Research & Study Tool

Jaundice Management: From Screening to Therapy

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I. Key points of country specific Guidelines

US Guideline on Hyperbilirubinemia: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation 2022

Selected Key Points:

TcB Screening: **Although TcB measurements do not directly assess bilirubin levels, they are valid and reliable when used as a screening test to identify infants who require a TSB measurement. Using TcB measures in this way may result in a reduction in blood draws. Implementing universal TcB screening during the nursery stay and at subsequent public health nurse visits has been associated with a reduction in both blood draws and the likelihood of having a TSB level 20 mg/dL.**

There is a good correlation between TcB measures and TSB concentrations, with the TSB generally within 3 mg/dL of the TcB among newborn infants with TSB concentrations <15 mg/dL. TSB should be measured if the TcB exceeds or is within 3 mg/dL of the phototherapy treatment threshold or if the TcB is ≥15 mg/dL. Use TSB as the definitive test to guide phototherapy and escalation-of-care decisions, including exchange transfusion.

Phototherapy: The general approach is to provide intensive phototherapy to as much of the infant's surface area as possible. Intensive phototherapy requires a narrow spectrum LED blue light with an **irradiance of at least 30 mW/cm2 per nm at a wavelength around 475 nm.** Light outside the 460 to 490 nm range provides unnecessary heat and potentially harmful wavelengths. **Different irradiance measurement devices can lead to varying results,** so it is reasonable to follow the manufacturer recommendations regarding how and when to measure irradiance.

Interrupting phototherapy for breastfeeding does not impact the overall effectiveness of phototherapy if it is otherwise appropriately used.

Discontinuing phototherapy is an option when the TSB has decreased by at least 2 mg/dL below the hour-specific threshold at the initiation of phototherapy.

It is an option to measure TcB instead of TSB if it has been at least 24 hours since phototherapy was stopped.

Follow-up: The timing of follow-up bilirubin testing after discontinuing phototherapy should be based on the risk of rebound hyperbilirubinemia. […] at least 12 hours, and preferably 24 hours, should elapse to allow sufficient time for the bilirubin concentration to demonstrate whether there is rebound hyperbilirubinemia.

Kemper, Alex R, Thomas B Newman, Jonathan L Slaughter, M Jeffrey Maisels, Jon F Watchko, Stephen M Downs, Randall W Grout, et al. "Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation" 150, no. 3 (2022). https://publications.aap.org/pediatrics/article/150/3/e2022058859/188726/Clinical-Practice-Guideline-Revision-Management-of.

Link: https://publications.aap.org/pediatrics/article/150/3/e2022058859/188726/Clinical-Practice-Guideline-Revision-Management-of

UK Guideline: Jaundice in newborn babies under 28 days **2023**

Selected Key Points:

TcB Screening: In babies who have a gestational age of 35 weeks or more and who are over 24 hours old:

- use a transcutaneous bilirubinometer to measure the bilirubin level
- if a transcutaneous bilirubinometer is not available, measure the serum bilirubin
- if a transcutaneous bilirubinometer measurement indicates a bilirubin level greater than 250 micromol/litre, measure the serum bilirubin to check the result
- use serum bilirubin measurement if bilirubin levels are at or above the relevant treatment thresholds for their age, and for all subsequent measurements.

Phototherapy: Use phototherapy (phototherapy given using an artificial light source with an appropriate spectrum and irradiance. This can be delivered using light-emitting diode [LED], fibreoptic or fluorescent lamps, tubes or bulbs) to treat significant hyperbilirubinaemia (see the threshold table and the treatment threshold graphs) in babies.

Consider intensified phototherapy (phototherapy that is given with an increased level of irradiance with an appropriate spectrum. Phototherapy can be intensified by adding another light source or increasing the irradiance of the initial light source used) to treat significant hyperbilirubinaemia in babies if any of the following apply

- the serum bilirubin level is rising rapidly (more than 8.5 micromol/litre per hour)
- the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours or more since birth (see threshold table and the treatment threshold graphs)
- the bilirubin level fails to respond to initial phototherapy (that is, the level of serum bilirubin continues to rise, or does not fall, within 6 hours of starting phototherapy).

If the serum bilirubin level falls during intensified phototherapy to a level 50 micromol/litre below the threshold for which exchange transfusion is indicated reduce the intensity of phototherapy

Stop phototherapy once serum bilirubin has fallen to a level at least 50 micromol/ litre below the phototherapy threshold (see threshold table and the treatment threshold graphs). Check for rebound of significant hyperbilirubinaemia with a repeat serum bilirubin measurement 12–18 hours after stopping phototherapy. Babies do not necessarily have to remain in hospital for this to be done.

National Institute for Health and Care Excellence. “NICE: Jaundice in Newborn Babies under 28 Days.” National Institute for Health and Care Excellence, October 31, 2023. www.nice.org.uk/guidance/cg98.

Link: www.nice.org.uk/guidance/cg98

Canadian Guideline: for detection and management of hyperbilirubinemia in term and late preterm newborns (≥35 weeks gestational age) **2025**

Selected Key Points:

TcB Screening: Every newborn should have a thorough clinical assessment within 24 hours of birth, including assessment for hyperbilirubinemia and bilirubin neurotoxicity risk factors (Tables 1a, 1b) and clinical assessment for jaundice. 8. A process should be in place for post-discharge follow-up of newborns at risk for hyperbilirubinemia, including resources to support timely TSB or TcB measurement(s) and mechanisms to provide prompt treatment of hyperbilirubinemia when required. Any newborn with suspected significant hyperbilirubinemia on assessment, at any age, should have their TSB or TcB measured without delay.

When TcB testing is used to monitor infants with hyperbilirubinemia, obtain confirmatory testing with TSB if the TcB level is within 50 µmol/L of the hour-specific phototherapy threshold OR if the TcB is above 250 µmol/L.

Phototherapy: The efficacy of phototherapy depends on light source intensity, the distance between light source and skin, the surface area being exposed, and duration of treatment. Intensive phototherapy is defined by using narrow spectrum lights at a wavelength of around 460 to 490 nm with an irradiance of at least 30 µW/cm2/nm. The current recommended approach is to provide intensive phototherapy for any infant who reaches threshold based on hour-specific TSB values (Figures 2, 3). Use of additional light sources, including a fiberoptic blanket or pad, may increase the body surface area exposed without necessarily increasing delivered irradiance. Because irradiance decay occurs in all types of phototherapy lamps with ongoing use, devices should be checked regularly by measuring the spectral irradiance using a radiometer.

Discontinue phototherapy at ΔTSB >30 µmol/L below treatment threshold for infants born ≥38 weeks GA and at ΔTSB >60 µmol/L for those born 35 to 37 weeks GA to minimize risk for rebound hyperbilirubinemia. 17. Measure TSB after stopping phototherapy to check for rebound hyperbilirubinemia. TcB can be used for follow-up if phototherapy has been discontinued for ≥18 hours.

Family centered care during Phototherapy: Phototherapy can interfere with breastfeeding and skin-to-skin care and may generate parental anxiety related to the hospitalization of an otherwise healthy newborn . Encourage family involvement with treatment by briefly interrupting phototherapy for feeding at the breast or skin-to-skin care (for 20 to 30 minutes, 8 to 10 times per day can be considered in the mild hyperbilirubinemia setting. Using a fiberoptic blanket or pad during phototherapy helps allow breastfeeding and skin-to-skin contact to continue.

Ng, Eugene, Gabriel Altit, Chloe Joynt, Nicole Radziminski, and Michael Narvey. “Canadian Guidelines for Detection and Management of Hyperbilirubinemia in Term and Late Preterm Newborns (≥35 Weeks Gestational Age).” Canadian Paediatric Society, March 18, 2025. https://cps.ca/en/documents/position/hyperbilirubinemia-newborns.

Link: https://cps.ca/en/documents/position/hyperbilirubinemia-newborns

Swiss Guideline: Empfehlungen zur Betreuung von Neugeborenen mit Hyperbilirubinämie 2023

Englisch Translation (original text below):

Selected Key Points

TcB screening: As a substitute for blood-based TSB determination, icterus can also be estimated using specific transcutaneous (Tc) bilirubin measuring devices. However, it must always be clear that this measurement is based on a calculation algorithm based on the photospectrometric absorption measurement of an area of skin. [...] This skin measurement is then converted into a serum bilirubin concentration according to a conversion factor. The measurement methods are therefore completely different, but the results are ultimately comparable. The great advantage of TcB determination is that it reduces the number of blood samples and the associated pain. However, TSB determination remains the clinical standard for therapy indication. Due to the possible difference between the TcB value and the TSB value, a TSB determination should be carried out for high TcB values, i.e. all those that are less than 50 µmol/l below the intervention limit or are ≥250 µmol/l. TcB determination is also applicable and reliable in premature infants.

- TcB may be used for newborns with a gestational age ≥ 32+0 weeks
- TcB may be used from the chronological age of 24 hours
- TcB may also be used in dark-skinned patients.
- In patients with a TcB value of < 50 µmol/l below the therapy limit, as well as with a TcB value ≥250 µmol/l, a control measurement using TSB should be carried out to assess the need for therapy.
- Therapy indications are based on TSB and not TcB values.
- TcB may also be used to assess the progression of bilirubin in patients after phototherapy, but no earlier than 24 hours after the end of phototherapy.

Recommendations for performing standard phototherapy: with bilirubin levels slightly above the phototherapy limit, no icterus praecox, no immune hemolysis (see Figure 7):

- Dress child with small diaper
- Eye protection
- **a lamp with an effective intensity of 20-30 µW/cm2/nm**
- **for premature babies with a birth weight <750 g, start with an intensity of 10-20 µW/cm2/nm**
- Distance between child and light source according to manufacturer's instructions, normally approx. 30 cm (except with light mat) Change the position of the child every 2-3 hours 72
- Illumination of the maximum body surface area
- Short therapy breaks (maximum 30' every 4 hours) for breastfeeding (remove eye protection)
- Clinical monitoring of temperature, heart rate and respiration every 4-8 hours during FT, measure weight daily
- Measurement of TSB after the first 4 to 6 hours after the start of FT to ensure that the bilirubin level decreases

In term and more mature preterm babies, intermittent phototherapy (on/off every 12 hours) is just as effective as continuous phototherapy and can therefore be used when TSB levels are not too high

Recommendations for the implementation of intensified phototherapy: with increasing bilirubin levels under standard phototherapy:

- this is defined as having an effective intensity of at least 30 µW/cm2/nm
- ideally FT using light-emitting diodes (minimum heat production with sufficient minimum distance between lamp and child according to the manufacturer's specifications)
- it is essential to use several lamps; the exposed body surface is more important than the number of devices, therefore it is advantageous to irradiate both the dorsal and the ventral body surface by using a fiberoptic light mat and light emitting diode.
- Intensified phototherapy should not be interrupted if possible and the bilirubin value should be checked after 2-4 hours until a clear decrease in the TSB value is measured (see figure).

