JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Neonatal Hyperbilirubinemia Clinical Pathway

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This pathway is intended as a guide for physicians, physician assistants, nurse practitioners, and other healthcare providers. It should be tailored to the care of specific patients based on their individual circumstances and the clinician's professional judgment.

JOHNS HOPKINS
All Children's Hospital

Johns Hopkins All Children's Hospital

Neonatal Hyperbilirubinemia Clinical Pathway

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Summary:

This clinical pathway was developed by a consensus group of Johns Hopkins All Children's Hospital (JHACH) physicians, advanced practice providers, and nurses to standardize the management of pediatric patients undergoing evaluation for neonatal hyperbilirubinemia. This clinical pathway addresses the following questions or problems:

1. How to evaluate for neonatal hyperbilirubinemia
2. When to consider hospital admission
3. When to initiate treatment (i.e., phototherapy, intravenous immunoglobulin [IVIG], exchange transfusion [ET])
4. When to initiate intravenous (IV) fluids
5. How to optimize breastfeeding and when to initiate supplementation
6. When to end phototherapy and when to obtain rebound total serum bilirubin (TsB)
7. When to discharge infants ≥ 35 weeks' gestational age (GA)
8. Management of hyperbilirubinemia in premature infants < 35 weeks' gestational age

Background:

Neonatal hyperbilirubinemia is the most commonly encountered clinical issue in newborn babies. A number of risk factors contribute to severe hyperbilirubinemia in newborn infants with gestational age ≥ 35 weeks. Evaluation and management of hyperbilirubinemia vary among clinical providers despite the publication of the AAP clinical practice guideline.[6] In some instances, phototherapy is initiated earlier than the recommended TsB threshold based on the risk factors and postnatal age. More importantly, significant variation exists in the TsB value at which phototherapy is discontinued and in the timing of rebound bilirubin level collection, leading to increased length of hospitalization, interruption in breastfeeding, family dissatisfaction, and denials by insurance companies.

Clinical Management:

Emergency Center (EC) Patients

Initial Assessment:

Obtain history (including prenatal, birth and postnatal), pattern and quality of stooling and voiding, mode of feeding (mother's own milk and/or formula), volume of feeding, physical exam (including neurologic, hydration status, and jaundice), vital signs, growth parameters (i.e., weight).

Initial Evaluation:

a. Obtain baseline laboratory tests: complete blood count (CBC), reticulocyte count, comprehensive metabolic profile (CMP), and neonatal type and screen-direct antiglobulin test (DAT) immunoglobulin G (IgG), if the infant's blood type and DAT status are unknown.

   If labs are abnormal and/or suggestive of infection and/or the infant has clinical signs/symptoms of sepsis, a full sepsis workup, including cerebrospinal fluid (CSF) culture, blood culture, urinalysis (UA), and urine culture (via catheter specimen), should be obtained before initiation of broad-spectrum antibiotics in order to assess for neonatal sepsis. Refer to the *Febrile Neonate* and *Urinary Tract Infection (UTI)* clinical pathways for additional recommendations and guidance.

b. If history and laboratory data *are not* suggestive of dehydration and/or poor oral intake, hemolysis, and no clear etiology for jaundice, obtain catheter urinalysis and urine culture, as data reveal a significant number of neonates with jaundice as the presenting sign of UTI. Of note, if a urinalysis is suspicious for UTI from a catheter specimen, a blood culture and lumbar puncture should be obtained before initiating broad-spectrum antibiotics to assess for neonatal sepsis. Refer to the *Febrile Neonate* and *UTI* clinical pathways for additional recommendations and guidance.

   Consider consultation with Infectious Disease (ID) regarding the appropriate antibiotic choice and treatment duration for a confirmed neonatal UTI based on a catheter specimen.

c. If history and laboratory data *are not* suggestive of dehydration and/or poor oral intake *and* are suggestive of hemolysis (particularly if bilirubin levels do not respond to or require additional phototherapy), evaluate further for:

   - Isoimmune hemolytic disease
   - Glucose-6-phosphate dehydrogenase (G6PD) deficiency

- Red blood cell (RBC) enzyme deficiencies
- RBC membrane defects
- Gilbert Syndrome
- Infection

d. Assess for significant hyperbilirubinemia risk factors:

- Lower gestational age (i.e., risk increases with each additional week less than 40 weeks)
- Jaundice in the first 24 hours (h) after birth
- Pre-discharge transcutaneous bilirubin (TcB) or TSB concentration close to the phototherapy threshold
- Hemolysis from any cause, if known or suspected, based on a rapid rate of increase in the TSB or TcB of >0.3 milligrams per deciliter (mg/dL) per hour in the first 24 h or >0.2 mg/dL per hour thereafter
- Phototherapy during a previous hospitalization
- Parent or sibling requiring phototherapy or exchange transfusion (ET)
- Family history or genetic ancestry suggestive of inherited red blood cell disorders, including G6PD deficiency
- Exclusive breastfeeding with suboptimal intake
- Scalp hematoma or significant bruising
- Down Syndrome
- Macrosomic infant of a diabetic mother

e. Assess for neurotoxicity risk factors:

