

Hyperbilirubinemia Guideline

*(Note: Pediatric Gastroenterology (GI) should be consulted for persistent jaundice or direct hyperbilirubinemia)
Neonatology should be consulted urgently for TSB approaching escalation of care*

Definition:

Hyperbilirubinemia is an elevation in total bilirubin beyond the level considered normal for age. Neonatal hyperbilirubinemia is a common problem that can cause neurotoxicity, kernicterus, and long-term disability if left untreated. Phototherapy is an effective treatment for hyperbilirubinemia.

Incidence:

Hyperbilirubinemia, more commonly known as newborn jaundice, is a fairly common presentation in the neonatal period. Reportedly anywhere from 60-84% of infants born at 35 weeks or greater will be diagnosed as having hyperbilirubinemia. An even larger percentage of infants born preterm will be affected.

Etiology:

Although there are a variety of syndromes and medical issues, such as sepsis, that can lead to elevated bilirubin in infants, in the typical healthy newborn, there are 4 general known causes: 1) physiologic jaundice, 2) breastfeeding jaundice which should be known as suboptimal intake jaundice, 3) breast milk jaundice, and 4) hemolytic jaundice. The physiologic causes can be found in the pathogenesis section below.

Physiological jaundice is most commonly seen within 24 hours to 5 days following birth, and is a result of increased bilirubin, partly due to a newborn's immature hepatic system, which can struggle to break down the increased load. Suboptimal intake jaundice (previously known as breastfeeding jaundice) typically occurs in those infants that are exclusively breastfed and is a result of decreased caloric intake while the mother's milk is still in the process of coming in. The cause of breast milk jaundice remains unknown. However, this is thought to be due to the increased enterohepatic circulation of bilirubin and b-glucuronidase, resulting in deconjugation of bilirubin. Hemolytic jaundice is a result of the destruction of blood products through ABO incompatibility, rhesus factor hemolysis, or minor heme antibody-led hemolysis. This leads to increased bilirubin production, which may result in jaundice.

Lastly, there is pathological jaundice which will be excluded from this guideline, as those diagnoses may require other interventions and workups that are outside the scope of this guideline.

Epidemiology:

All infants may be at risk of developing jaundice, however, certain risk factors can be useful for identifying which infants may be more likely to develop significant hyperbilirubinemia. Risk factors include:

- Lower gestational age (ie, the risk increases with each additional week less than 40 wk)
- Jaundice in the first 24 hours after birth
- Predischarge transcutaneous bilirubin (TcB) or total serum bilirubin (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 mg/dL per hour in the first 24 h or >0.2 mg/dL per hour thereafter.
- Need for Phototherapy before discharge
- Parent or sibling requiring phototherapy or exchange transfusion

- Family history or genetic ancestry suggestive of inherited red blood cell disorders, including glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Exclusive breastfeeding with suboptimal intake
- Scalp hematoma or significant bruising
- Down syndrome
- Polycythemia

Other components of the history which may reveal additional risk factors include family history of neonatal jaundice, chronic liver disease, and history of hematologic or metabolic conditions.

Pathogenesis:

Bilirubin is a breakdown product of heme, derived from hemoglobin and other heme proteins. When it is initially broken down, it is released into the blood in its unconjugated form. Unconjugated bilirubin from all over the body is transported through the blood to the liver, bound to albumin. It cannot be excreted from the body until it is changed into conjugated bilirubin. In the liver, an enzyme called uridine 5'-diphospho-glucuronosyltransferase (B-UGT) converts bilirubin into the conjugated form, allowing it to be easily excreted in urine and feces. Conjugated bilirubin is also known as direct bilirubin.

Anything that causes increased bilirubin products in the blood (i.e. RBC breakdown), decreases enterohepatic circulation or interferes with B-UGT can cause levels of bilirubin to rise in the blood. Newborns often have multiple factors that increase their overall risk of severe hyperbilirubinemia.

If bilirubin is not excreted and levels increase above a certain threshold in the blood, it will deposit in extravascular tissue and cross the blood-brain barrier. Deposition in the skin causes jaundice, and deposition in the basal ganglia and substantia nigra in the brain can cause acute bilirubin encephalopathy (short-term sequelae) and kernicterus (long-term sequelae).

Phototherapy treatment involves using a specific wavelength of light that converts unconjugated bilirubin to a water-soluble form in which it can be excreted.

Differential Diagnosis:

Unconjugated Hyperbilirubinemia

Increased production of bilirubin:

- Hemolysis
 - Isoimmune: ABO incompatibility, Rh, or minor blood group antigen incompatibility.
 - Erythrocyte membrane defects: spherocytosis, elliptocytosis.
 - Enzyme defects: G6PD deficiency, pyruvate kinase deficiency, etc.
 - Hemoglobinopathies
 - Disseminated intravascular coagulopathy.
- Cephalohematoma or extensive bruising
- Polycythemia - Infant of a diabetic mother, delayed cord clamping.