Selected Key Points

TcB Screening: Als Ersatz für die blutige TSB-Bestimmung kann der Ikterus auch mittels spezifischer transkutaner (Tc) Bilirubinmessgeräte abgeschätzt werden. Es muss aber immer klar sein, dass dieser Messung ein Berechnungsalgorithmus zugrunde liegt, basierend auf der photospektrometrischen Absorptionsmessung eines Hautareales. […] Diese Hautmessung wird dann gemäss eines Umrechnungsfaktors in eine Serumbilirubinkonzentration umgerechnet. Die Messmethoden sind also völlig verschieden, die Resultate aber schlussendlich vergleichbar. Der grosse Vorteil der TcB-Bestimmung ist es, die Anzahl der Blutentnahmen und damit verbundene Schmerzen zu verringern. Als klinischer Standard zur Therapie-Indikation gilt aber weiterhin die TSB Bestimmung. Aufgrund der möglichen Differenz des TcB-Wertes gegenüber dem TSB-Wert, soll bei hohen TcB-Werten, also all jenen, die weniger als 50 µmol/l unterhalb der Interventionsgrenze liegen oder ≥250 µmol/l betragen, eine TSB Bestimmung erfolgen. Die TcB- Bestimmung ist auch bei Frühgeborenen anwendbar und verlässlich.

- TcB darf bei Neugeborenen mit einem Gestationsalter ≥ 32+0 Wochen verwendet werden
- TcB darf ab dem chronologischen Alter von 24h verwendet werden.
- TcB darf auch bei dunkelhäutigen Patienten verwendet werden.
- Bei Patienten mit einem TcB-Wert von < 50 µmol/l unterhalb der Therapiegrenze, sowie bei einem TcBWert ≥250 µmol/l, soll eine Kontroll-Messung mittelsTSB erfolgen, um die Notwendigkeit der Therapie zu beurteilen.
- Therapieindikationen werden aufgrund von TSB- und nicht von TcB-Werten gestellt.
- TcB darf für die Beurteilung des Bilirubinverlaufes auch bei Patienten nach Fototherapie verwendet werden, jedoch frühestens 24 Stunden nach Beendigung derselben.

Empfehlungen zur Durchführung der Standard-Fototherapie: bei Bilirubinwerten leicht über der Fototherapiegrenze, kein Ikterus praecox, keine Immunhämolyse (siehe Abbildung 7):

- Kind mit kleiner Windel bekleiden
- Augenschutz
- **eine Lampe mit einer effektiven Intensität von 20-30 µW/cm2/nm**
- **bei Frühgeborenen mit Geburtsgewicht <750 g soll mit einer Intensität von 10-20 µW/cm2/nm angefangen werden**
- Abstand Kind-Lichtquelle gemäss Angaben des Herstellers, normalerweise ca 30cm (ausser bei Leuchtmatte) Wechsel der Lagerung des Kindes alle 2-3 Stunden 72
- Beleuchung der maximalen Körperoberfläche
- kurze Therapiepausen (maximal 30' alle 4h) zum Stillen (Augenschutz dabei entfernen)
- klinische Überwachung von Temperatur, Herzfrequenz und Atmung alle 4-8 Stunden während der FT, messen des Gewichtes täglich
- Messung des TSB nach den ersten 4 bis 6 Stunden nach Beginn der FT, um sicherzustellen, dass ein Rückgang des Bilirubinwerdes erfolgt

Bei Termingeborenen und reiferen Frühgeborenen ist eine intermittierende Fototherapie (jeweils 12 Stunden an/aus) ebenso wirksam, wie eine kontinuierliche Fototherapie und kann deshalb bei nicht allzu hohen TSB-Werten eingesetzt werden

Empfehlungen zur Durchführung der intensivierten Fototherapie: bei steigendem Bilirubinwert unter Standard-Fototherapie:

- diese wird definiert mit einer effektiven Intensität von mindestens 30 µW/cm2/nm
- idealerweise FT mittels Leuchtdioden (minimale Wärmeproduktion bei ausreichendem Minimalabstand Lampe-Kind gemäss Angabe der Hersteller)
- zwingend mehrere Lampen benutzen; die exponierte Körperoberfläche ist wichtiger als die Anzahl der Geräte, daher ist es von Vorteil, sowohl die dorsale als auch die ventrale Körperoberfläche zu bestrahlen, durch Einsatz von fiberoptischer Leuchtmatte und Leuchtdiode.
- die intensivierte Fototherapie soll möglichst nicht unterbrochen und der Bilirubinwert nach 2-4 Stunden kontrolliert werden bis eine deutliche Abnahme des TSB-Wertes gemessen wird (siehe Abbildung).

Fontana, M., C. Hagmann, M. Wolff, J. Meng-Hentschel, M. Roth-Kleiner, S. Zoubir, and M. Wolff. "Empfehlungen Zur Betreuung von Neugeborenen Mit Hyperbilirubinämie." Schweizerischen Gesellschaft für Neonatologie, December 15, 2022. https://www.paediatrieschweiz.ch/empfehlungen-zur-betreuung-von-neugeborenen-mit-hyperbilirubinaemie/.

Link: https://www.paediatrieschweiz.ch/empfehlungen-zur-betreuung-von-neugeborenen-mit-hyperbilirubinaemie/

German Guideline: Hyperbilirubinämie des Neugeborenen – Diagnostik und Therapie (S2k-Leitlinie) / In Überarbeitung	2015

Translation of Selected Key Points (Original text below):

TcB screening: Screening of all newborns for potentially dangerous hyperbilirubinemia is carried out sequentially by physical examination (visible icterus or sclerenicterus?), transcutaneous bilirubin determination (TcB) and, if necessary, blood-based measurement of total serum bilirubin (GSB) (Table 1). The GSB is decisive for therapy, without deduction of any direct serum bilirubin that may also be measured. **The TcB measurement is much more informative than a visual assessment and allows the number of blood-based measurements to be reduced. Transcutaneous measurements can be carried out in premature infants with similar reliability as in mature newborns.** Deviations between TcB and GSB measurements become relevant at the latest at TcB values that are 2 mg below the respective phototherapy limit; in these cases, a blood-based GSB check is indicated. **Even blood-based measurement methods in the laboratory or on site ("point of care") exhibit considerable discrepancies between them, so there is no real gold standard. Immediately after phototherapy, transcutaneous measurements are associated with larger deviations between GSB and TcB; the difference normalizes within 24 hours.**

Phototherapy: The effectiveness of phototherapy depends on the applied dose, the light spectrum, the distance from the light source and the exposed surface. **Intensive phototherapy means using a light source with a blue-green spectrum between 430 and 490 nm and a radiation intensity of 30 µW/ cm² per nm**. This is best achieved with special blue fluorescent tubes or blue light-emitting diodes (LEDs). The lower effectiveness of fiberoptic mats is due to the comparatively smaller exposed area, but they can be used with blue light tubes or LED devices for combined sandwich phototherapy from above and below. In order to achieve a rapid decrease in very high bilirubin levels, the effectiveness of phototherapy can be improved by reducing the distance between the light source and the body surface, the above-mentioned sandwich method as well as by using additional side-mounted lamps, reflective metal foils or white cloths. With continued phototherapy, equilibration processes between the skin, blood and other organs become the limiting factor for the drop in serum bilirubin; intermittent phototherapy with 12-hour breaks is then similarly effective to continuous therapy

TcB Screening: Das Screening aller Neugeborenen auf eine potentiell gefährliche Hyperbilirubinämie erfolgt sequenziell durch körperliche Untersuchung(sichtbarer Ikterus bzw. Sklerenikterus?) , transkutane Bilirubinbestimmung (TcB) und ggf. blutige Messung des Gesamt-Serum Bilirubins (GSB)(Tabelle 1). Therapieentscheidend ist das GSB, ohne Abzug eines evtl. mitgemessenen direkten Serumbilirubins. **Die TcB - Messung ist wesentlich aussagekräftiger als eine visuelle Beurteilung und erlaubt es, die Anzahl blutiger Messungen zu reduzieren. Transkutane Messungen sind bei Frühgeborenen mit ähnlicher Verlässlichkeit durchführbar wie bei reifen Neugeborenen**. Abweichungen zwischen TcB-und GSB -Messungen werden spätestens bei TcB-Werten, die 2 mg unter der jeweiligen Phototherapiegrenze liegen, relevant, in diesen Fällen ist entsprechend eine blutige GSB-Kontrolle indiziert . **Auch blutige Messmethoden im Labor oder vor Ort ("point -of care")weisen untereinander erhebliche Diskrepanzen auf , es gibt insofern keinen wirklichen Goldstandard. Unmittelbar nach einer Phototherapie sind transkutane Messungen mit größeren Abweichungen zwischen GSB und TcB verbunden, die Differenz normalisiert sich innerhalb von 24h.**

Fototherapie: Die Effektivität der Phototherapie hängt von der applizierten Dosis, dem Lichtspektrum, dem Abstand von der Lichtquelle und der belichteten Oberfläche ab**. Intensive Phototherapie bedeutet den Einsatz einer Lichtquelle mit blau-grünem Spektrum zwischen 430 bis 490 nm und einer Strahlungsintensität von 30 µW/ cm² pro nm. Dies wird am besten mit speziellen blau fluoreszierenden Leuchtstoffröhren81oder mit Blaulichtdioden (LED) erreicht.** Die geringere Effektivität fiberoptischer Matten beruht auf der vergleichsweise kleineren exponierten Fläche, allerdings können sie mit Blaulichtröhren oder LED-Geräten zur kombinierten Sandwich-Phototherapie von oben und unten eingesetzt werden. Um bei sehr hohen Bilirubinwerten einen schnellen Abfall zu erreichen, kann die Effektivität der Phototherapie durch eine Verringerung der Distanz zwischen Lichtquelle und Körperoberfläche, die oben erwähnte Sandwich-Methode sowie durch zusätzlich seitlich angebrachte Lampen, reflektierende Metallfolien oder weiße Tücher verbessert werden. Bei fortgesetzter Phototherapie werden Äquilibrierungsvorgänge zwischen Haut, Blut und anderen Organen zur limitierenden Größe für den Abfall des Serumbilirubins, eine intermittierende Phototherapie mit 12-stündigen Pausen ist dann ähnlich effektiv wie eine Dauertherapie

Bührer, Christoph, Monika Berns, and al et. "Hyperbilirubinämie Des Neugeborenen – Diagnostik Und Therapie (S2k-Leitlinie)." Gesellschaft für Neonatologie und Pädiatrische Intensivmedizin, January 8, 2015. https://gnpi.de/wp-content/uploads/2020/07/024-007l_S2k_Hyperbilirubinaemie_Neugeborenen_Diagnostik_Therapie_2015-08.pdf.

Link: https://gnpi.de/wp-content/uploads/2020/07/024-007l_S2k_Hyperbilirubinaemie_Neugeborenen_Diagnostik_Therapie_2015-08.pdf

II. Transcutaneous Jaundice Screening

The **Jaundice Meter JM-105** and its predecessor JM-103 which uses the same optical pathway system have been subject of clinical studies to demonstrate clinical performance. **In total, during the last decade studies with almost 30.000 early and late preterm** as well as term infants of different races / ethnicities have been conducted with the JM-105 & JM-103. The results of those studies confirm that these transcutaneous bilirubinometers are valuable and reliable screening tools in assessing neonatal hyperbilirubinemia.

i. Accuracy, safety & measuring Sites of TcB

Impact of a Transcutaneous Bilirubinometry Program on Resource Utilization and Severe Hyperbilirubinemia	**2012**

Objective: Our goal was to assess the impact of programmatic and coordinated use of transcutaneous bilirubinometry (TcB) on the incidence of severe neonatal hyperbilirubinemia and measures of laboratory, hospital, and nursing resource utilization.