- Albumin < 3.0 grams (g)/dL
- Gestational age
- G6PD deficiency, or other hemolytic conditions
- Isoimmune hemolytic disease (e.g., positive DAT)
- Sepsis
- Significant clinical instability in the past 24h

f. Assess for signs of acute bilirubin encephalopathy (ABE):

- Hypertonia
- Arching
- Retrocollis
- Opisthotonos
- High-pitched cry
- Recurrent apnea

g. Plot the total serum bilirubin on Hour-Specific Nomogram, Phototherapy Nomogram and Exchange Nomogram (www.bilitool.org or www.peditools.org/bili2022).

Hospital Admission

For JHACH patients, the Neonatal Intensive Care Unit (NICU) should be the first point of contact for ALL infants who require hospital admission, including discussions regarding unit assignment (i.e., NICU vs Pediatric Intensive Care Unit [PICU] vs Pediatric Medicine) and the need for NICU consults when infants are admitted to units outside the NICU. Possible scenarios for hospital admission include:

- Infant with signs/symptoms of acute bilirubin encephalopathy, irrespective of bilirubin level
- TsB ***at or above*** phototherapy threshold
- TsB ***less than 3 mg/dL below*** phototherapy threshold *and* signs/symptoms of acute hemolysis
- Provider discretion to start phototherapy if TsB is <3 mg/dL below the threshold to prevent readmission
- Start phototherapy STAT in the EC

EC Discharge Criteria

Consider discharge to home from EC if TsB is ***below*** phototherapy threshold *and* meets the following criteria:

- No risk factors for neurotoxicity
- Demonstrating adequate oral intake/hydration status
- Without signs/symptoms of acute hemolysis
- Close follow-up assured with PCP within 24 h of EC discharge

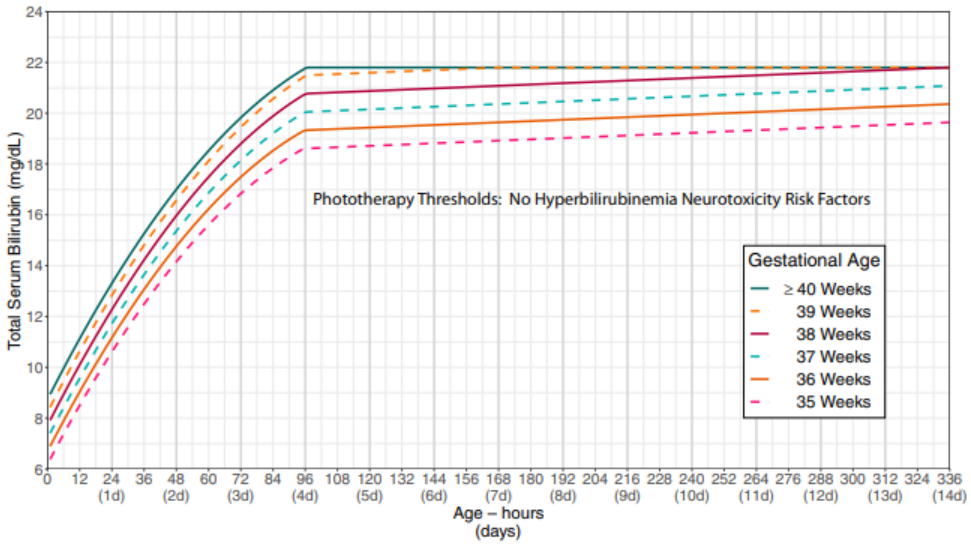


FIGURE 2

Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Note that infants <24 hours old with a TSB at or above the phototherapy threshold are likely to have a hemolytic process and should be evaluated for hemolytic disease as described in recommendation 14. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 1.

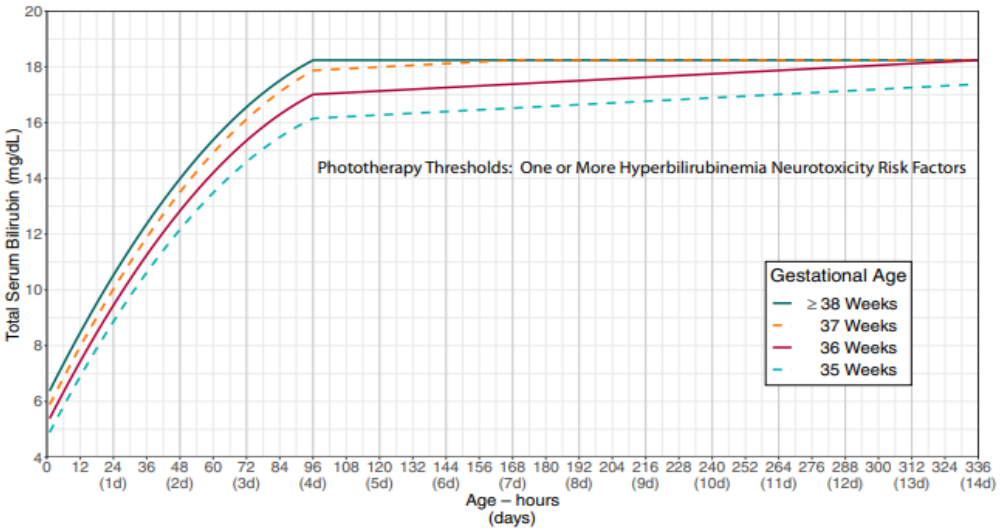


FIGURE 3

Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract the direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 2.