Impaired conjugation or decreased hepatocellular uptake:

- Gilbert syndrome - decreased B-UGT
- Crigler-Najjar syndrome, types I and II - decreased or absent B-UGT function.
- Medications: aspirin, cephalosporins, sulfonamides (interfere with bilirubin to albumin binding), rifampin (competes with bilirubin for hepatocellular uptake).
- Congenital hypothyroidism - decreased B-UGT enzyme activity

Increased enterohepatic circulation:

- poor feeding
- infrequent stooling
- bowel obstruction.

Mixed etiology:

- Physiologic jaundice and prematurity related jaundice
- Breastfeeding/breast milk jaundice

Conjugated Hyperbilirubinemia

- Obstruction of biliary system
 - Biliary atresia
 - Choledochal cyst
 - Alagille syndrome
- Metabolic liver diseases and systemic conditions:
 - Infection: TORCH infections, sepsis, or UTI
 - Acute liver injury related to ischemia, hypoxia, or acidosis
 - Parenteral nutrition-associated cholestasis
 - Gestational alloimmune liver disease
- Bile acid synthesis, storage, or transport defect
 - Progressive familial intrahepatic cholestasis
 - Dubin Johnson syndrome
 - Rotor syndrome

Guideline Inclusion Criteria:

- Previously healthy infants
- Age >24 hours and ≤14 days
- > 35+0 weeks gestational age

Guideline Exclusion Criteria:

- Conjugated hyperbilirubinemia defined as > 2 mg/dL or greater than 20% of the TSB concentration
- Suspected acute bilirubin encephalopathy or displaying clinical findings associated with acute bilirubin encephalopathy such as hypotonia, weak suck or high pitched cry
- Suspected sepsis, history of fever or ill-appearing on assessment

Diagnostic Evaluation:

TABLE 1. Laboratory Evaluation of the Jaundiced Infant of 35 or More Weeks' Gestation

Indications	Suggested labs
Jaundice in first 24 hours of life	<ul style="list-style-type: none"> ● Transcutaneous total bilirubin (TcB) or total serum bilirubin (TSB)
Jaundice appears excessive for infant's age	<ul style="list-style-type: none"> ● TcB or TSB
Infant receiving phototherapy or TSB rising rapidly and unexplained by history or exam	<ul style="list-style-type: none"> ● Blood type ● direct antiglobulin test (DAT) if positive or unknown maternal Ab screen ● Complete blood count ● Peripheral smear ● Direct bilirubin ● Repeat TSB within 4 to 24 hours depending on hour of life and prior TSB level
TSB approaching Escalation of Care levels (TSB within 2 of exchange transfusion level)	<ul style="list-style-type: none"> ● STAT labs: total and direct serum bilirubin, CBC, albumin, serum chemistries, type and cross match ● Notify blood bank ● Measure TSB at least q 2 hrs
Elevated direct (or conjugated) bilirubin level (exclusion criteria)	<ul style="list-style-type: none"> ● Urinalysis ● Urine culture ● Consider sepsis evaluation (CBC, blood culture, UA, urine culture, lumbar puncture) ● Consider work-up for biliary atresia
Jaundice present beyond 3 weeks of age (exclusion criteria)	<ul style="list-style-type: none"> ● Total and direct bilirubin ● Evaluate for cholestasis if elevated direct bilirubin ● Check newborn screen for thyroid, galactosemia ● Consider evaluating for hypothyroidism especially if concerning on exam ● Consider work up of biliary atresia

Critical Points of Evidence

Fluids/Nutrition:

Evidence Supports

- Promoting oral feeding during phototherapy to make up for insensible losses that are increased by the treatment.
- The AAP recommends the implementation of maternity care practices that promote comprehensive, evidence-based, family-centered breastfeeding support. Clinicians should promote breastfeeding support for all mothers and breast milk feeding within the first hour after birth with frequent feeding on

demand (ie, at least 8 times in 24 hours). Signs of suckling adequacy include appropriate urine output and transitional stooling, normal weight loss by hour of age and delivery method, absence of maternal discomfort, and audible swallowing as the mother's milk volumes increase. Breastfed infants who are adequately hydrated should not routinely receive supplementation with commercially available infant formula. (see [LIGHT Algorithm for Breastfeeding Infants 5 Days Old with Hyperbilirubinemia](#))

- Infants requiring Escalation of Care levels (TSB within 2 of exchange transfusion level) should receive intravenous hydration (see [Escalation of Care Algorithm](#))

Evidence Lacking/Inconclusive

- There is no clear evidence demonstrating that IV fluid supplementation contributes to preventing infants from having acute bilirubin encephalopathy, kernicterus, or cerebral palsy in otherwise healthy full-term newborns.