Methods: We compared the neonatal hyperbilirubinemia-related outcomes of 14 796 prospectively enrolled healthy infants $35 weeks gestation offered routine TcB measurements in both hospital and community settings by using locally validated nomograms relative to a historical cohort of 14 112 infants assessed by visual inspection alone.

Results: **There was a 54.9% reduction (odds ratio [OR]: 2.219 [95% confidence interval (CI): 1.543–3.193]; P , .0001) in the incidence of severe total serum bilirubin values** (≥342 μmol/L; ≥20 mg/dL) after implementation of routine TcB measurements. **TcB implementation was associated with reductions in the overall incidence of total serum bilirubin draws** (134.4 vs 103.6 draws per 1000 live births, OR: 1.332 [95% CI: 1.226–1.446]; P , .0001) and overall phototherapy rate (5.27% vs 4.30%, OR: 1.241 [95% CI: 1.122–1.374]; P , .0001), a reduced age at readmission for phototherapy (104.3 6 52.1 vs 88.9 6 70.5 hours, P , .005), and duration of phototherapy readmission (24.8 6 13.6 vs 23.2 6 9.8 hours, P , .05). There were earlier (P , .01) and more frequent contacts with public health nurses (1.33 vs 1.66, P , .01) after introduction of the TcB program.

Conclusions: Integration of routine hospital and community TcB screening within a comprehensive public health nurse newborn follow-up program is associated with significant improvements in resource utilization and patient safety.

Wainer, S., S. M. Parmar, D. Allegro, Y. Rabi, and M. E. Lyon. “Impact of a Transcutaneous Bilirubinometry Program on Resource Utilization and Severe Hyperbilirubinemia.” PEDIATRICS 129, no. 1 (January 1, 2012): 77–86. https://doi.org/10.1542/peds.2011-0599.

Link: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2011-0599

Accuracy of enhanced transcutaneous bilirubinometry according to various measurement sites	2021

Objective: The goal of the study was to provide missing data on the accuracy of enhanced transcutaneous bilirubinometry in a monoracial population of term neonates, considering three different measurement sites.

Material and methods: Transcutaneous bilirubin was measured using the **JM-105 device on the forehead, chest, and abdomen.** Blood sampling for total serum bilirubin concentration has been performed within 10 minutes of transcutaneous measurements. Paired transcutaneous bilirubin and total serum bilirubin measurements were statistically analyzed.

Results: The study group consisted of 102 healthy term Slovak infants. The correlation between total serum bilirubin and transcutaneous bilirubin was significant (coefficient of determination R2: 0.9045 forehead, 0.8808 sternum, 0.8467 abdomen). Transcutaneous measurements underestimated serum bilirubin levels significantly when total serum bilirubin values were higher than 15 mg/dL, irrespective of the site of transcutaneous measurements. The lowest mean difference between total serum bilirubin and transcutaneous bilirubin was identified on the sternum (median: -1.1 mg/dL). The area under the curve was >0.97 and >0.93 for detecting total serum bilirubin levels >10 mg/dL and >13 mg/dL, respectively, for all measurement sites. **Transcutaneous measurements on the forehead and sternum provided very high sensitivity, with the best performance at the forehead.**

Conclusion: Transcutaneous bilirubinometry using an enhanced device is an accurate, sensitive, and convenient screening method in term Caucasian neonates. **Transcutaneous bilirubin measurements on the forehead, sternum, and abdomen are reliable, with the best performance on the forehead.** It is necessary to confirm higher transcutaneous bilirubin values with a total serum bilirubin measurement.

Matasova, Katarina. “Accuracy of Enhanced Transcutaneous Bilirubinometry Considering Various Measurement Sites.” Türk Pediatri Arşivi, 2020. https://doi.org/10.14744/TurkPediatriArs.2020.54514.

Link: https://pubmed.ncbi.nlm.nih.gov/34013224/

ii. Reduction in Blood Draws & Costs effectiveness

Reducing Outpatient Infant Blood Draws with Transcutaneous Measurement of Bilirubin 2020

Introduction: Newborn jaundice is a common outpatient problem. Transcutaneous bilirubin (TcB) measurements correlate well with total serum bilirubin (SB) measurements below 15mg/dl and are efficient and noninvasive. Some concern exists that TcB measurement may subsequently lead to an increase in the number of SB measurements performed in the outpatient setting. We aimed to implement the use of a TcB device in an outpatient clinic. By doing so, we sought to increase the number of newborns screened solely by TcB as opposed to SB, by 30%, within 12 months.

Methods: We conducted plan-do-study-act cycles with targeted interventions to promote the use of TcB in an outpatient clinic for eligible newborns older than 35 weeks gestational age, aged 1–20 days, and without a history of transfusion, phototherapy, extensive bruising, or risk of hemolysis. We used statistical process control methods to measure proportions of newborns evaluated with TcB (run chart) and patients-between SB measurements (G-chart) over time in the outpatient clinic.

Results: We collected preintervention data for 18-months and intervention data for 12 months. For newborns attending the outpatient clinic, the proportion of TcB measurements increased after implementation of the use of TcB measurement. There was an increase in patients-between SB measurements. At project inception, SB was drawn for every 8 eligible patients. By the end of the project, there were 98 eligible newborns between instances of SB testing.

Conclusion: Implementation of a quality-improvement initiative to measure TcB in the outpatient clinic was feasible and reduced the number of SB tests.

The use of TcB may reduce the overall cost of testing for hyperbilirubinemia in this patient population, as the device has a one-time cost as opposed to the ongoing costs of laboratory testing. **The estimated cost per TcB screen in hospital and community (urban and rural) settings was $3.54 and $3.76, respectively. The estimated cost per SB screen in hospital and urban and rural community settings was $15.82, $50.21, and $65.03, respectively. In addition to anticipated cost-saving of the actual test, the bilirubinometer also saves time for providers and families as results are immediately available.**

Kilmartin, Keira C, Emily J McCarty, Catherine D Shubkin, and Alison Volpe Holmes. “Reducing Outpatient Infant Blood Draws with Transcutaneous Measurement of Bilirubin,” 2020.

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC7351454/pdf/pqs-5-e335.pdf

Cost savings with transcutaneous screening versus total serum bilirubin measurement for newborn jaundice in hospital and community settings: a cost-minimization analysis 2018

Background: Leading authorities in North America recommend universal screening via total serum bilirubin (TSB) measurement or transcutaneous bilirubinometry (TcB) for kernicterus prevention. **We assessed costs associated with these 2 screening methods** in hospital and in urban and rural community settings.

Methods: Our tertiary care centre in Saskatoon, with about 5600 births per year, serves the local population of 300 000; in addition, 30% of patients are referred from outside the local community and surrounding area. We obtained health administrative data for two 6-month periods: before (June 1 to Nov. 30, 2015 [TSB program]) and after (June 1 to Nov. 30, 2016 [TcB–TSB program]) implementation of universal screening with TcB. Data on nurses' time and mileage were collected to assess the mean time for screening and sample transportation. We performed a cost-minimization analysis.

Results: **The observed requirement for TSB blood draws decreased by 71.4% after implementation of TcB** (1383.2/1000 live births to 397.8/1000 live births), whereas the overall number of screens increased from 1383.2 to 2758.6/1000 live births. The mean time per screen decreased from 12.52 (95% confidence interval [CI] 10.44–14.59) minutes with TSB to 2.94 (95% CI 2.55–3.33) minutes with TcB ($p < 0.001$). **The estimated cost per TcB screen in hospital and community (urban and rural) settings was $3.54 and $3.76, respectively, and the estimated cost per TSB screen in hospital and in urban and rural community settings was $15.82, $50.21 and $65.03, respectively. The estimated overall 6-month savings with the TcB–TSB hospital and community programs were $19 760 and $6417, respectively.**

Interpretation: The TcB–TSB program reduced nurses' time to screen and provided immediate results at the point of care. **Transcutaneous bilirubinometry reduced the requirement for painful heel pokes while improving access to screening and decreasing the overall program cost.**

McClean, Stephanie, Krista Baerg, Julie Smith-Fehr, and Michael Szafron. "Cost Savings with Transcutaneous Screening versus Total Serum Bilirubin Measurement for Newborn Jaundice in Hospital and Community Settings: A Cost-Minimization Analysis." CMAJ Open 6, no. 3 (July 2018): E285–91. https://doi.org/10.9778/cmajo.20170158.

Link: http://cmajopen.ca/lookup/doi/10.9778/cmajo.20170158

'Halving the heel pricks': evaluation of a neonatal jaundice protocol incorporating the use of a transcutaneous bilirubinometer 2010

Aim: **This study aimed to assess the impact of implementing a new jaundice protocol** incorporating the use of the Konica Minolta/Air Shields JM 103 Jaundice Meter (JM103) (Konica Minolta Sensing Inc., Osaka, Japan) in the setting of an Australian post-natal ward.

Methods: A before-and-after study was completed following the introduction of a protocol integrating the use of the JM103 monitor on to the post-natal ward. Eligible infants were ≥ 36 weeks gestation, > 24 h and < 8 days of age. The number of Total Serum Bilirubin tests (TSBRs) were compared for the 12 months prior (T1) with a 6-month period and 6 months after protocol introduction (T2). Transcutaneous bilirubin (TcBR) results were also collected in T2. Rates of phototherapy and peak TSBRs at commencement were also compared as measures of safety.

Results: Four hundred and twenty-six of the 2197 live births in T1 required one or more TSBRs compared with 119 of the 1169 live births in T2. This represents an odds ratio of 0.47 (95% confidence interval 0.38-0.58) for infants in T2 having ≥ 1 TSBR compared with T1. There was no difference between the groups for rates of phototherapy (3.8% vs. 3.0%; P= 0.2) nor any difference between the groups for peak SBR during phototherapy (301.9 μmol/L (standard deviation, SD 58) for T1 vs. 303.2 μmol/L (SD 54) for T2; P= 0.45). **The estimated cost saving per year is $6966.00.**

Conclusion: **TcBR measurement in conjunction with our protocol significantly reduces painful procedures and costs without increasing the risk of delaying treatment with phototherapy**.

Hartshorn D, Buckmaster A. 'Halving the heel pricks': evaluation of a neonatal jaundice protocol incorporating the use of a transcutaneous bilirubinometer. J Paediatr Child Health. 2010 Oct;46(10):595-9. doi: 10.1111/j.1440-1754.2010.01801.x. Epub 2010 Aug 17. PMID: 20722994.

Link: https://pubmed.ncbi.nlm.nih.gov/20722994/

iii. Different ethnicities & skin tones

Comparison between the Transcutaneous and Total Serum Bilirubin Measurement in Malay Neonates with Neonatal Jaundice 2022

Background: This study aims to investigate the **reliability of the Dräger Jaundice Meter JM-105** for the screening of neonatal jaundice in **Malay neonates.**

Methods: A cross-sectional study was conducted in a university hospital involving 130 jaundiced neonates requiring serum bilirubin determination from day 2 to day 7 of life.