Figures 2 and 3 reprinted from: Kemper AR, Newman TB, Slaughter JL, et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics.* 2022;150(3):e2022058859

Admission and Inpatient Management:

Guidelines for Administration of Phototherapy

- Recommend initiation of intensive phototherapy= 30 µW/cm2/nm (e.g., overhead light and biliblanket) and optimize exposed surface area.
- Measure the irradiance level with a bilimeter upon initiation of phototherapy, upon addition of another phototherapy device, and at least every 12 hours.
- If concern for hemolysis or an approaching escalation of care threshold (i.e., within 2 mg/dL below the exchange transfusion threshold), recheck TsB within 3-6 hours of initiation of phototherapy. If low concern for hemolysis, recheck TsB within 12-24 hours after initiation of phototherapy.

    - If repeat TsB levels are not rising with administration of phototherapy, repeat TsB levels every 12-24 hours until discontinuation
    - If repeat TsB levels are rising in spite of administration of phototherapy:

        - Repeat TsB every 6 h until stable or falling. TsB levels can be further spaced to every 12-24 h once declining TsB levels have been established.
        - Ensure maximization of current-intensive phototherapy with consideration for additional phototherapy exposure and limiting time out of phototherapy
        - Assess for additional etiologies (i.e., Isoimmune Hemolytic Disease, G6PD deficiency, RBC enzyme deficiencies, RBC membrane defects, Gilbert's disease, infection, etc.).
        - Consult NICU STAT if there is a poor response to phototherapy or if TsB meets or exceeds the Escalation of Care threshold.

Guidelines for Discontinuation of Phototherapy and Obtaining Rebound Bilirubin Levels

- Discontinue phototherapy if TsB level is ≥ 2 mg/dL below the phototherapy threshold at initiation.
- If the infant is at lower risk for rebound hyperbilirubinemia (i.e., no concern for hemolysis, phototherapy started ≥48 hr old), discharge home with PCP follow-up in 1 day.
- If the infant is at risk for rebound hyperbilirubinemia (e.g.., concern for hemolysis, phototherapy started when ≤48 hr old), consider rebound TSB level 6-12 hours after phototherapy discontinuation.

    - If rebound TsB is not obtained, follow up in 24 hours with primary care provider (PCP) to repeat TsB.
    - If rebound TsB is obtained and is ≥ the phototherapy threshold, restart phototherapy and refer to the Inpatient Management Pathway.

Breastfed Infant Management

a. For infants not on supplementation for another medical indication *and* TSB within 3 mg/dL of the phototherapy threshold, document recent weight and perform a Breastfeeding Assessment:

- Consult Lactation, if available
- Risk factors for delayed lactogenesis
- Lactation history
- Maternal breast shape, breast change
- LATCH scores and latch depth
- Feeding frequency
- Infant transfer at the breast

b. Assessment of signs for suboptimal intake:

- Ineffective latch and/or suck
- Sleepy and difficult to wake up for feeding
- Delayed colostrum or milk supply
- Weight loss > 10% from birth weight
- Laboratory abnormalities (e.g., hypoglycemia, hypernatremia)
- Ineffective milk transfer
- Uric acid crystals in urine
- < 4 stools on day 4 or meconium stools on day 5

c. If there are NO signs of suboptimal intake, continue to encourage breastfeeding with a deep latch, 9+ feeds in 24 hours, and consider other etiologies for hyperbilirubinemia (e.g., hemolysis, especially if ≤ 24 hr old).

d. If there ARE signs of suboptimal intake:
- and breastmilk volumes **ARE** increasing:
    - Encourage increased breastfeeding frequency, 9+ feeds in 24 hours, deep latch
    - Milk expression after feeds and offer expressed breast milk
- and breastmilk volumes are **NOT** increasing:
    - Encourage increased breastfeeding frequency, 9+ feeds in 24 hours, deep latch
    - Milk expression after feeds and offer any expressed breast milk.
    - Start supplementation with donor milk or formula and continue until breastmilk volumes are adequate

e. Suggested supplementation volumes (phototherapy by itself is not an indication for supplementation):

- 0-24 hours of life: supplement 2-10 ml each feed
- 24-48 hours of life: supplement 5-15 ml each feed
- 48-72 hours of life: supplement 15-30 ml each feed
- 72-96 hours of life: supplement 30-60 ml each feed

f. In order to optimize intensive phototherapy, it is recommended to keep the biliblanket under the infant during breastfeeding sessions and limit breastfeeding sessions to no more than 20 minutes.