Treatment/Equipment:

Evidence Supports

- Intensive phototherapy is recommended at the total serum bilirubin thresholds in Figure 3 (infants with no known hyperbilirubinemia neurotoxicity risk factors) or Figure 4 (infants with at least 1 recognized hyperbilirubinemia neurotoxicity risk factor besides gestational age) on the basis of gestational age, hyperbilirubinemia neurotoxicity risk factors, and age of the infant in hours. Clinical decision support tool includes <https://peditools.org/bili2022/>
- Care should be escalated when an infant's TSB reaches or exceeds the escalation-of-care threshold, defined as 2 mg/dL below the exchange transfusion threshold, as detailed in Figure 5 (infants with no known hyperbilirubinemia neurotoxicity risk factors) or Fig 6 (infants whose TSB is increasing despite phototherapy or infants with at least 1 recognized hyperbilirubinemia neurotoxicity risk factor). See Figure 2 for the algorithm recommended by the AAP. Clinical decision support tool includes <https://peditools.org/bili2022/>
- Putting LED lights within 10cm of the infant to improve irradiance levels. (LED lights and fluorescent lights may be placed as close as possible to an infant whereas halogen lights cannot.) The use of an open bassinet may be preferred due to the difficulty of placing an LED light within 10cm of a baby while in an incubator. (Management of Hyperbili)
- Use of LED lights in the blue-green light spectrum 430 to 490 nm exposed to greatest body surface area
- LED lights are to be used instead of fluorescent or halogen lights due to lower heat emission leading to potentially fewer side effects, and improved cost-effectiveness
- Keep irradiance measurement > 30 microwatts/cm²/nm up to a max of 55 microwatts/cm²/nm
- Use of biliblanket in combination with overhead conventional light improves the rate of decrease compared to conventional overhead light or biliblanket alone
- Use of phototherapy is contraindicated in congenital porphyria or in patients being treated with photosensitizing drugs
- The use of reflective materials to line the sides of the crib has a meaningful reduction in bilirubin and decreases length of hospital stay and should be considered if bilirubin is approaching exchange transfusion level.
- High-risk indicator for hearing loss (red flag) - Hearing check for infants with hyperbilirubinemia at levels requiring exchange transfusion.

Evidence Against

- No evidence that biliblanket is more favorable on parent-child bonding or nurse satisfaction than conventional overhead phototherapy

Discontinuing Treatment:

Evidence Supports

- Discontinuing phototherapy is an option when the TSB has decreased to at least 2 mg/dL below the hour-specific threshold at the initiation of phototherapy. A longer period of phototherapy is an option if there are risk factors for rebound hyperbilirubinemia (eg, gestational age <38 weeks, age <48 hours at the start of phototherapy, hemolytic disease).

Laboratory Testing:

Evidence Supports

- If an infant has direct hyperbilirubinemia, further workup for cholestasis should be evaluated.
- Infants with direct bilirubinemia should have a urinalysis and urine culture. Clinicians should also consider an evaluation for sepsis if warranted.
- Glucose-6-phosphate dehydrogenase (G6PD) level should be obtained for a jaundiced infant receiving phototherapy with a family history or genetic factor increasing the likelihood of G6PD deficiency and/or for an infant with poor response to phototherapy.
- For hospitalized infants, TSB should be measured within 12 hours after starting phototherapy. The timing of the initial TSB measure after starting phototherapy and the frequency of TSB monitoring during phototherapy should be guided by the age of the child, the presence of hyperbilirubinemia neurotoxicity risk factors, the TSB concentration, and the TSB trajectory.
- Repeat bilirubin measurement after phototherapy is discontinued is based on the risk of rebound hyperbilirubinemia.
 - Infants who received phototherapy during the birth hospitalization and who were later readmitted for exceeding the phototherapy threshold should have bilirubin measured the day after phototherapy discontinuation.
 - Infants readmitted because they exceeded the phototherapy threshold following discharge but who did not receive phototherapy during the birth hospitalization and infants treated with home phototherapy who exceeded the phototherapy threshold should have bilirubin measured 1 to 2 days after phototherapy discontinuation or clinical follow-up 1 to 2 days after phototherapy to determine whether to obtain a bilirubin measurement. Risk factors for rebound hyperbilirubinemia to consider in this determination include the TSB at the time of phototherapy discontinuation in relationship to the phototherapy threshold, gestational age <38 weeks, the adequacy of feeding and weight gain, and the other hyperbilirubinemia and hyperbilirubinemia neurotoxicity risk factors.

Risk Factors for Neurotoxicity:

- Gestational age < 38 weeks (risk increases with the degree of prematurity). Gestational age is required to identify the phototherapy thresholds and exchange transfusion thresholds
- albumin < 3.0 g/dL
- isoimmune hemolytic disease (ie positive direct antiglobulin test/DAT), G6PD deficiency or other hemolytic conditions
- sepsis
- significant clinical instability in the previous 24 hr

Consults/Referrals:

- Obtain Neonatology consult if the patient meets Escalation of Care threshold (2 mg/dl from exchange transfusion level)
- Consider Gastroenterology consult if Direct Bilirubin is persistently elevated

- Lactation Consultation for all breastfeeding mothers

Admission Criteria:

- Meets criteria for needing phototherapy (use the following phototherapy guidelines from the AAP: Pediatrics. 2022;150(3). doi:10.1542/peds.2022-058859)
- Persistently elevated total bilirubin with evidence of dehydration (>10% loss from birth weight, sunken fontanel, lethargic, poor feeding, decreased urine output or stool output)
- For infants ≤ 2.7 kg recommend discussion with NICU for placement for use of infant warmer to prevent hypothermia.