Results: The mean total serum bilirubin (TSB) was 232 µmol/L, whereas the mean transcutaneous bilirubin (TcB) measured at the forehead and sternum were 222 µmol/L and 223 µmol/L, respectively. Further, TcB underestimates TSB with a mean difference of 10.10 µmol/L at the forehead and 9.27 µmol/L at the sternum. **A positive linear relationship was observed between TSB with TcB forehead (r = 0.82) and TcB sternum (r = 0.80).** A good discriminations ability was observed for both the TcB forehead (receiver operating characteristics [ROC] curve = 89.8%) and sternum (ROC curve = 89.7%) at a TSB level of 205 µmol/L. **The sensitivity ranges from 84.4% to 85.3%, while the specificity ranges from 77.4% to 76.4%.**

Conclusion: Our study demonstrates a strong linear relationship and good diagnostic accuracy of TcB values compared to TSB values. To conclude, TcB measured at the forehead or sternum is a good alternative as a non-invasive screening tool for non-severe hyperbilirubinemia in Malay neonates.

Department of Paediatrics, School of Medical Sciences Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, Mazrah Mohamed, Nor Rosidah Nor Rosidah, Department of Paediatrics, School of Medical Sciences Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, Hospital Universiti Sains Malaysia, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, Noraida Ramli, Department of Paediatrics, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, et al. "Comparison between the Transcutaneous and Total Serum Bilirubin Measurement in Malay Neonates with Neonatal Jaundice." Malaysian Journal of Medical Sciences 29, no. 1 (February 23, 2022): 43–54. https://doi.org/10.21315/mjms2022.29.1.5.

Link: http://www.mjms.usm.my/MJMS29012022/MJMS29012022_5.pdf

Reliability of transcutaneous bilirubin determination based on skin color determined by a neonatal skin color scale of our own 2021

Abstract: Measurement of transcutaneous bilirubin (TcB) is widely used to estimate serum bilirubin (SB). However, its reliability depending on skin tone is still controversial. Ethnic classification does not correlate well with skin tone. We aimed to determine the reliability of transcutaneous bilirubin in a multiethnic population based on skin color according to our neonatal skin color scale. We conducted a prospective, observational study comparing SB and TcB among different skin colors. With the blood sample routinely obtained at 48–72 h for the screening of inborn errors of metabolism, we determined SB and TcB with a jaundice meter. We obtained data from 1359 newborns (color 1 337, color 2 750, color 3 249, color 4 23) and analyzed 1549 dyads SB/TcB. **Correlation between TcB and serum bilirubin was very good (R2 = 0.908–0.956), globally and by color group, with slight differences between darker and lighter skin colors.** Bland-Altman plots showed different mean bias depending on skin color.

Conclusions: Our study not only supports the reliability of TcB to assess SB regardless of skin color, but also supports the fact that TcB tends to overestimate SB in a higher degree in dark-skinned neonates. This may help reduce the number of blood samples for newborns.

Maya-Enero, Silvia, Júlia Candel-Pau, Jordi Garcia-Garcia, Xavier Duran-Jordà, and María Ángeles López-Vílchez. "Reliability of Transcutaneous Bilirubin Determination Based on Skin Color Determined by a Neonatal Skin Color Scale of Our Own." European Journal of Pediatrics 180, no. 2 (February 2021): 607–16. https://doi.org/10.1007/s00431-020-03885-0.

Link: https://link.springer.com/article/10.1007/s00431-020-03885-0

Predictability of transcutaneous bilirubinometry in late preterm and term infants at risk for pathological hyperbilirubinemia 2021

BACKGROUND: The aim was to **assess the predictability of transcutaneous bilirubinometry** in late preterm and term neonates at risk for pathological hyperbilirubinemia, and **to identify the neonatal population in which transcutaneous bilirubin most accurately predicts serum bilirubin level** (SB, mg/dl).

METHODS: The correlations between transcutaneous bilirubin (TCB, mg/dl) and SB in different neonatal population subsets; and between TSB (TCB-SB) and relevant neonatal variables and clinical groups were analyzed.

RESULTS: TCB correlated with SB ($r = 0.82$, $p < 0.05$) in the cohort ($n = 350$) and in population subsets ($r = 0.81–0.9$, $p < 0.001$). **Black infants with gestational age (GA) >35 weeks** and chronological age (CA) >3 days recorded **strongest correlation ($r = 0.9$, $p < 0.001$)** followed by Blacks, and non-Black infants with CA >3 days and GA >35 weeks. TSB was positive in Blacks, and in infants with CA <3 days, or with no phototherapy. TSB was negative in non-Blacks, in infants with positive direct Coombs test (DC+) or those receiving phototherapy. Black race [beta (SE) = 1.3(0.33), $p < 0.001$] had positive, while CA [beta (SE) = −1.74 (0.36), $p < 0.001$], DC + status [beta (SE) = −0.72 (0.25), $p = 0.004$] and receipt of phototherapy [beta (SE) = −0.84 (0.21), $p < 0.001$] each had negative correlation with TSB. TSB for Blacks was >Whites, Hispanics and Asians.

CONCLUSION: SB is best predicted by TCB in Black infants with CA over 3 days and GA over 35 weeks. Variability in SB estimation by TCB is race, CA and immune mediated hemolysis specific.

Dianova, E., J. Fogel, and R.P. Verma. “Predictability of Transcutaneous Bilirubinometry in Late Preterm and Term Infants at Risk for Pathological Hyperbilirubinemia.” Journal of Neonatal-Perinatal Medicine 14, no. 2 (March 16, 2021): 261–67. https://doi.org/10.3233/NPM-200486.

Link: https://journals.sagepub.com/doi/10.3233/NPM-200486

iv. Studies on other TcB devices

A Prospective Comparison of Transcutaneous and Serum Bilirubin Within Brief Time Intervals 2017

Background: The American Academy of Pediatrics recommends screening newborns ≥35 weeks' gestation with total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) to detect hyperbilirubinemia. Retrospective studies show TcB measurements strongly correlate with TSB; however, few prospective trials document this relationship. Furthermore, Dräger's newest TcB instrument, JM-105, remains unstudied in the United States. We measure TcB on foreheads and sternums of newborns **using JM-105 and Bilichek** devices within 30 minutes of TSB measurement. We find best overall TcB/TSB correlation with JM-105 on the sternum (mean TcB-TSB difference: −0.21 ± 1.15 mg/dL). Correlations between paired measurements for TcB on the sternum using JM-105 were 0.93 for all TSB levels (n = 178), 0.82 for TSB > 10 (n = 19), 0.69 for TSB > 12 (n = 11), and 0.52 for TSB > 15 (n = 6). TcB accuracy via JM-105 on the sternum significantly differed among races (P < .001). For 5% of paired measurements, TcB with JM-105 on the sternum underestimated TSB by ≥2 mg/dL, and for <1% by ≥3 mg/dL.

Discussion: **This study found that the Dräger JM-105 most accurately predicted the TSB when used on the mid-sternum when compared to the forehead and to the Bilichek meter on both sites.** Based on these results and on results from previous studies that have found the Dräger to be preferable to the Bilichek, we recommend that pediatric newborn nurseries and clinics use the Dräger JM-105 when screening infants for TcB.

Conclusion: Pediatricians in the newborn nursery and outpatient setting should continue to **screen with transcutaneous bilimeters, ideally on the sternum and with the Dräger JM-105.** Serum bilirubin should be drawn with discretion, ideally only when the TcB is within 3 mg/dL of the phototherapy treatment threshold for age. This will save practices money, but most importantly decrease stressful, painful, and unnecessary heel sticks in infants.

Jones, Denise F., Abigail R. McRea, James D. Knowles, Feng-Chang Lin, Erin Burnette, Lara A. Reller, and Jacob A. Lohr. "A Prospective Comparison of Transcutaneous and Serum Bilirubin Within Brief Time Intervals." Clinical Pediatrics 56, no. 11 (October 2017): 1013–17. https://doi.org/10.1177/0009922817701170.

Link: https://pubmed.ncbi.nlm.nih.gov/28366015/

Accuracy of transcutaneous bilirubin measured by the BiliCare device in late preterm and term neonates 2016

Objective: The objective of this study is to **explore the accuracy and performance of a new transcutaneous bilirubinometer (TCB)** for the screening of jaundice in late preterm and term infants.

Methods: A cross-sectional study was conducted. TCB measurements were performed using **the BiliCareTM** bilirubinometer. Paired TCB and serum bilirubin (SB) measurements were analysed.

Results: One hundred and fourteen paired samples were collected from 93 healthy late preterm and term infants. Bilirubin measurements were done at median (interquartile range) of 50.5 (34, 72) hours. The mean (SD) difference between the TCB and SB was 1.87 (1.98) mg/dL. A TCB cutoff level at 8.0 mg/dL provides a sensitivity of 97.3% with a negative predictive value (NPV) of 87.5% to detect a SB level of at least 8.0 mg/dL. For SB levels of at least 10.0 mg/dL, a TCB cutoff at 9.0 mg/dL shows a sensitivity of 97.5%; NPV 95.4%. For a SB level of at least 13.0 mg/dL, a TCB cut-off at 12 or 13 mg/dL had a sensitivity of 92.9% and NPV of 98.7%.

Conclusion: The BiliCareTM demonstrated good performance with positive bias for the screening of jaundice in healthy late preterm or term infants. However, if adopted, proper cut-off levels should be chosen because of sub-optimal device precision.

An in vitro study by the manufacturer documents the accuracy of the BiliCare device within 1.5 mg/dL (25.7 mmol/L) occurring at least 66% of the time. We found that 35.1% of our paired measurements had a difference of ≤1.5 mg/dL compared with the corresponding SB level. A wide range of 1.96 SD around the mean difference indicates poor precision of the device.

Kitsommart, Ratchada, Buranee Yangthara, Punnanee Wutthigate, and Bosco Paes. "Accuracy of Transcutaneous Bilirubin Measured by the BiliCare Device in Late Preterm and Term Neonates." The Journal of Maternal-Fetal & Neonatal Medicine, January 13, 2016, 1–20. https://doi.org/10.3109/14767058.2016.1140141.

Link: http://www.tandfonline.com/doi/full/10.3109/14767058.2016.1140141

Comparison of the transcutaneous bilirubinometers BiliCare and Minolta JM-103 in late preterm and term neonates 2015

Objective: To assess the agreement of **transcutaneous bilirubin (TcB) measurement with the Bilicare System in comparison to TcB measured with JM-103 and total serum bilirubin (TSB).**

Methods: Caucasian infants with gestational age ≥35 weeks with non-hemolytic jaundice received TcB measurement with both **Bilicare and JM-103 devices**. TSB was also obtained in infants at risk of phototherapy.

Results: We studied 458 infants measuring TcB with Bilicare and JM-103, correlating the results and with TSB. The mean difference ± 2SD between Bilicare and JM-103 TcB was 2.02 ± 4.46 mg/dL and decreased from 2.88 ± 3.17 to 1.20 ± 4.55, and to -0.95 ± 4.58 mg/dL at mild, moderate and high TcB values, respectively.

The **number of TSB measurements theoretically needed** in our population by measuring TcB **with Bilicare (249/458; 55%) was significantly higher** than that actually found measuring TcB with JM-103 (132/458; 29%) (p50.001). Moreover, we found that only in 43% (106/249) of cases in which Bilicare TcB measurement suggested the need of TSB measurement JM-103 TcB measurement did confirm this recommendation, while, on the contrary, **in 12% (22/249) of cases in which Bilicare TcB measurement did not suggest the need of TSB measurement whereas JM-103 TcB measurement did indicate the need of TSB**.

