for newborns, but also for other patients suffering from excessive hyperbilirubinemia, such as that caused by the Crigler-Najjar syndrome.

Hendrik J Vreman, Ronald J Wong, David, Stevenson, Roger K Route, Sidney D Reader, Martin M Fejer, Rena Gale and Daniel S Seidman


http://www.nature.com/pr/journal/v44/n5/full/pr1998537a.html
Objective: It is unclear whether aggressive phototherapy to prevent neurotoxic effects of bilirubin benefits or harms infants with extremely low birth weight (1000 g or less).

Result: The aggressive-phototherapy group and the conservative-phototherapy group were generally similar, with small differences in the percentages of male infants and black infants.

Conclusion: Aggressive phototherapy did not significantly reduce the rate of death or neurodevelopmental impairment. The rate of neurodevelopmental impairment alone was significantly reduced with aggressive phototherapy. This reduction may be offset by an increase in mortality among infants weighing 501 to 750 g at birth.
Objective: The objective of this study is to determine whether irradiance levels of phototherapy (PT) devices in Dutch neonatal intensive care units (NICUs) increased between 2008 and 2013.

Result: Five types of closed incubators (Giraffe, Dräger Caleo, Dräger 8000, Weyer Thermocare Vita and Hill-Rom Air-Shields) and one open incubator (Dräger Babytherm) were used. Among seven overhead devices (Medela, Dräger, Ohmeda Spot, Giraffe Blue Spot Lite, Natus neoBLUE, Natus neoBLUE Mini and Infantulus) four light-emitting diode (LED)-based devices were in use in 2013 versus one in 2008.

Conclusion: Irradiance of PT devices still varies, but has markedly improved since 2008 due to shorter distances between PT device and infant, and introduction of better performing LED-based devices.
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Thank you for your attention.