Intravenous Fluids Administration Management

a. IV fluids and/or supplemental formula are routinely NOT indicated unless clinical signs of dehydration are suspected. It is important to underscore that enteral feeds hasten the elimination of bilirubin.
b. Encourage frequent feedings every 2-3 hours and, for breastfed infants, engage a Lactation Specialist for additional breastfeeding support.
c. Consider initiating IVF based on the following clinical factors:

- Weight loss disproportionate for postnatal age
- Hypernatremia
- Increased urine specific gravity
- Poor oral intake
- Decreased urine output
- Signs of poor perfusion
- TsB above or within 3 mg/dL of the exchange level

Escalation of Care Management

Defined as within 2 mg/dL below the exchange transfusion level:

a. If not already a patient in the NICU, consult Neonatology and admit to NICU STAT
b. If there are signs of acute bilirubin encephalopathy, then proceed to the “Is TsB ≥ Exchange Transfusion Threshold” section below
c. If there are no signs of acute bilirubin encephalopathy:
    - Start intensive phototherapy STAT:
        - Overhead lights plus blanket LED devices, if available
        - Ensure maximization of current intensive phototherapy with optimized surface exposure and allow no time out of phototherapy for anything that is not medically necessary (roll down diaper, etc.)
        - Position the infant under the center of the device

        - Decrease the distance between the device and the infant
            - Ensure irradiance >30 µW/cm2 /nm

- Obtain STAT labs, if not already done:
    - CBC, reticulocyte count, CMP, Neonatal Type & Screen-DAT IgG, UA, and urine culture
    - Consider sepsis evaluation (blood culture, CSF studies, as well as UA and urine culture if not already obtained); G6PD deficiency test, blood smear, and haptoglobin
    - Obtain STAT TsB at least every 2 hours

- Obtain STAT vascular access:
    - Place peripheral IV
    - Consider umbilical lines (double-lumen umbilical venous catheter [UVC]) with radiograph (XR) to confirm placement

- Ensure hydration:
    - Total fluids 80-120 mL/kg/day (by mouth [PO] + IV)
    - IV fluids with D10W +/- electrolytes based on age and serum chemistry results
    - Enteral feeds PO + gavage feeds at 80 mL/kg/day

- Consider IVIG administration:
    - For infants with isoimmune hemolytic disease, if TsB reaches or exceeds the escalation of care threshold
    - IVIG dose is 1 g/kg over 2 hours and may be repeated in 12 hours, if needed

Exchange Transfusion Threshold

If TsB > exchange transfusion threshold:

- Continue phototherapy, hydration, and other interventions as above.
    - Place NPO, obtain consent, and prepare for urgent exchange transfusion
    - Notify the blood bank and place a central line (if not yet placed)
- If, while preparing for the exchange transfusion but before starting the procedure, a TsB concentration is **<** the exchange transfusion threshold and the infant does not show signs of acute bilirubin encephalopathy, then the exchange transfusion may be deferred while continuing intensive phototherapy and following the TsB every 2 hours until the TsB is below the escalation of care threshold.
    - Do not delay performing the exchange transfusion while awaiting lab results

- Perform exchange transfusion:
    - Double volume ET: 160 mL/kg total blood
    - Packed RBC and fresh frozen plasma (FFP) to reconstitute a hematocrit (HCT) of 40-50%
    - Cross-matched, < 48 hr old, irradiated blood
    - Aliquots by patient weight:
        - >3 kg: 10-15 mL/aliquot
        - 2-3 kg: 10 mL/aliquot
        - 1-2 kg: 10 mL/aliquot (5 ml/aliquot if closer to 1 kg)
    - Lab monitoring before, during, and after ET (i.e., platelets, glucose, serum calcium/ionized calcium, albumin, serum chemistry, TsB
    - Continuous cardiac and pulse oximetry
    - Refer to the hospital protocol for procedure details

- The bilirubin to albumin ratio (B/A) in relation to gestational age (GA) and risk can be used in conjunction with the TsB in determining the need for an exchange transfusion:
    - ≥ 8.0 if the GA ≥ 38 weeks and no neurotoxicity risk factors
    - ≥ 7.2 if the GA ≥ 38 weeks and at least 1 neurotoxicity risk factor
    - ≥ 7.2 if the GA is 35 – 37 weeks and no neurotoxicity risk factors
    - ≥ 6.8 if the GA is 35 – 37 weeks and at least 1 neurotoxicity risk factor

- If TsB **<** Exchange Transfusion Threshold, continue intensive phototherapy

Johns Hopkins All Children's Hospital
Neonatal Hyperbilirubinemia Clinical Pathway

EC Management: Neonatal Hyperbilirubinemia Clinical Pathway
Infants ≥ 35 Weeks Gestation

Scan the QR code or click the link to access the AgileMD algorithm for EC management:

https://t.jh.edu/NeonatalHyperbilirubinemiaEmergency

Inpatient Management: Neonatal Hyperbilirubinemia Clinical Pathway
Infants ≥ 35 Weeks Gestation

Scan the QR code or click the link to access the AgileMD algorithm for inpatient management:

https://t.jh.edu/NeonatalHyperbilirubinemiaInpatient

Additional Considerations:

Patient Class

All patients with neonatal indirect hyperbilirubinemia should be placed in “inpatient” status if admitted for phototherapy.