Conclusions: Bilicare and JM-103 TcB measurements are well correlated, but **Bilicare overestimates TcB for mild and moderate values and under-estimates it for high values compared to JM-103. This could increase the prescription of TSB measurements for less serious cases and decrease them in the most worrisome.**

Pratesi, Simone, Luca Boni, Lorenzo Tofani, Elettra Berti, Sara Sollai, and Carlo Dani. "Comparison of the Transcutaneous Bilirubinometers BiliCare and Minolta JM-103 in Late Preterm and Term Neonates." The Journal of Maternal-Fetal & Neonatal Medicine, December 2, 2015, 1–5. https://doi.org/10.3109/14767058.2015.1113521.

Link: http://www.tandfonline.com/doi/full/10.3109/14767058.2015.1113521

Transcutaneous bilirubin measurement at the time of hospital discharge in a multiethnic newborn population 2011

Background: Severe neonatal hyperbilirubinemia continues to occur in healthy newborns. Recent guidelines have supported using transcutaneous devices in estimating bilirubin levels. Previous studies using these devices are limited.

Methods: Newborns requiring serum bilirubin level measurements before hospital discharge were recruited prospectively. The agreement between a transcutaneous bilirubin (TCB) and total serum bilirubin (TSB) level was assessed. Sensitivity analysis was conducted. Our study compared the accuracy of the TSB measurement with the TCB measurement using a **BiliChek meter (Respironics Inc, USA)** in an ethnically diverse population of term and near-term infants, when used by various health care personnel just before discharge.

Results: A total of 430 infants were enrolled. Correlation between the values was high (Pearson's correlation coefficient 0.83; Lin's concordance coefficient 0.81 [95% CI 0.77 to 0.84]; P<0.001). The mean (± SD) TSB level was 194±60 µmol/L. The TCB measurement tended to overestimate the value (mean difference 12.7), with wide 95% limits of agreement (−52 µmol/L to 77 µmol/L). Sensitivity and specificity analysis of TCB values allowed estimation of clinically important TSB levels.

Conclusions: **The TCB correlated, but was imprecise in predicting TSB.** TCB values can be used at the time of discharge to safely plan care for jaundiced infants if the limits of agreement are considered and clinical judgment is maintained.

Campbell, Douglas M, Karoon C Danayan, Valleverdina McGovern, Sohail Cheema, Brenda Stade, and Michael Sgro. "Transcutaneous Bilirubin Measurement at the Time of Hospital Discharge in a Multiethnic Newborn Population." Paediatrics & Child Health 16, no. 3 (March 2011): 141–45. https://doi.org/10.1093/pch/16.3.141.

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC3077302/pdf/pch16141.pdf

v. TcB use in preterm infants

Transcutaneous bilirubin levels in extremely preterm infants less than 30 weeks gestation **2023**

Objective: The primary objective of this study was to determine the relationship between **transcutaneous bilirubin (TcB) levels and total serum bilirubin (TSB) levels in extremely preterm infants**.

Study design: We conducted a prospective multicenter study of extremely preterm infants less than 30 weeks gestation in California. Difference between paired TcB and TSB values were compared based on gestational age, birth weight, maternal race/ethnicity, chronological age as well as during and after phototherapy.

Results: TSB values ranged from 0 to 12.6 mg/dl and the TcB values ranged from 0 to 14.2 mg/dl. TSB was predicted with a high degree of accuracy at TSB = 2.37 + 0.54 (TcB) with r = 0.786. **There was good correlation across gestational age, birth weight, race/ethnic, chronological age subgroups as well as during and after phototherapy.**

Conclusion: Our study supports the use of TcB as a screening tool for monitoring jaundice in extremely preterm infants.

Sankar, Meera N. "Transcutaneous Bilirubin Levels in Extremely Preterm Infants Less than 30 Weeks Gestation." Journal of Perinatology, 2023.

Link: https://www.nature.com/articles/s41372-022-01477-4#:~:text=Results,TcB)%20with%20r%20%3D%200.786.

A Comparison Between Transcutaneous Bilirubin and Total Serum Bilirubin Levels for the Management of Jaundice in Preterm Neonates by Bland-Altman Plot **2021**

Objective: To **compare the bilirubin levels measured by transcutaneous bilirubinometer and serum samples** for the management of jaundice in preterm neonates.

Methods: The study was a prospective comparative observational study conducted in a tertiary care neonatal unit of Odisha from January 2019 to June 2020. All inborn and outborn neonates with a gestational age of 28+0/7 weeks to 36+6/7 weeks with the clinical diagnosis of neonatal jaundice were included in the study. Transcutaneous bilirubin (TcB) was estimated by **Draeger jaundice meter JM-105** and simultaneously venous blood and total serum bilirubin levels (TSB) were measured by diazonium method. The comparison between TcB and TSB values was analyzed by direct linear correlation in scatter plot and Bland-Altman plot.

Results: A total of 167 preterm neonates (66, 28-33 6/7 and 111, 34-366/7), with a mean gestational age 33.55 ±2.36 weeks and a mean birth weight of 1960 ± 613 grams, were analyzed. The mean TSB and TcB levels were 12.99 ± 3.47 mg/dl (min-max 4.9-18.3 mg/dl) and 14.156 ± 4.71 mg/dl (min-max 4-20.1 mg/dL), respectively. **The TcB is excellently correlated with TSB with a correlation coefficient of r =0.948, p ≤0.001.** The bias difference between TcB and TSB is -1.16 (95% CI: 2.35, -4.6) mg/dl. The correlation coefficients between 28-33+6/7 weeks gestational age groups (r = 0.944) and 34-36+6/7gestational age (r = 0.950) were similar.

Conclusion: TcB is well correlated with TSB level in preterm neonates. Hence, TcB can be used for the guidance of management in these neonates.

Panda, Santosh K, Abhinav Gaurav, Palash Das, Natabar Swain, and Soumini Rath. "A Comparison Between Transcutaneous Bilirubin and Total Serum Bilirubin Levels for the Management of Jaundice in Preterm Neonates by Bland-Altman Plot." Cureus, October 2, 2021. https://doi.org/10.7759/cureus.18442.

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC8559578/pdf/cureus-0013-00000018442.pdf

Transcutaneous versus Total Serum Bilirubin Measurements in Preterm Infants **2021**

Introduction: Transcutaneous bilirubin (TcB) measurement offers a noninvasive approach for bilirubin screening; however, its accuracy in preterm infants is unclear. **This study determined the agreement between TcB and total serum bilirubin (TSB) among preterm infants.**

Methods: A multisite prospective cohort study was conducted at 3 NICUs in Ontario, Canada, September 2016 to June 2018. Among 296 preterm infants born at 240/7 to 356/7 weeks, 856 TcB levels were taken at the forehead, sternum, and before and after the initiation of phototherapy with TSB measurements. Bland-Altman plots and 95% limits of agreement (LOA) expressed agreement between TcB and TSB. **[Used Device: Dräger JM-105]**

Results: The overall mean TcB-TSB difference was −24.5 µmol/L (95% LOA −103.3 to 54.3), 1.6 µmol/L (95% LOA −73.4 to 76.5) before phototherapy, and −31.1 µmol/L (95% LOA −105.5 to 43.4) after the initiation of phototherapy. The overall mean TcBTSB difference was −15.2 µmol/L (95% LOA −86.8 to 56.3) at the forehead and −24.4 µmol/L (95% LOA −112.9 to 64.0) at the sternum. The mean TcB-TSB difference was −31.4 µmol/L (95% LOA −95.3 to 32.4) among infants born 24–28 weeks, −25.5 µmol/L (95% LOA −102.7 to 51.8) at 29–32 weeks, and −15.9 µmol/L (95% LOA −107.4 to 75.6) at 33–35 weeks. Measures did not differ by maternal ethnicity.

Conclusion: **Among preterm infants, TcB may offer a noninvasive, immediate approach to screening for hyperbilirubinemia with more careful use in preterm infants born at <33 weeks' gestation, as TcB approaches treatment thresholds.** Its underestimation of TSB after the initiation of phototherapy warrants the use of TSB for clinical decision-making after the initiation of phototherapy.

Jegathesan, Thivia, Douglas M. Campbell, Joel G. Ray, Vibhuti Shah, Howard Berger, Robin Z. Hayeems, Michael Sgro, and for the NeoHBC. "Transcutaneous versus Total Serum Bilirubin Measurements in Preterm Infants." Neonatology 118, no. 4 (2021): 443–53. https://doi.org/10.1159/000516648.

Link: https://www.karger.com/Article/FullText/516648

vi. TcB use after Phototherapy

Transcutaneous bilirubin reliability during and after phototherapy depending on skin color **2023**

Abstract: Measurement of transcutaneous bilirubin (TcB) is a non-invasive, widely used technique to estimate serum bilirubin (SB). However, its reliability in multiethnic populations during and after phototherapy is still controversial even in covered skin. The aim of this study was to determine the reliability of TcB in covered (cTcB) and exposed (eTcB) skin during and after phototherapy in a multiethnic population of term and preterm neonates according to Neomar's neonatal skin color scale. Prospective, observational study comparing SB and TcB. We determined SB when clinically indicated and, at the same time, measured cTcB under a photo-opaque patch and eTcB next to it with a jaundice meter (Dräger JM-105TM). All dyads TcB-SB were compared, both globally and according to skin color. We obtained data from 200 newborns (color1: 44, color2: 111, color3: 41, color4: 4) and compared 296 dyads TcB/SB. Correlation between cTcB and SB is strong during (0.74–0.83) and after (0.79–0.88) phototherapy, both globally and by color group. The SB-cTcB bias depends on gestational age during phototherapy and on skin color following phototherapy. **The correlation between eTcB and SB during phototherapy is not strong (0.54), but becomes so 12 h after discontinuing phototherapy (0.78).**

Conclusions: **Our study supports the reliability of cTcB to assess SB during and after phototherapy, with differences among skin tones after the treatment**. The use of cTcB and Neomar's scale during and mainly after phototherapy may help reduce the number of blood samples required.

Candel-Pau, Júlia, Silvia Maya-Enero, Jordi Garcia-Garcia, Xavier Duran-Jordà, and María Ángeles López-Vílchez. "Transcutaneous Bilirubin Reliability during and after Phototherapy Depending on Skin Color." European Journal of Pediatrics 183, no. 7 (April 6, 2024): 2819–30. https://doi.org/10.1007/s00431-024-05516-4.

Link: https://link.springer.com/10.1007/s00431-024-05516-4

Transcutaneous Bilirubin Accuracy Before, During, and After Phototherapy: A Meta-Analysis **2023**

CONTEXT: Transcutaneous bilirubinometry (TcB) is used as a valid screening to identify neonates requiring measurement of total serum bilirubin (TSB) before phototherapy. Its use during and after phototherapy is not advised yet because of unknown reliability.

OBJECTIVES: **To determine the agreement of TcB and TSB measurements before, during, and after phototherapy.**

DATA SOURCES: PubMed Medline, Cochrane Library, and references of eligible studies were searched.