Follow-Up Care:

- Follow up with a primary care doctor within 24 to 48 hours. Repeat bilirubin measurement after phototherapy is based on the risk of rebound hyperbilirubinemia.
 - Infants who received phototherapy during the birth hospitalization and who were later readmitted for exceeding the phototherapy threshold should have bilirubin measured the day after phototherapy discontinuation.
 - Infants readmitted because they exceeded the phototherapy threshold following discharge but who did not receive phototherapy during the birth hospitalization and infants treated with home phototherapy who exceeded the phototherapy threshold should have bilirubin measured 1 to 2 days after phototherapy discontinuation or clinical follow-up 1 to 2 days after phototherapy to determine whether to obtain a bilirubin measurement. Risk factors for rebound hyperbilirubinemia to consider in this determination include the TSB at the time of phototherapy discontinuation in relationship to the phototherapy threshold, gestational age <38 weeks, the adequacy of feeding and weight gain, and the other hyperbilirubinemia and hyperbilirubinemia neurotoxicity risk factors.
- Weight and percent change from birth weight should be recorded.
- Infants should be assessed for adequate intake, stooling patterns, and urine output.
- If a provider is unsure about the degree of jaundice, a total serum bilirubin should be obtained. Visually diagnosing jaundice can be prone to error, especially in dark-skinned infants.

Prevention:¹

- Promote and support breastfeeding
- Establish nursery protocols for identifying and evaluating hyperbilirubinemia
- Measure bilirubin levels in all infants with jaundice in the first 24 hours after delivery
- Recognize that visual estimation of bilirubin levels is inaccurate
- Interpret all bilirubin levels according to the infant's age in hours
- Identify preterm breastfed infants and provide close monitoring
- Perform a thorough risk assessment for all infants
- Provide parents with written and verbal information about newborn jaundice
- Provide appropriate follow-up
- Treat newborns, when indicated, with phototherapy or exchange transfusion

Outcome Measures:

1. Proportion of infants receiving inpatient phototherapy for subthreshold TSB (≥ 0.3 mg/dL below phototherapy threshold) goal is < 10%
2. Proportion of infants who receive a DAT in all appropriate instances. The goal is 100% of infants with blood type O mothers who undergo inpatient phototherapy will have DAT status assessed.

3. Proportion of infants without hemolysis concerns who start inpatient phototherapy at ≥ 48 hours of age and who have rebound bilirubin measured < 18 hours after phototherapy discontinuation. Goal is $< 10\%$
4. Proportion of infants who receive unnecessary IVF. The goal is that $< 5\%$ of well-appearing infants who receive inpatient phototherapy and do not have concerns for dehydration or meet the escalation of care threshold will receive IV fluids.

Balancing Measures:

1. Incidence of reaching escalation of care threshold: Percent of infants who reach or exceed escalation of care threshold (2 mg/dL below exchange transfusion threshold) at the start of or during inpatient phototherapy
2. Incidence of total serum bilirubin (TSB) > 25 mg/dL: Percent of infants who have a TSB > 25 mg/dL at the start of or during inpatient phototherapy)
3. Phototherapy duration- Number of hours infants undergo inpatient phototherapy (approximated)
4. Hospitalization duration - Numbers of hours infants are hospitalized during phototherapy admission
5. Readmission or re-initiation of phototherapy: Percent of infants who are reinitiated on or readmitted for inpatient phototherapy within 4 days of previous inpatient phototherapy discontinuation

Methods

Existing External Guidelines/Clinical Pathways

Existing External Guideline/Clinical Pathway	Organization and Author	Last Update
Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation	American Academy of Pediatrics	2022

Any published clinical guidelines have been evaluated for this review using the **AGREE II criteria**. The comparisons of these guidelines are found at the end of this document. **AGREE II criteria** include evaluation of: Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, and Editorial Independence.

Review of Relevant Evidence: Search Strategies and Databases Reviewed

Search Strategies	Document Strategies Used
Search Terms Used:	Inclusion: neonatal, neonate, newborn, physiologic Jaundice: hyperbilirubinemia, jaundice, unconjugated, conjugated Nutrition: breastfeeding, IV fluids, intravenous fluids, formula feeding, donor milk Phototherapy: irradiance, warmer, isolette, overhead lights, biliblanket, phototherapy, Labs: direct bilirubinemia
Years Searched - All Questions	1980-2022
Language	English
Age of Subjects	≤ 14 days infants, ≥ 35 weeks GA, inpatient admissions

Search Engines	PubMed, Cochrane, Google Scholar
EBP Web Sites	UpToDate
Professional Organizations	American Academy of Pediatrics
Joint Commission	
Government/State Agencies	None
Other	