Discharge:

- If all hospital discharge criteria have been met.
- Needs follow-up with PCP within 24-48 hr (based on risk for rebound hyperbilirubinemia) of discharge has been assured.
- Verbal and written information regarding signs/symptoms of jaundice warranting immediate medical attention is distributed to caregivers.

Outcome Measures:

1) Rate of readmissions for jaundice or hyperbilirubinemia
2) Rate of administration of IV fluids
3) Rate of obtaining rebound bilirubin levels prior to discharge
4) Length of stay for patients in the EC
5) Total length of stay for patients in the hospital
6) Length of phototherapy (time initiated to time discontinued)

Neonatal Hyperbilirubinemia Clinical Pathway
Infants < 35 Weeks Gestation

Background:

Hyperbilirubinemia in premature infants less than 35 weeks gestational age (GA) is more prevalent and protracted than in term infants and carries a higher risk for the development of bilirubin-induced neurologic dysfunction (BIND) at lower total serum bilirubin (TsB) values. This is thought to be due to central nervous system immaturity and associated comorbidities that may potentiate bilirubin toxicity.[9]

Risk Factors:

Inherent to premature infants are:

- Increased red blood cell breakdown causes a higher bilirubin load
- Immature liver function leading to decreased bilirubin clearance and conjugation
- Increased enterohepatic circulation due in part to the delay in initiating and advancing enteral feeds

Clinical Presentation:

Premature infants are at higher risk for BIND, and unfortunately, the acute signs and symptoms of BIND in premature infants are subtle and non-specific and may present primarily as recurrent apneic episodes. It has been reported that the increased maximum total bilirubin level in premature infants is independently associated with hearing screen failure. Further prospective studies are needed to determine whether this increased risk of hearing screen failure translates into an increased risk of hearing loss.[10]

In unstable VLBW preterm infants, increasing levels of total plasma bilirubin were also found to be directly associated with increasing risk of death or adverse neurodevelopmental outcomes at 18-22 months of age.[11]

Bilirubin Measurement:

Even though the accuracy of transcutaneous bilirubin (TcB) measurements has been validated in infants 28-34 6/7 weeks GA [12, 13], the tool is not uniformly used in the premature baby population. A 2018 study found that only 28% of NICUs in California actually use TcB measurement in this patient population.[14]

Management Approach:

Unlike in term infants, evidence-based guidelines for initiating phototherapy and performing exchange transfusions in infants < 35 weeks GA are lacking. This is due in part to the lack of reliable, predictive measures of bilirubin neurotoxicity and uncertainties about the risk-benefit ratio of interventions in this at-risk patient population.

Initiation of Phototherapy:

The expert opinion consensus on initiating phototherapy in infants < 35 weeks was proposed by Maisels in 2012.[17] It has since been routinely followed by the majority of NICUs in the U.S.

Postmenstrual age is to be used to compute the need for phototherapy as follows:

- GA <28 weeks – TSB 5 - 6 mg/dL (86 to 103 micromol/L)
- GA 28 to 29 weeks – TSB 6 - 8 mg/dL (103 to 137 micromol/L)
- GA 30 to 31 weeks – TSB 8 - 10 mg/dL (137 to 171 micromol/L)
- GA 32 to 33 weeks – TSB 10 - 12 mg/dL (171 to 205 micromol/L)
- GA 34 to <35 weeks – TSB 12 - 14 mg/dL (205 to 239 micromol/L)

Given concerns about increased mortality among infants < 1000 grams exposed to aggressive phototherapy, it is recommended to start with an irradiance of 15 microW/cm per nanometer (nm). If TSB continues to rise, increase the exposed surface area. Only if a poor response is still observed, increase the irradiance in increments as needed up to a max of 30 microW/cm per nm.

Special Considerations for Infants 24–28 weeks GA and/or Extremely Low Birth Weight (ELBW) Infants:

Is bilirubin harmful?

Uncertainties remain as to the safe levels of TsB in this very premature patient population. Some observational studies have raised concerns that very low TSB levels (≤ 5 mg/dL) may cause long-term neurodevelopmental deficits. Others suggested that moderate TsB levels may actually be of benefit, given the antioxidant properties of bilirubin.

Is phototherapy (PT) safe?