STUDY SELECTION: Prospective and retrospective cohort and cross-sectional studies reporting BlandAltman statistics of paired TcB and TSB measurements in term and preterm newborns.

DATA EXTRACTION: Meta-analysis was performed using the Mantel-Haenszel weighted approach. The agreement between TcB and TSB in lmol/L was described by pooled mean differences (MDs) and limits of agreement (LoA).

RESULTS: **Fifty-four studies were included**. The pooled MD before phototherapy is 2.5 lmol/L (LoA -38.3 to 43.3). The pooled MD during phototherapy is -0.3 lmol/L (LoA -34.8 to 34.2) on covered skin and -28.6 lmol/L (LoA -105.7 to 48.5) on uncovered skin. The pooled MD after phototherapy is -34.3 lmol/L (LoA -86.7 to 18.1) on covered skin and -21.1 lmol/L (LoA -88.6 to 46.4) on uncovered skin. Subgroup analysis revealed the best agreement at the forehead. We did not find any difference in agreement between term and preterm neonates.
LIMITATIONS: Language restriction.

CONCLUSIONS: **TcB measurements before and during phototherapy on covered skin show good agreement compared with TSB in term and preterm newborns. More studies are needed to evaluate the accuracy after phototherapy.**

Ten Kate, Lisa, Tiemen Van Oorschot, Jessica Woolderink, Sarah Teklenburg-Roord, and Jolita Bekhof. "Transcutaneous Bilirubin Accuracy Before, During, and After Phototherapy: A Meta-Analysis." Pediatrics 152, no. 6 (December 1, 2023): e2023062335. https://doi.org/10.1542/peds.2023-062335.

Link: https://publications.aap.org/pediatrics/article/152/6/e2023062335/195647/Transcutaneous-Bilirubin-Accuracy-Before-During

Accuracy of transcutaneous bilirubin on covered skin in preterm and term newborns receiving phototherapy using a JM-105 bilirubinometer	**2019**

Objective: Determine the suitability of **transcutaneous bilirubin (TCB) as a tool to assess the effectiveness of phototherapy on patched skin.**

Study design: A prospective observational study was conducted. We covered a fragment of skin (sternum) with a photo-opaque patch. Several simultaneous TCB and TSB measurements were performed with the JM-105 bilirubinometer. Bland and Altman test evaluated the agreement between bilirubin levels.

Result: A total of 217 patients were studied, 48.8% were preterm. The mean difference between TSB and TCB before the start of treatment was 1.07 mg/dL. During phototherapy, differences on covered skin were 0.52, 0.27, and 0.39 mg/dL at 24, 48, and 72 h of therapy respectively. The best correlation was observed at 48 h in preterm infants.

Conclusion: **The measurement of TCB on patched skin (PTCB) is useful for monitoring the response to phototherapy in term and preterm infants.** We use a patch with a removable flap that eases successive measures without disturbing the patients.

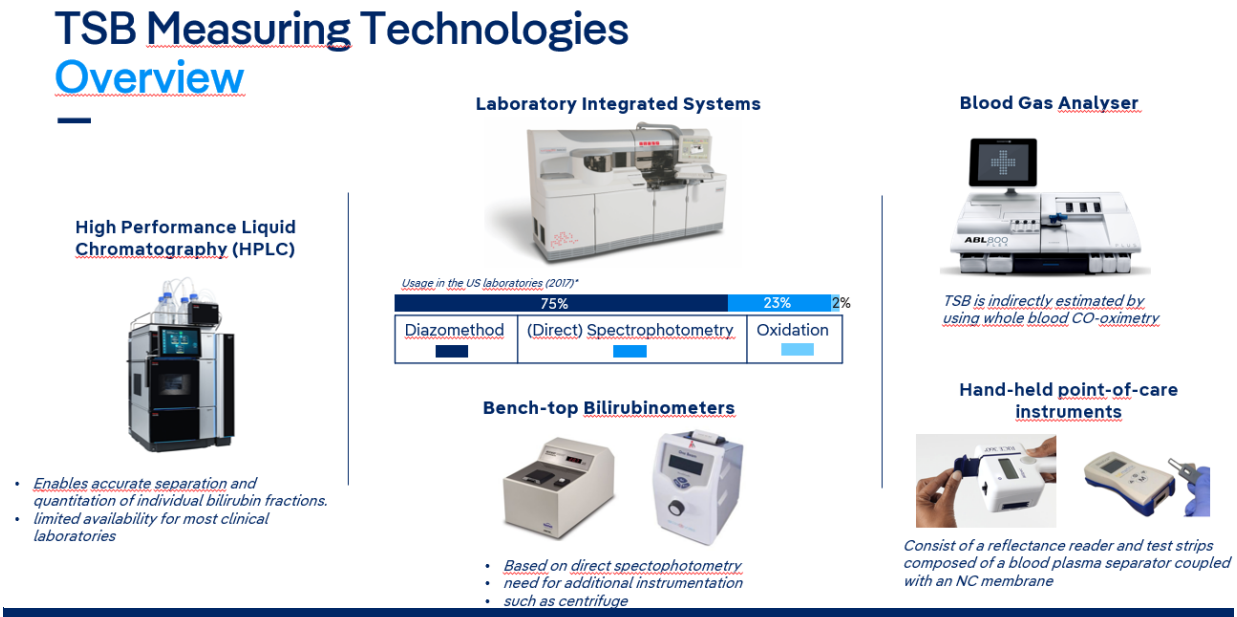
Costa-Posada U, Concheiro-Guisán A, Táboas-Ledo MF, González-Colmenero E, González-Durán ML, Suarez-Albo M, Duran Fernández-Feijoo C, Pumarada-Prieto M, Martínez-Reglero C, Fernández-Lorenzo JR. Accuracy of transcutaneous bilirubin on covered skin in preterm and term newborns receiving phototherapy using a JM-105 bilirubinometer. J Perinatol. 2020 Feb;40(2):226-231. doi: 10.1038/s41372-019-0557-9. Epub 2019 Nov 25. PMID: 31767979; PMCID: PMC6985020.

Link: https://pubmed.ncbi.nlm.nih.gov/31767979/

vii. TSB Methods

Accurate quantification of neonatal bilirubin presents a significant challenge, especially in the context of managing neonatal hyperbilirubinemia. There is a variety of different methods to determine the total serum bilirubin (TSB). The goal of precise, accurate and specific measurement of bilirubin and its subfractions in serum has not yet been achieved, despite many different methods being available. In addition to the traditional photometric diazo procedures, drychemistry methods, direct spectrophotometry in serum and whole blood and for scientific purposes separations by HPLC were established.

Studies show partially strong differences between methods. The methods can therefore also impact the correlation between TSB and TcB values e.g. from the Dräger Jaundice Meter JM-105. While a constant offset could be adjusted for, missing precision can lead to different clinical decisions.



Accuracy of bilirubin on the Siemens RAPIDPoint 500 blood gas analyser: A data mining study 2022

Aim: Blood gas analysers which can measure bilirubin in whole blood are commonly available in neonatal intensive care units; however, the accuracy of these measurements is not well established. We sought to determine accuracy of whole blood bilirubin on the Siemens RAPIDPoint 500 blood gas analyser with reference to formal laboratory total serum bilirubin on the Ortho Vitros 5600.

Methods: A method comparison of the bilirubin results from the blood gas analysers compared with the chemistry analysers was performed by data mining of results obtained as part of routine patient care. Results were included if patients underwent bilirubin testing by blood gas analyser and formal TSB, with both samples being collected within 20 min. Retrospective laboratory data was collected over a 28-month period, 1 January 2019 to 1 May 2021.

Results: 449 eligible sample pairs were included. A Bland-Altman plot was generated to identify systematic differences between the methods. A mean bias of -11 µmol/L was observed with 95% limits from -60 µmol/L to 38 µmol/L. Some blood gas bilirubin results were up to 70 µmol/L lower than formal TSB measurements around the clinically significant concentration range of 200 to 300 µmol/L.

Conclusion: **Clinicians need to be aware of potential differences between the results from their blood gas analysers compared to formal TSB results. Sole reliance on blood gas bilirubin results which underestimate TSB may lead to under-recognition of neonatal jaundice that meets treatment thresholds.** Formal measurement of TSB should be sought to inform decisions regarding treatment of neonatal jaundice.

Mukerji, Shohini, Himanshu Popat, and Jason ZY Chung. "Accuracy of Bilirubin on the Siemens RAPIDPoint 500 Blood Gas Analyser: A Data Mining Study." Journal of Paediatrics and Child Health, February 7, 2022, jpc.15890. https://doi.org/10.1111/jpc.15890.

Link: https://onlinelibrary.wiley.com/doi/10.1111/jpc.15890

Accuracy and Reliability of Whole Blood Bilirubin Measurements Using a Roche Blood Gas Analyzer for Neonatal Hyperbilirubinemia Screening and Risk Stratification 2022

Background: Accurate bilirubin measurements are essential for appropriate management of neonatal hyperbilirubinemia. This study aimed to evaluate the accuracy and reliability of whole blood bilirubin measurements obtained using a Roche blood gas analyzer (Roche TBiL), with total serum bilirubin (TSB) measurements determined by the Ortho VITROS 4600 chemistry system (Ortho TSB) serving as a reference.

Materials and Methods: Medical records of hospitalized neonates that underwent simultaneous Roche TBiL and Ortho TSB measurements were reviewed for eligibility selection and data collection. The correlations and differences between two sets of results were determined using Passing–Bablok regression analysis and a Bland–Altman plot, respectively. For eligible newborns, the risk of developing severe hyperbilirubinemia was assessed using the Bhutani nomogram. Weighted kappa analysis was used to evaluate the agreement between risk prediction by the two methods.

Results: We obtained 618 paired Roche TBiL and Ortho TSB results from 309 neonates. Roche TBiL and Ortho TSB measurements showed a good correlation (r = 0.923; 95% CI: 0.905–0.938). Passing–Bablok regression analysis yielded the following equation: Roche TBiL = 0.794 × Ortho TSB + 1.255 mg/dL, with a slope of 0.794 (95% CI: 0.763–0.825) and intercept of 1.255 (95% CI: 1.042–1.417). The average difference between the two methods was 0.1 ± 1.448 mg/dL. A total of 207 neonates were eligible for evaluation of the agreement between the risk-grading methods. Although kappa analysis showed good agreement between the methods, with a weighted kappa of 0.681 (95% CI: 0.610–0.751) across all populations, the values for approximately half of the neonates at intermediate and high risk of hyperbilirubinemia (33/72) were underestimated by Roche TBiL.

Conclusion: **Our results indicate that Roche TBiL and Ortho TSB measurements in the neonatal population are not consistent.** As a point-of-care and trace blood assay, Roche blood gas bilirubin measurements can facilitate primary screening of neonatal hyperbilirubinemia, but **it seems to lack accuracy regarding risk stratification, particularly for high-risk newborn individuals.**

Wang, Qing, Tianyi Zhang, Yuanxi Lin, Li Jiang, Wenlong Zhou, and Xiaolong Zong. “Accuracy and Reliability of Whole Blood Bilirubin Measurements Using a Roche Blood Gas Analyzer for Neonatal Hyperbilirubinemia Screening and Risk Stratification.” Frontiers in Pediatrics 10 (July 4, 2022): 910566. https://doi.org/10.3389/fped.2022.910566.