Evidence Found with Searches

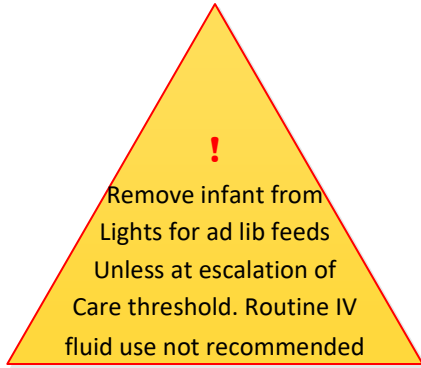
Check Type of Evidence Found	Summary of Evidence – All Questions
<input checked="" type="checkbox"/>	Systematic Reviews
<input type="checkbox"/>	Meta-analysis articles
<input checked="" type="checkbox"/>	Randomized Controlled Trials
<input checked="" type="checkbox"/>	Non-randomized studies
<input checked="" type="checkbox"/>	Review articles
<input type="checkbox"/>	Government/State agency regulations
<input checked="" type="checkbox"/>	Professional organization guidelines, white papers, ect.

Evaluating the Quality of the Evidence

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
Strong	Desirable effects clearly outweigh undesirable effects or vice versa
Weak	Desirable effects closely balanced with undesirable effects
Type of Evidence	
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence

Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence
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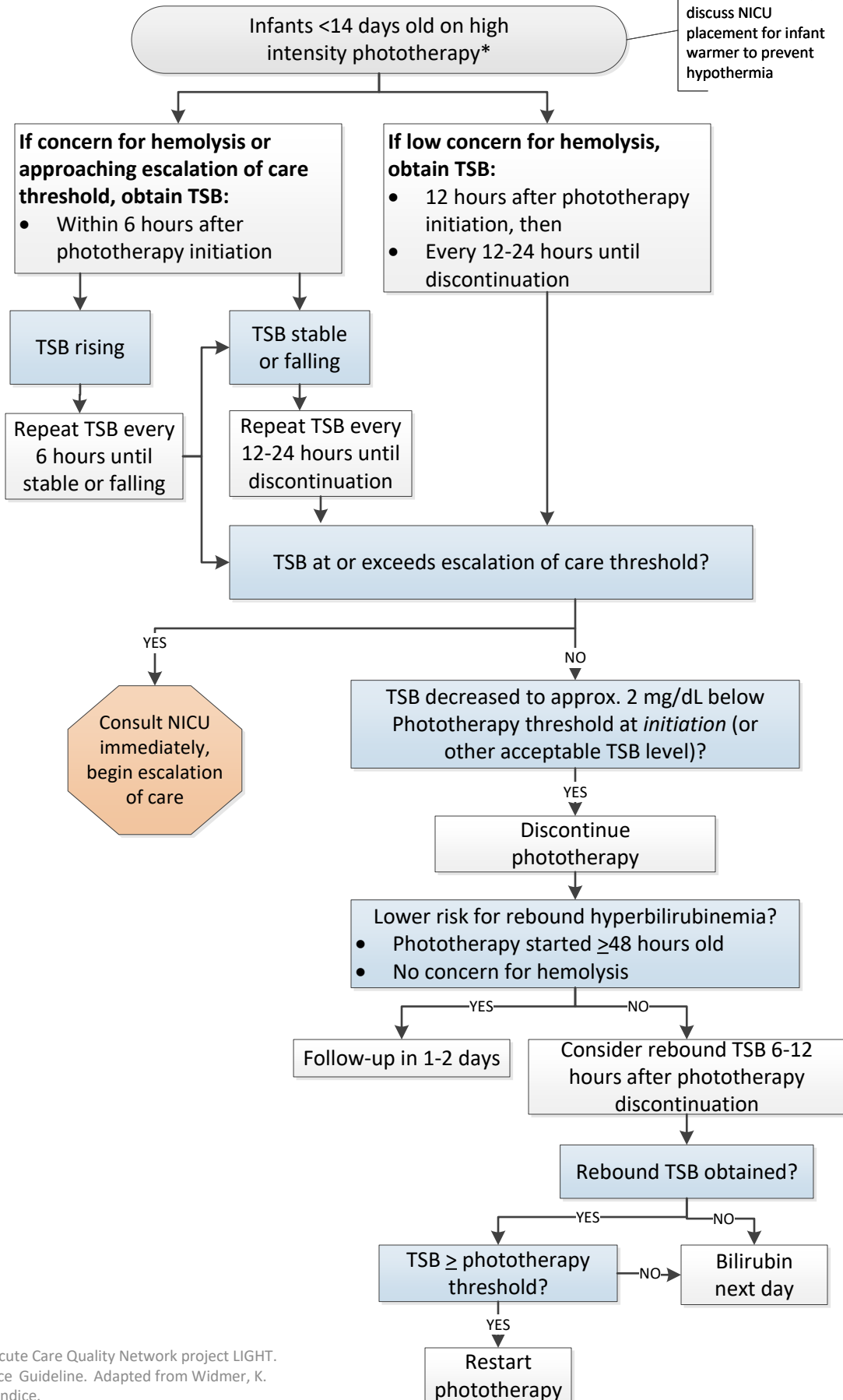
* If weight ≤ 2.7 kg discuss NICU placement for infant warmer to prevent hypothermia