A multicenter, randomized National Institute of Child Health and Human Development (NICHD) Neonatal Research Network study published in 2008 compared aggressive to conservative PT among 1974 ELBW infants. Infants were stratified into 2 groups: birth

weight (BW) 501 - 750 grams (g) and BW 751- 1000 g. Conservative PT was initiated, continued, or restarted for TSB ≥ 8 mg/dL for infants with BW 501 to 750 g and for TsB ≥ 10 mg/dL for infants with BW 751 to 1000 g. Aggressive phototherapy was initiated, continued, or restarted for infants in either group with TSB ≥ 5 mg/dL.[17]

They found:

1) No significant difference in the rate of death or neurodevelopmental impairment (the primary outcome) at 18 to 22 months of corrected gestational age (CGA) between neonates randomized to either conservative or aggressive PT

2) A significant reduction in the rate of neurodevelopmental impairment among the aggressive PT group

3) The rate of death among infants with BW 501 to 750 g was higher with aggressive PT. The difference was not statistically significant (p=0.15), but a post hoc, Bayesian analysis estimated an 89% probability that aggressive phototherapy increased the rate of deaths in this subgroup. This finding was considered worrisome and warranted serious attention, given an earlier trial[18] that raised similar concerns and the study's limited power. The etiology for such a correlation is postulated to be secondary to oxidative injury to cell membranes and deoxyribonucleic acid (DNA).

Because of the reported increased mortality in infants with BW 501 to 750 g, prudence has been advocated, at least in infants with a BW <750 g, to initiate phototherapy at lower irradiance levels and only to increase these levels, or to increase the surface area of the infant exposed to phototherapy, if the TSB continues to rise.[15]

A sub-study of the NICHD Neonatal Research Network PT trial was performed to evaluate the efficacy of phototherapy (PT) devices and the outcomes of ELBW infants treated with those devices. It included 1404 infants treated with a single type of PT device during the first 24±12 h of treatment. Their standard of care included the following guidelines to intensify PT for TSB values of:

- 11 mg/dL in 501- to 750-g infants
- 13 mg/dL in 751- to 1000-g infants

The definition of ‘high TSB’ was predefined as a TSB within 2 mg/dl of the predetermined exchange transfusion criterion (≥11 mg dl^{-1} for 501 to 750 g infants and ≥13 mg/dl for 751 to 1000 g infants). An exchange transfusion was indicated if the TSB exceeded the threshold values after 8 h of intensified treatment.[19]

In an UpToDate review[20], Bhutani suggested the following guidelines for increasing the irradiance level in infants 24 to 26 weeks GA when TSB continues to rise despite adequate phototherapy:

- 24 to <26 weeks GA:
  - Start with 15 to 25 microW/cm^2/nm to one (dorsal/ventral) body surface
  - Increase to 15 to 25 microW/cm^2/nm on both ventral and dorsal body surfaces
  - Pre-exchange – 25 microW/cm^2/nm to both ventral and dorsal body surfaces

- 26 to 28 weeks GA:
  - Start with 25 to 30 microW/cm^2/nm to one (dorsal/ventral) body surface
  - Increase to 25 to 30 microW/cm^2/nm to both ventral and dorsal body surfaces
  - Pre-exchange – 30 microW/cm^2/nm to both ventral and dorsal body surfaces

Information on the management of hyperbilirubinemia in infants <501 grams is currently lacking. The PT initiation threshold may be lower than reported, and provider discretion is advised.

Clinical Management:

Infants born at <35 weeks' gestation should have their TsB checked regularly in the first week of life, per NICU standard of care. Indications for initiating PT or performing an exchange transfusion are based on expert consensus.[12]

	Phototherapy	*Exchange transfusion*
Gestational age (week)	*Initiate phototherapy total serum bilirubin (mg dl^{-1})*	*Total serum bilirubin (mg dl^{-1})*
<28 0/7	5–6	11–14
28 0/7–29 6/7	6–8	12–14
30 0/7–31 6/7	8–10	13–16
32 0/7–33 6/7	10–12	15–18
34 0/7–34 6/7	12–14	17–19

Reprinted from: Maisels MJ, Coffey MP, Kring E. Transcutaneous bilirubin levels in newborns <35 weeks' gestation. *J Perinatol.* 2015;35(9):739-744.

Important Information:

- Use PMA for phototherapy. Consider discontinuation of phototherapy when TsB is 1–2 mg/dL below the initiation level for the infant's PMA.

- Prophylactic phototherapy in case of skin bruising is not routinely recommended.

- For infants at higher risk, it is suggested to follow TsB every 12 hours until phototherapy is started, then proceed per guidelines.

- For infants > 28 weeks or > 1000 g, using TcB or bilirubin measurement via blood gas analyzer could be an option to minimize blood draws in stable patients with significant skin bruising.

- For infants < 28 weeks or < 1000 g, using bilirubin measurement via a blood gas analyzer could be an option to minimize blood draws in stable patients with significant skin bruising.

- Use total bilirubin. Do not subtract direct-reacting or conjugated bilirubin from the total.

- Given the high risk and complications of exchange transfusion in infants < 35 weeks, it is recommended that exchange transfusion be performed if the TsB value is at the exchange level after 8 hours of intensive and optimized phototherapy. Exceptions would be at the physician's discretion.