Link: https://www.frontiersin.org/articles/10.3389/fped.2022.910566/full

viii. Checklist for Transcutaneous Bilirubin Screening Devices:

Key considerations when investing in a Jaundice Meter

Criteria for safe and efficient TcB Jaundice Screening:

- ☐ Accuracy (σ) of +/- 1.5mg/dL or +/- 25.5 µmol/L
- ☐ Non-invasive and pain-free transcutaneous measuring
- ☐ Proven track record with high amount of clinical evidence >30.000 patients involved
- ☐ Pulse xenon arc lamp light source with two-optical path technology
- ☐ Daily check of light source as performance indicator
- ☐ Reusable probe, no disposables needed
- ☐ Hand held contour designed for easy handling

Hygienic design focus

- ☐ Plain surfaces
- ☐ No gaps or edges that are difficult to reach
- ☐ Compatible with many disinfection agents

Workplace Integration

- ☐ Barcode Reader to easily enter nurse and patient ID
- ☐ Electronic data transfer (via HL7) to reduce manual documentation
- ☐ LCD Touch Screen
- ☐ Lightweight <205g and compact, with simple user interface

III. Phototherapy

Phototherapy (PT) is commonly used to treat neonatal jaundice but there is substantial variation in the application. Lamola introduced a pharmacological perspective on the topic of phototherapy to use photons as a drug when prescribing PT and Maisels confirms that one "should apply the same therapeutic rigour to the use of phototherapy as [...] to the use of a pharmacologic agent in the newborn."

i. Principles of Phototherapy as a drug

A Pharmacologic View of Phototherapy **2016**

Background: Because of its efficacy in reducing the need for exchange transfusion, the concomitant reduction in the incidence of kernicterus, and its apparent safety, noninvasive phototherapy to reduce the body burden of unconjugated bilirubin has been widely used for nearly decades. However, it is now opined that phototherapy may be overprescribed.

Optimum phototherapy light source:
Light generation technology, the elucidation of skin optics, and progress in understanding of phototherapy processes have converged to provide a strong conclusion for the optimum light source: an array of narrow-band (<25 nm at half height) LEDs with peak wavelength near 475 nm, capable of providing a uniform irradiance greater than or equal to 30 mW/cm2/nm over a 1500-cm2 area. Such a source is superior in every important respect: action spectrum overlap, irradiance control, uniformity, stability, safety, and lifetime cost.

Best practices for effective phototherapy to reduce bilirubin load:
1. Use photons as a drug when prescribing neonatal phototherapy
2. Use of narrow-spectrum blue light (475 nm)
3. Measure irradiance for specific wavelength
4. Use least irradiance dose to achieve an efficient decrease in bilirubin load
5. Consider infants' Hb as a potential barrier for effective bilirubin photodegradation

Consideration: By considering the photons of therapy light as molecules of a drug, this view connects therapeutic efficacy with photon wavelength, photon dose, dose rate and regimen, efficiency of photon absorption by bilirubin, quantum yields of photoproducts, and their metabolic courses.
Based on this view, recommendations to ultimately improve efficacy and safety are presented.
Special attention is given to phototherapy regimens for low gestational age, low birthweight infants.

Lamola, Angelo A. "A Pharmacologic View of Phototherapy." Clinics in Perinatology 43, no. 2 (June 2016): 259–76. https://doi.org/10.1016/j.clp.2016.01.004.

Link: https://linkinghub.elsevier.com/retrieve/pii/S0095510816000051

Phototherapy in the neonatal intensive care unit – quantity and quality **2018**

Summary:
If we do use phototherapy, it is important that it is used correctly and, like any drug, it should be administered in an appropriate dose (measured as irradiance). The data of Mreihil and colleagues [...] **remind us that 'prolonged exposure to phototherapy lights may be detrimental to jaundiced infants and that efforts should be made to keep exposure short, particularly in the most immature infants'**, and they recognise the need for more attention to 'precision and quality'. PT is a ubiquitous intervention that has helped millions of newborns throughout the world, **but it has some potentially harmful side effects**. The balance of the risks versus benefits of PT will likely vary both with the status of the infant and with the way we deliver

[...] Changes we need if we want to provide effective PT and improve outcomes: (i) Use photons as a drug when prescribing phototherapy (ii) use a narrowspectrum blue light (450 nm) (iii) measure irradiance for specific wavelength and (iv) use the least irradiance dose to achieve an efficient decrease in bilirubin load'. **I would add one other recommendation to these 'best practices' and that is to use phototherapy for the shortest possible time.** However we plan to use it, and **we should apply the same therapeutic rigour to the use of phototherapy as we do to the use of a pharmacologic agent in the newborn which simply means using the lowest effective dose for as shorter time as possible**. Finally, as noted by Stevenson, we should consider a 'nonphototherapy' option for the treatment of hyperbilirubinaemia in ELBW infants.

Maisels, M Jeffrey. "Phototherapy in the Neonatal Intensive Care Unit – Quantity and Quality." Acta Paediatrica 107, no. 4 (April 2018): 551–53. https://doi.org/10.1111/apa.14241.

Link: https://onlinelibrary.wiley.com/doi/10.1111/apa.14241

ii. Wavelength, footprint & efficacy

Irradiance footprint of phototherapy devices: a comparative study **2021**

Background: Phototherapy (PT) is the standard treatment of neonatal unconjugated hyperbilirubinemia. The irradiance footprint, i.e., the illuminated area by the PT device with sufficient spectral irradiance, is essential for PT to be effective. Irradiance footprint measurements are not performed in current clinical practice. We describe a user-friendly method to systematically evaluate the high spectral irradiance (HSI) footprint (illuminated area with spectral irradiance of ≥30 µW cm−2 nm−1) of PT devices in clinical practice.

Materials and methods: Six commercially available LED-based overhead PT devices were evaluated in overhead configuration with an incubator. Spectral irradiance (µW cm−2 nm−1) and HSI footprint were measured with a radiospectrometer (BiliBlanket Meter II).

Results: The average measured spectral irradiance ranged between 27 and 52 µW cm−2 nm−1 and HSI footprint ranged between 67 and 1465 cm2, respectively. Three, two, and **one PT devices [Bililux] out of six covered the average BSA of an infant born at** 22, 26–32, and **40 weeks of gestation**, respectively.

Conclusion: Spectral irradiance of LED-based overhead PT devices is often lower than manufacturer's specifications, and HSI footprints not always cover the average BSA of a newborn infant. The proposed measurement method will contribute to awareness of the importance of irradiance level as well as footprint measurements in the management of neonatal jaundice.

Dam-Vervloet, Alida J., Nienke Bosschaart, Henrica L. M. van Straaten, Lieke Poot, and Christian V. Hulzebos. "Irradiance Footprint of Phototherapy Devices: A Comparative Study." Pediatric Research, November 2, 2021. https://doi.org/10.1038/s41390-021-01795-x.

Link: https://www.nature.com/articles/s41390-021-01795-x

Bilirubin isomers during LED phototherapy of hyperbilirubinemic neonates, blue-green (~478 nm) vs blue **2024**

Background: The clinical part of this randomized controlled trial concerning phototherapy of neonates with hyperbilirubinemia showed that the recommended blue-green LED light (≈478 nm) was 31% more efficient than standard blue LED light (≈459 nm) measured by the decline in total serum bilirubin. Lumirubin has biologic effects. The aim was to compare the serum bilirubin isomers, efficacy, and biologic effects between the two phototherapy groups.

Methods: Inclusion criteria: neonates healthy except for hyperbilirubinemia, gestational age ≥33 weeks, birth weight ≥1800 g, and postnatal age >24 h. Forty-two neonates were randomized to receive overhead blue-green light and 44 blue light. Treatment 24 h. The light irradiance was equal.

Results: The percentage decrease of combined bilirubin isomers was 47.8% for blue-green light vs 33.4% for blue light, the ratio being 1.43. Corresponding values for Z,Z-bilirubin were 55.6% vs 44.2%, the ratio being 1.26. The increase in the absolute serum concentrations of the photoisomer Z,E-bilirubin and thereby combined photoisomers were greater using blue light.

Conclusion: Blue-green light was essentially more efficient determined by the decline of combined bilirubin isomers and Z,Zbilirubin itself. Regarding biological effects neonates receiving blue-green light might be more affected than neonates receiving blue light.

Impact:

Phototherapy of hyperbilirubinemic neonates using blue-green LED light with a peak emission of 478 nm was 43% more efficient than standard blue LED light with a peak emission of 459 nm was measured by the decline of serum combined bilirubin isomers, and the decline of toxic Z,Z-bilirubin was 26% greater.

Ebbesen, Finn, Poul H. Madsen, Maria Rodrigo-Domingo, and Mette L. Donneborg. "Bilirubin Isomers during LED Phototherapy of Hyperbilirubinemic Neonates, Blue-Green (~478 Nm) vs Blue." Pediatric Research, September 4, 2024. https://doi.org/10.1038/s41390-024-03493-w.

Link: https://www.nature.com/articles/s41390-024-03493-w

Blue-Green (~480 nm) versus Blue (~460 nm) Light for Newborn Phototherapy—Safety Considerations 2022

Background: We have previously shown that the **phototherapy of hyperbilirubinemic neonates using blue-green LED light with a peak wavelength of ~478 nm is 31% more efficient** for removing unconjugated bilirubin from circulation than blue LED light with a peak wavelength of ~452 nm. Based on these results, we recommended that the phototherapy of hyperbilirubinemic newborns be practiced with light of ~480 nm.

Aim: Identify and discuss the most prominent potential changes that have been observed in the health effects of phototherapy using either blue fluorescent- or blue LED light and speculate on the expected effects of changing to blue-green LED light phototherapy. Search the phototherapy literature using the terms neonate, hyperbilirubinemia, and phototherapy in the PubMed and Embase databases. Transitioning from blue fluorescent light to blue-green LED light will expose neonates to less light in the 400–450 nm spectral range, potentially leading to less photo-oxidation and geno-/cytotoxicity, reduced risk of cancer, and decreased mortality in extremely low-birthweight neonates. The riboflavin level may decline, and the increased production and retention of bronze pigments may occur in predisposed neonates due to enhanced lumirubin formation. The production of pre-inflammatory cytokines may rise. Hemodynamic responses and transepidermal water loss are less likely to occur. The risk of hyperthermia may decrease with the use of blue-green LED light and the risk of hypothermia may increase. **Parent–neonate attachment and breastfeeding will be positively affected because of the shortened duration of phototherapy. The latter may also lead to a significant reduction in the cost of phototherapy procedures as well as the hospitalization process.**

Ebbesen, Finn, Hendrik Jan Vreman, and Thor Willy Ruud Hansen. "Blue-Green (~480 Nm) versus Blue (~460 Nm) Light for Newborn Phototherapy—Safety Considerations." International Journal of Molecular Sciences 24, no. 1 (December 27, 2022): 461. https://doi.org/10.3390/ijms24010461.

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC9820095/

iii. Continuous vs intermittent Phototherapy

Blue- Continuous versus intermittent phototherapy in treatment of neonatal jaundice: a randomized controlled trial 2024

Abstract: Phototherapy (PT) is a widely used treatment for neonatal jaundice, yet the ideal model of application remains controversial. **In this study, the effects of continuous phototherapy (CPT) and intermittent phototherapy (IPT) models were compared in the treatment of neonatal indirect hyperbilirubinemia (IHB) and whether IPT is a superior modality is investigated**. Single-centre parallel randomized controlled open label trial. A computer-based table of random numbers was used to allocate treatments. Newborns ≥ 34 weeks' gestation who received phototherapy in our neonatal intensive care unit (NICU) between July 2022 and April 2023 were included. CPT was applied continuously for 6 h, and IPT was applied as 2 cycles of 1 h on and 2 h off in a 6-h session. Rebound TSB was measured 8 h after phototherapy was stopped in both groups. Phototherapy duration, TSB reduction rate and rebound bilirubin rate were compared between intervention groups.

One hundered and four neonates met the inclusion criteria during the study period. CPT and IPT were each used in 52 newborns. Demographic characteristics of the study groups, including sex, mode of delivery, birth weight, admission weight, age at postnatal presentation, diet, discharge weight, and history of PT in siblings, were similar ($p > 0.05$). The most common cause of IHB in both groups was ABO incompatibility. The median phototherapy time was 12 h (6–15) in the CPT group and 4 h (2–4) in the IPT group ($p < 0.001$). The mean rate of bilirubin decrease was 1.12 ± 0.73 mg/dl/h in those who underwent IPT and 0.51 ± 0.33 mg/ dl/h in those who underwent CPT ($p < 0.001$). The mean rebound bilirubin rate 8 h after phototherapy was 0.08 ± 0.28 mg/ dl/h in the CPT group, and −0.01 ± 0.17 mg/dl/h in the IPT group ($p = 0.039$). The length of hospital stay was longer in the CPT group ($p = 0.032$). Skin rash, diarrhoea and increased body temperature were less frequent in the IPT group ($p < 0.001$).

Conclusions: In this study, **IPT was found to be at least as effective as CPT in reducing total serum bilirubin**. Even though the **duration of PT is shorter in IPT, the slower rate of rebound bilirubin, shorter hospital stays and lower incidence of side effects indicated that intermittent phototherapy is superior to continuous phototherapy**. Choosing IPT over CPT is a more rational approach in neonatal jaundice.

Demirel, Hande Nur, Sibel Sevuk Ozumut, and Husnu Fahri Ovalı. "Continuous versus Intermittent Phototherapy in Treatment of Neonatal Jaundice: A Randomized Controlled Trial." European Journal of Pediatrics 183, no. 8 (May 20, 2024): 3389–96.

Link: https://link.springer.com/10.1007/s00431-024-05610-7

Continuous vs Intermittent Phototherapy in the Management of Non-Haemolytic Neonatal Hyperbilirubinemia - A Randomised Non - Inferiority Study 2020

Introduction: Phototherapy is used to manage neonatal hyperbilirubinemia in early life. **We aimed to compare between intermittent and continuous phototherapy in reducing TSB**, rate of fall of bilirubin, duration of phototherapy and duration of hospitalisation in neonates with non-haemolytic hyperbilirubinemia.

Methods: Total 190 neonates who were > 34 weeks and birth weight ≥ 2000 gm were included. They were randomised into group A (continuous phototherapy) and group B (intermittent phototherapy). **Group A received phototherapy for three hours and 45 minutes off and group B received phototherapy for three hours and then three hours off.** TSB levels estimation were done in both groups and compared after each 12 hours, 24 hours, and 48 hours of commencing phototherapy.

Results: The mean TSB at presentation was 15.64 ± 2.19 mg/dl for continuous and 15.03 ± 1.07 mg/dl for intermittent group. Mean TSB at 12, 24, 48 hours were 13.26 ± 2.4 mg/dl, 10.8 ± 1.72 mg/dl, 10.16 ± 0.95 mg/dl respectively for continuous and 12.6 ± 1.65 mg/dl, 10.04 ± 1.8 mg/dl, 9.1 ± 0.66 mg/dl respectively for intermittent group ($p < 0.05$). The mean rate of fall in serum bilirubin was 0.22 ± 0.12 mg/dl/hr for group A and 0.21 ± 0.08 mg/dl/hr for group B ($p = 0.45$). There was not much difference in mean duration of hospitalisation in both groups ($p = 0.547$).

Conclusions: Intermittent phototherapy is a non-inferior option to continuous phototherapy, in the management of non-haemolytic hyperbilirubinemia with additional advantages of less interrupted mother infant bonding and decreased irradiance.

Patil, Mallanagouda M, Gowthami G S, Hidaytullah R Bijapure, Anil Kumar Sajjan, S S Kalyanshettar, and S V Patil. "Continuous vs Intermittent Phototherapy in the Management of Non-Haemolytic Neonatal Hyperbilirubinemia - A Randomised Non - Inferiority Study." Journal of Nepal Paediatric Society 40, no. 3 (December 15, 2020): 185–89. https://doi.org/10.3126/jnps.v40i3.29535.

Link: https://www.nepjol.info/index.php/JNPS/article/view/29535

Analysis of therapeutic effect of intermittent and continuous phototherapy on neonatal hemolytic jaundice 2019

Abstract: **Clinical efficacy and adverse reaction rates of ABO hemolytic jaundice in patients with continuous and intermittent blue light irradiation were compared**, to provide reference for clinical treatment of neonatal ABO hemolytic jaundice. A retrospective analysis of 307 patients with neonatal hemolytic jaundice admitted to Qilu Hospital of Shandong University (Qingdao) from January 2010 to December 2017 was undertaken. A total of 165 cases of children with continuous blue light irradiation and 142 cases of intermittent blue light irradiation were analyzed. Also the serum bilirubin levels, phototherapy time and frequency, treatment efficiency and adverse reaction rates were compared between the groups. **The phototherapy time of children in the continuous phototherapy group was significantly higher from the intermittent phototherapy group, and the difference was statistically significant (t=26.800, P<0.001).** Before treatment, there was no significant difference in serum bilirubin levels between continuous and intermittent phototherapy groups (P>0.050). Serum bilirubin levels of patients in continuous and intermittent phototherapy groups were lower than both previous and before treatment period, and differences were statistically significant (P<0.001). The overall effective rate of the continuous phototherapy group was higher than that of the intermittent phototherapy group (P>0.050). **The adverse reaction rates after treatment in the continuous phototherapy group was significantly higher than the intermittent phototherapy group (P<0.050).** After the symptomatic treatment in children, the adverse reactions ceased. **The therapeutic effect of intermittent blue light irradiation on neonatal ABO hemolytic jaundice was consistent with the continuous blue light irradiation treatment, and the intermittent blue light irradiation treatment has a low adverse reaction rate, and is worth promotion in clinical practice.**

Zhou, Shiying, Xiaoyan Wu, Aihua Ma, Min Zhang, and Yanli Liu. "Analysis of Therapeutic Effect of Intermittent and Continuous Phototherapy on Neonatal Hemolytic Jaundice." Experimental and Therapeutic Medicine, March 22, 2019. https://doi.org/10.3892/etm.2019.7432.

Link: http://www.spandidos-publications.com/10.3892/etm.2019.7432

iv. Quality Assurance of Phototherapy & Measurement

The concept of phototherapy as a drug aims to apply the same therapeutic rigor to the use of phototherapy as to the use of a pharmacological agent in the newborn. However, **there is no standard way of measuring the dosage** and current guidelines simply state to follow manufacturer's instructions. Variability in the intensity and wavelength of phototherapy devices can lead to inconsistent treatment outcomes. Not every light source ages the same. If a light source ages faster or stronger, there is a risk of a too low irradiation dose resulting in extended or ineffective treatment. Moreover, even if irradiance is measured results highly depend on the settings and the equipment used, thus potentially resulting in entirely different values. Establishing a robust quality assurance process for neonatal phototherapy is essential to ensure that all infants receive optimal care. By implementing these measures, healthcare facilities can ensure that phototherapy is both safe and effective, ultimately improving neonatal health outcomes and reducing the incidence of severe hyperbilirubinemia-related complications.

Neonatal Phototherapy—The Need to Measure and Document **2024**

Key Points:

Pediatricians work with the assumption that PT is safe. Perhaps this explains why PT, in contrast with other hospital-based medical treatments, departs from the standard practice of dose measurement and recordkeeping. By comparison, imagine treating a hospitalized patient with antibiotics without recording any details of the dose or length of time the medication was administered. Or imagine administering radiation therapy for a tumor without documenting the details of the radiation protocol or target area. It is axiomatic in medical practice that dosage information is recorded in the medical record. But this is not so for PT. The presumption of safety regarding PT goes against another axiom of medicine, that is, there is no treatment without side effects. There are many examples of widely accepted presumptions in medical practice that were proven wrong after rigorous studies were conducted.

Nevertheless, several studies have indicated an increased risk of adverse outcomes in infants who underwent PT. Morris et al noted that in a prespecified subgroup of their prospective study, aggressive treatment had a higher rate of mortality, "albeit not significantly so." The difference between the 2 groups was not the intensity of the light but rather the duration of exposure (ie, the total dose). The authors cautioned that "these findings are particularly worrisome because of the trend toward an increased rate of death in the only previous major trial assessing phototherapy for neonatal hyperbilirubinemia

This common practice of neither measuring nor recording dosage or treatment data in all newborns treated with PT, with the possible exception of infants being treated in the neonatal intensive care unit, has resulted in the absence of a large multicenter database. This prevents the possibility of large retrospective studies examining possible delayed adverse effects. The next challenge to further advance PT is to establish and require methods for universal measurement and recording of treatment data in every newborn. The basic information of irradiance, duration, surface area, and total dose should be recorded for each infant receiving PT. This will facilitate proper monitoring of the prescribed treatment in real time and will generate meaningful studies with accurate data.

Goldenhersh, Michael A., and Arthur I. Eidelman. "Neonatal Phototherapy—The Need to Measure and Document." JAMA Pediatrics 178, no. 6 (June 1, 2024): 515. https://doi.org/10.1001/jamapediatrics.2024.0558.

Link: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2817563

v. Checklist for Phototherapy equipment:

Key considerations when investing in a Phototherapy light

Criteria for effective and guideline conform phototherapy

- ☐ Treatment of unconjugated serum bilirubin within effective light spectrum (460-490 nm) peaking at 475nm
- ☐ Sufficient irradiance of >30 µW/cm2/nm
- ☐ Irradiance adjustment in 5 steps
- ☐ Radiometer calibrated to 460-490 nm for accurate readings
- ☐ Large surface area coverage for full term >1465 cm² with even distribution
- ☐ Eye protection for baby and staff such as: Eye shield or Light curtain

Hygienic design focus

- ☐ Plain surfaces
- ☐ No gaps or edges that are difficult to reach
- ☐ No fan
- ☐ No ventilation slots

Workplace Integration

- ☐ Easy integration into the workplace through selection of mounting option:
  - ☐ Trolly
  - ☐ Arm
  - ☐ Standalone/Hood version
- ☐ Compact and lightweight to be easy adjustable at the workplace
- ☐ Treatment timer
- ☐ Electronic data transfer to reduce manual documentation
- ☐ White observation light for quick checks
- ☐ Low noise level of 20dB(A) during normal operation
- ☐ Quite device handling

Link: https://nicmag.ca/pdf/NIC-37-4-Fall-2024-R20-web.pdf