- Information about hyperbilirubinemia management in infants < 25 weeks is currently lacking. Phototherapy and exchange transfusion initiation thresholds may be lower than what is reported in the tables above, and provider discretion is advised. Measure irradiance at regular intervals per NICU protocol.

- For infants <1000 g BW, start phototherapy at lower irradiance levels (15-20 Mwatts). If the TsB continues to rise, increase the exposed surface area. Increase the irradiance only if the TsB continues to rise.

- Increases of irradiance should be done in a stepwise fashion based on Bhutani's recommendations:

    - >26 to 28 weeks GA:
        - Start with 25 to 30 microW/cm^2/nm on one (dorsal/ventral) body surface
        - Increase to 25 to 30 microW/cm^2/nm to both ventral and dorsal body surfaces

        - Pre-exchange – 30 microW/cm^2/nm to both ventral and dorsal body surfaces

    - 24 to <26 weeks GA:
        - Start with 15 to 25 microW/cm^2/nm on one (dorsal/ventral) body surface
        - Increase to 15 to 25 microW/cm^2/nm to both ventral and dorsal body surfaces
        - Pre-exchange – 25 microW/cm^2/nm to both ventral and dorsal body surfaces

Indications for Exchange Transfusion:

Exchange transfusion carries a significant risk of complications that include cardio-respiratory arrest, arrhythmias, thrombosis, thrombocytopenia, hypothermia, necrotizing enterocolitis, and infection.[18]

The risk/benefit ratio of an exchange transfusion needs to be considered. Candidates for such an intervention would be infants who have neurologic signs suggestive of BIND or those who fail to respond to aggressive phototherapy with persistently rising TsB levels.

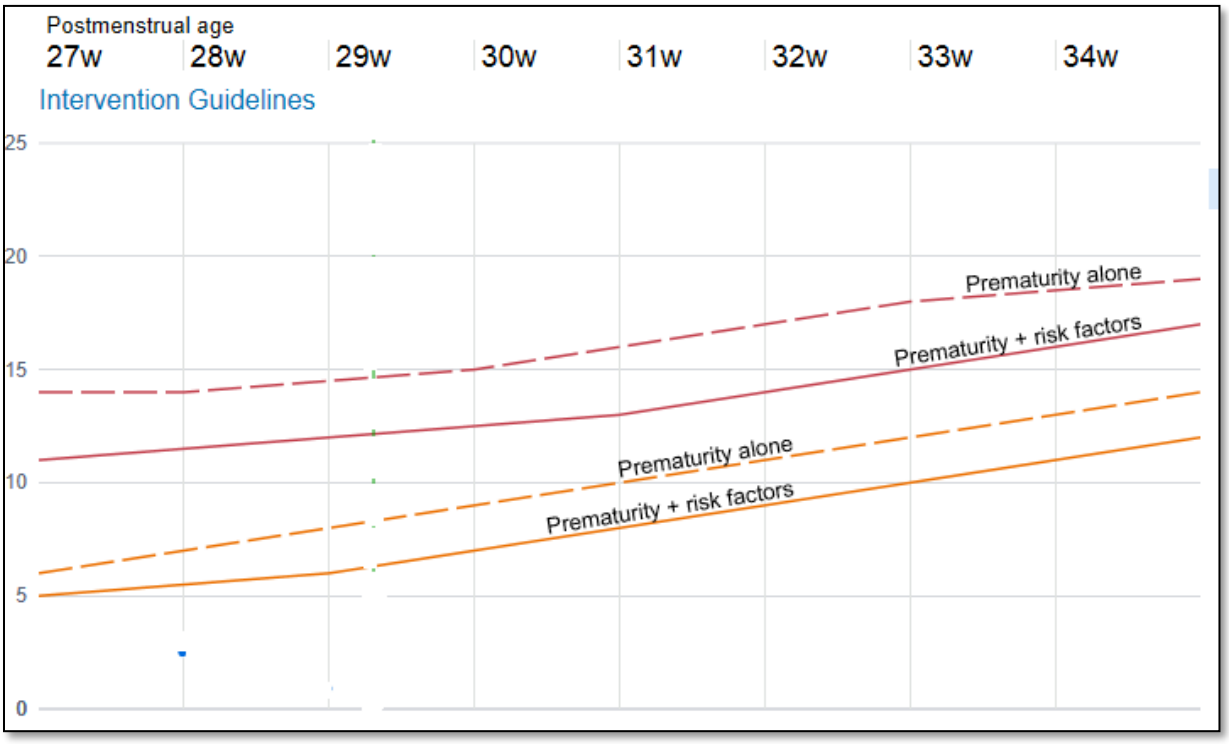
The expert opinion consensus on initiating exchange transfusion in infants 25 to 35 weeks GA was proposed by Maisels in 2012.[16] Postmenstrual age is to be used to compute the need for exchange transfusion as follows:

- GA <28 weeks – TSB 11 to 14 mg/dL (188 to 239 micromol/L)
- GA 28 to 29 weeks – TSB 12 to 14 mg/dL (205 to 239 micromol/L)
- GA 30 to 31 weeks – TSB 13 to 16 mg/dL (222 to 274 micromol/L)
- GA 32 to 33 weeks – TSB 15 to 18 mg/dL (257 to 308 micromol/L)
- GA >34 weeks – TSB 17 to 19 mg/dL (291 to 325 micromol/L)

Per the authors, “The wider ranges and overlapping of values in the exchange transfusion column reflect the degree of uncertainty in making these recommendations. They recommend using the lower range of the listed TSB levels for infants at greater risk for bilirubin toxicity – such as (1) lower gestational age, (2) lower serum albumin levels < 2.5 g/dL, (3) rapidly rising TSB, and (4) clinically unstable infants such as those with severe metabolic acidosis, sepsis, significant apnea or hypotension, among other conditions.”

*****Discuss with the Neonatology Attending before proceeding with exchange transfusion in this population. Refer to the AgileMD guideline for aliquot volumes in infants <1 kg.***

The graph below is in Epic, under **Bilirubin Activity**:



Stanford Children's Health Premie BiliRecs
Use the lower range of the listed TSB levels for infants at greater risk for bilirubin toxicity:
1. Serum albumin levels < 2.5 g/dL
2. Rapidly rising TSB levels suggesting hemolytic disease
3. Those who are clinically unstable, as described below:

When a decision is being made about the initiation of phototherapy or exchange transfusion, infants are considered to be clinically unstable if they have one or more of the following conditions:
A. Blood pH < 7.15
B. Blood culture positive sepsis in the prior 24 hours
C. Apnea and bradycardia requiring cardio-respiratory resuscitation (bagging and/or intubation) during the previous 24 hours
D. Hypotension requiring pressor treatment during the previous 24 hours
E. Mechanical ventilation at the time of blood sampling

Stanford Children's Health Premie BiliRecs, a free, publicly available clinical decision support tool found at https://pbr.stanfordchildrens.org/, which notes that its "[r]esults are based on An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation by Maisels et al. (J Perinatol 2012)." Used with permission.

Transfusion Guidelines Legend
- Prematurity alone
- Prematurity + additional neurotoxicity risk factors

Phototherapy Guidelines Legend
- Prematurity alone
- Prematurity + additional neurotoxicity risk factors

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Disclaimer:

Clinical Pathways are intended to assist physicians, physician assistants, nurse practitioners, and other health care providers in clinical decision-making by describing a range of generally acceptable approaches for diagnosing, managing, or preventing specific diseases or conditions. The provider must make the ultimate judgment regarding the care of a particular patient in light of the patient's individual circumstances.

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Appendix A: Neonatal Phototherapy Nursing Checklist:

- ☐ Phototherapy source ordered in the patient's EMR (Bili-blanket, spot, etc.)
- ☐ Bilimeter to test irradiance level (as per phototherapy order – generally 30-35 μW/cm^2/nm
- ☐ The infant should be in a diaper only, no clothes
- ☐ Position the phototherapy device at the bedside with lights set at the recommended distance from the infant. For fluorescent and LED lights, this is as close as possible to the infant's skin, typically less than 10 centimeters (cm). If using a halogen spotlight, keep the light at the manufacturer's recommended distance to avoid overheating.
- ☐ Isolette (Giraffe Omnibed) – please see attached neonatal quick reference
    - An Isolette is needed for most phototherapy. If the infant is on a bili-blanket only, they may be in an open crib if swaddled.
- ☐ Temperature probe and temperature probe cover for use in isolette
- ☐ Thermometer to measure axillary temperature
- ☐ Eye protection
- ☐ Bili-blanket: obtain a Bili-blanket cover and ensure that the illuminated side is facing the patient
- ☐ TsB order present with frequency listed

Further information may be found in:

MyLearning:

- ACH-Giraffe Bed video
- Mosby's Nursing Skills:

    Phototherapy (Maternal-Newborn)
    Phototherapy Blanket (Maternal-Newborn)

NICU Education Specialists: x72116 and x72881

Appendix B: Neonatal Thermoregulation Quick Reference

Giraffe Isolette:

- Infants should remain in servo (baby) mode, and their body temperature should be maintained at 36.5C - 37.5C.
    - Keep the isolette top closed as much as possible and work through portholes
- Place the temperature probe over the liver (not over bone) while supine or on the flank while prone
    - When using phototherapy lights, the **probe must be directly in the path of the radiant heat of the light**; do not place the probe in an area shielded from phototherapy light
    - Cover the probe with a reflective temp probe cover
    - Probe must be visible
- No clothing or swaddling

Thermoregulation

- Infant's axillary temperature should be 36.5-37.5.
- Keep the top of isolette down whenever possible
- Use the "air boost" button when working through portholes
- Check axillary temperature every 3 hours

- If there is more than a 0.5-degree difference between the axillary temperature and isolette temp probe temperature, then the two are not correlating.
    - Check temperature probe position and adjust if needed
    - Replace the temperature probe if necessary