Concern for Hemolysis

- TSB rises or declines very slowly under phototherapy
- Met phototherapy threshold ≤ 24 hours of age
- Rapid rate of rise (ROR) prior to phototherapy initiation (TcB/TSB increase ≥ 0.3 mg/dL/hr in 1st 24 hrs after birth or ≥ 0.2 mg/dL/hr thereafter)
- Meets escalation of care threshold (2 mg/dL below exchange transfusion threshold)

Additional Laboratory Recommendations

- If infant DAT unknown, obtain at phototherapy initiation if maternal antibody screen positive, maternal blood type O or Rh(D) neg, or rapid ROR
- Obtain Hct/CBC if DAT+ or concern for hemolysis (see above)
- Obtain G6PD testing if concern for unexplained hemolysis (e.g. TSB rises under phototherapy or requires escalation of care) or atypical development of severe hyperbilirubinemia
- Consider direct bilirubin if etiology unclear



This algorithm was developed for the VIP Pediatric Acute Care Quality Network project LIGHT. Content may differ from the AAP 2022 Clinical Practice Guideline. Adapted from Widmer, K. (2022). Evaluation and Management of Neonatal Jaundice.

FIGURE 1:

Clinical decision support tool:
<https://peditools.org/bili2022/>

Feeding Assessment Should Include:

- Risk factors for delayed lactogenesis
- Lactation History
- Maternal breast shape, breast changes
- LATCH scores
- Latch depth
- Feeding frequency
- Infant transfer at the breast

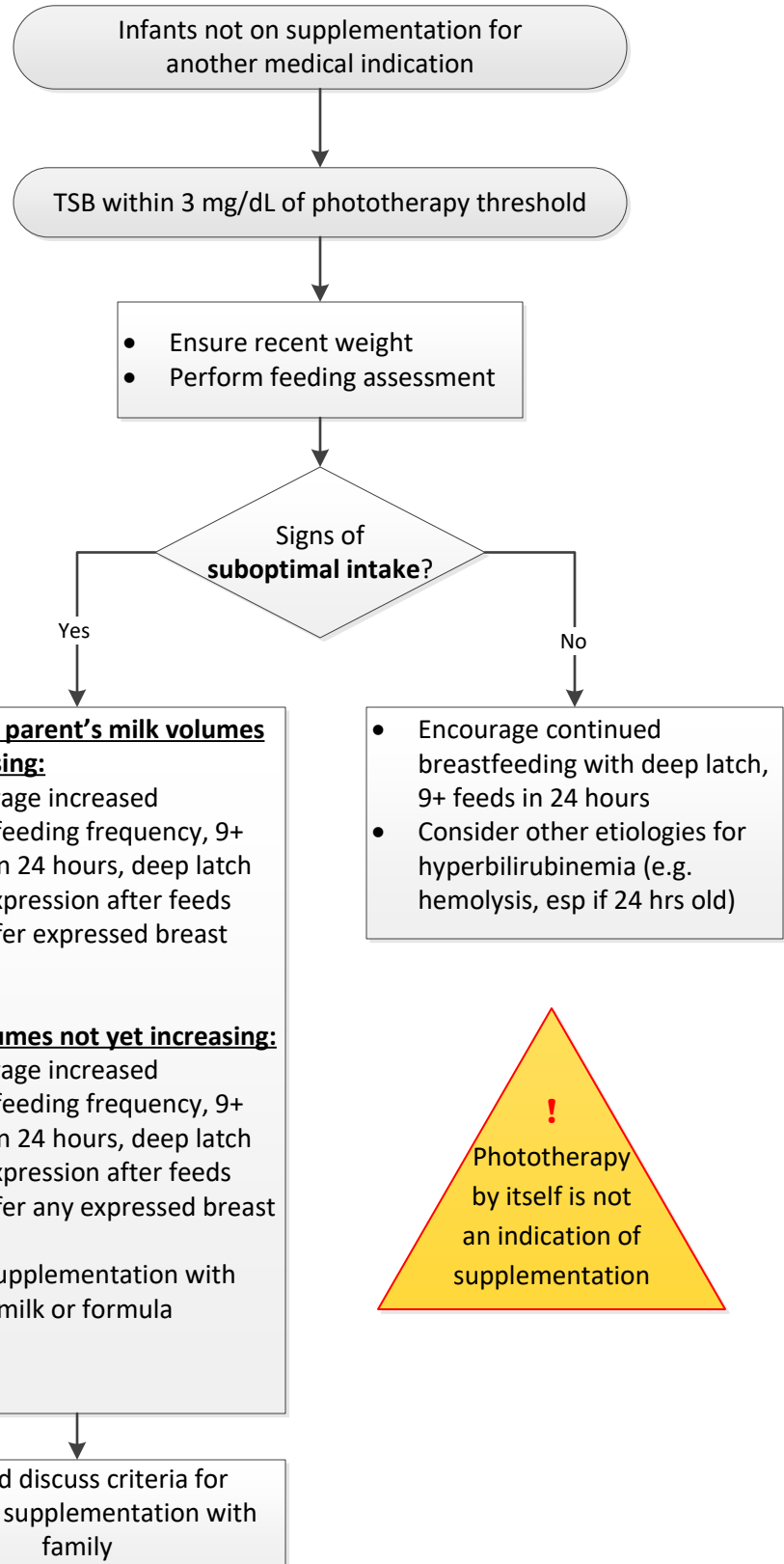
Signs of Suboptimal Intake May Include:

- Ineffective latch and/or suck
- Sleepy and difficult to wake for feedings
- Delayed colostrum or milk supply
- Weight loss >75th %ile on NEWT, esp. after first 24 hrs (<https://newbornweight.org>)
- Laboratory abnormalities (e.g. hypoglycemia)
- Ineffective milk transfer
- Uric acid crystals in urine
- <4 stools on day 4 or meconium stools on day 5

Suggested supplementation volumes by ABM^{1,2}

Time (hrs)	mL/feed*
0-24	2-10
24-48	5-15
48-72	15-30
72-96	30-60

*with expressed breast milk, donor breast milk (if available), or formula



1 Kellams A, Harrel C, Omega S, Gregory C, Rosen-Carole C. ABM clinical protocol #3: supplementary feedings in the healthy term breastfed neonate, revised 2017. Breastfeed Med. 2017;12:188-198. doi:10.1089/bfm.2017.29038.ajk

2 Flaherman VJ, Maisels MJ; Academy of Breastfeeding Medicine. ABM clinical protocol #22: guidelines for management of jaundice in the breastfeeding infant 35 weeks or more of gestation—revised. Breastfeed Med. 2017;12(5): 250–257

LIGHT Algorithm for Escalation of Care
Breastfeeding Infants 5 Days Old with Hyperbilirubinemia
DCMC Evidence-Based Outcomes Center

FIGURE 2:

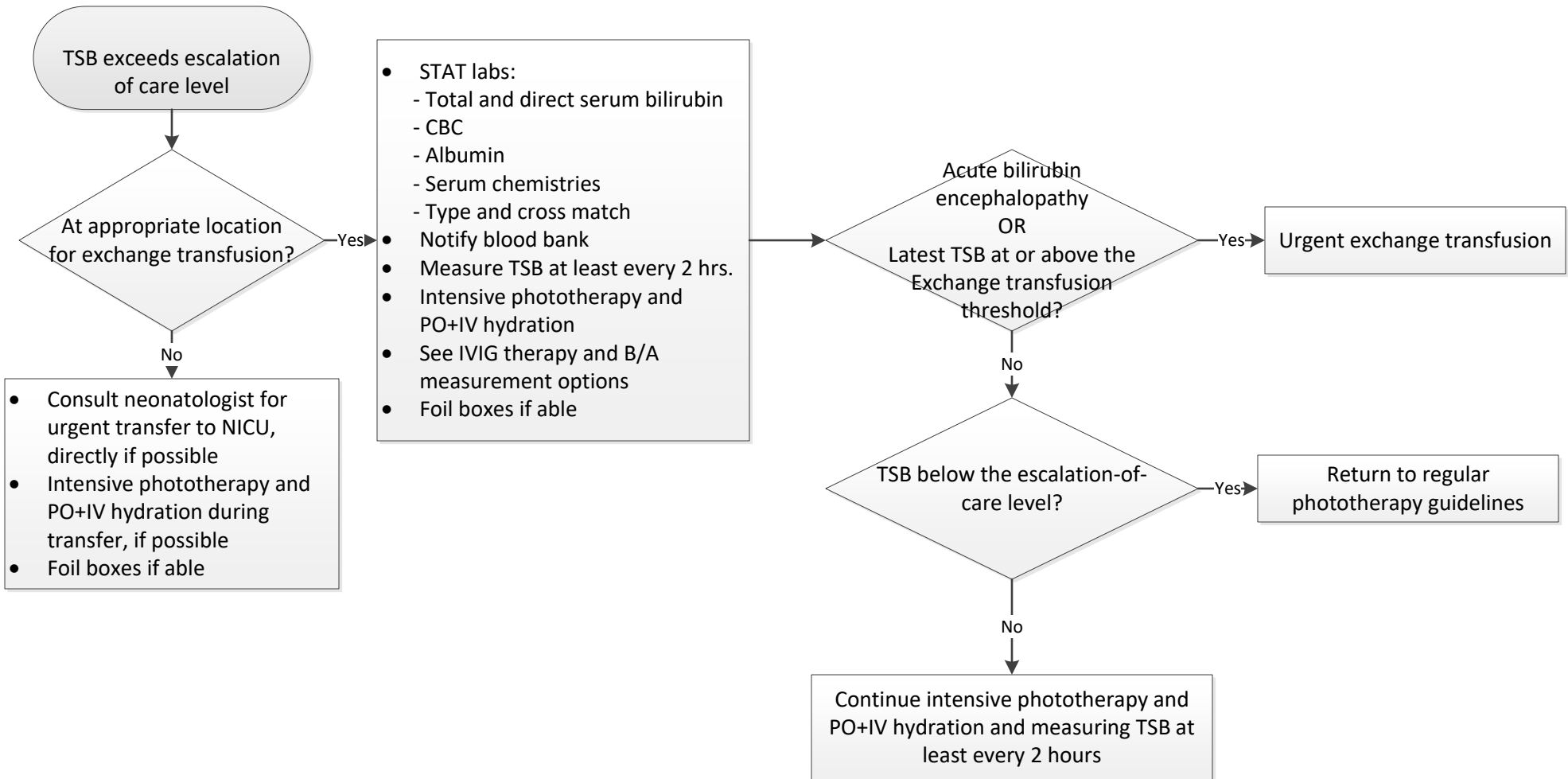


Figure legend: Approach to escalation of care. The escalation-of-care threshold is 2mg/dL below the exchange transfusion threshold. IVIG, intravenous immune globulin; bilirubin to albumin ratio.

*If direct bilirubin is elevated then GI should be consulted to evaluate for biliary atresia or other diseases.

Figure 3:

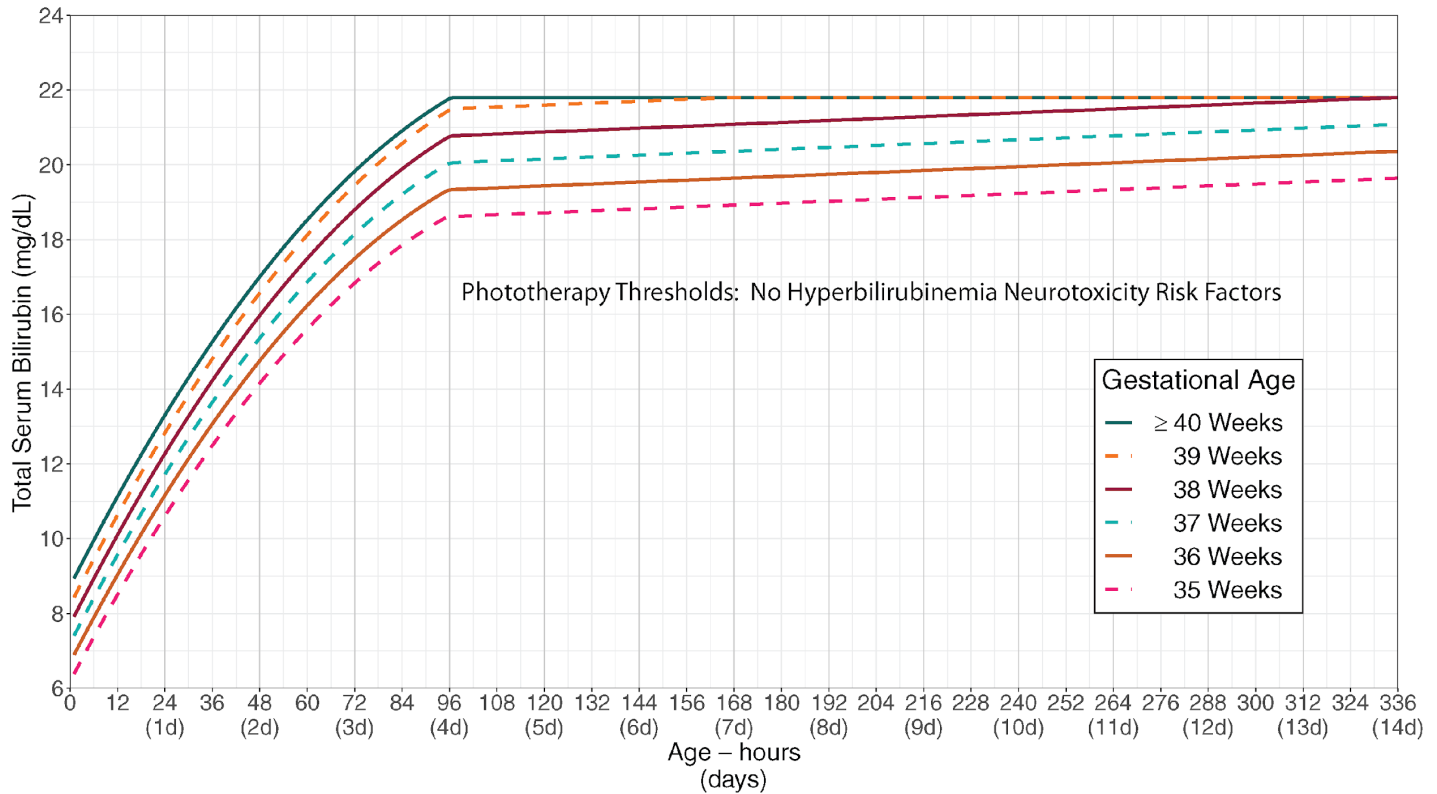


Figure Legend: Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed 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.

Clinical decision support tool: <https://peditools.org/bili2022/>

Figure 4:

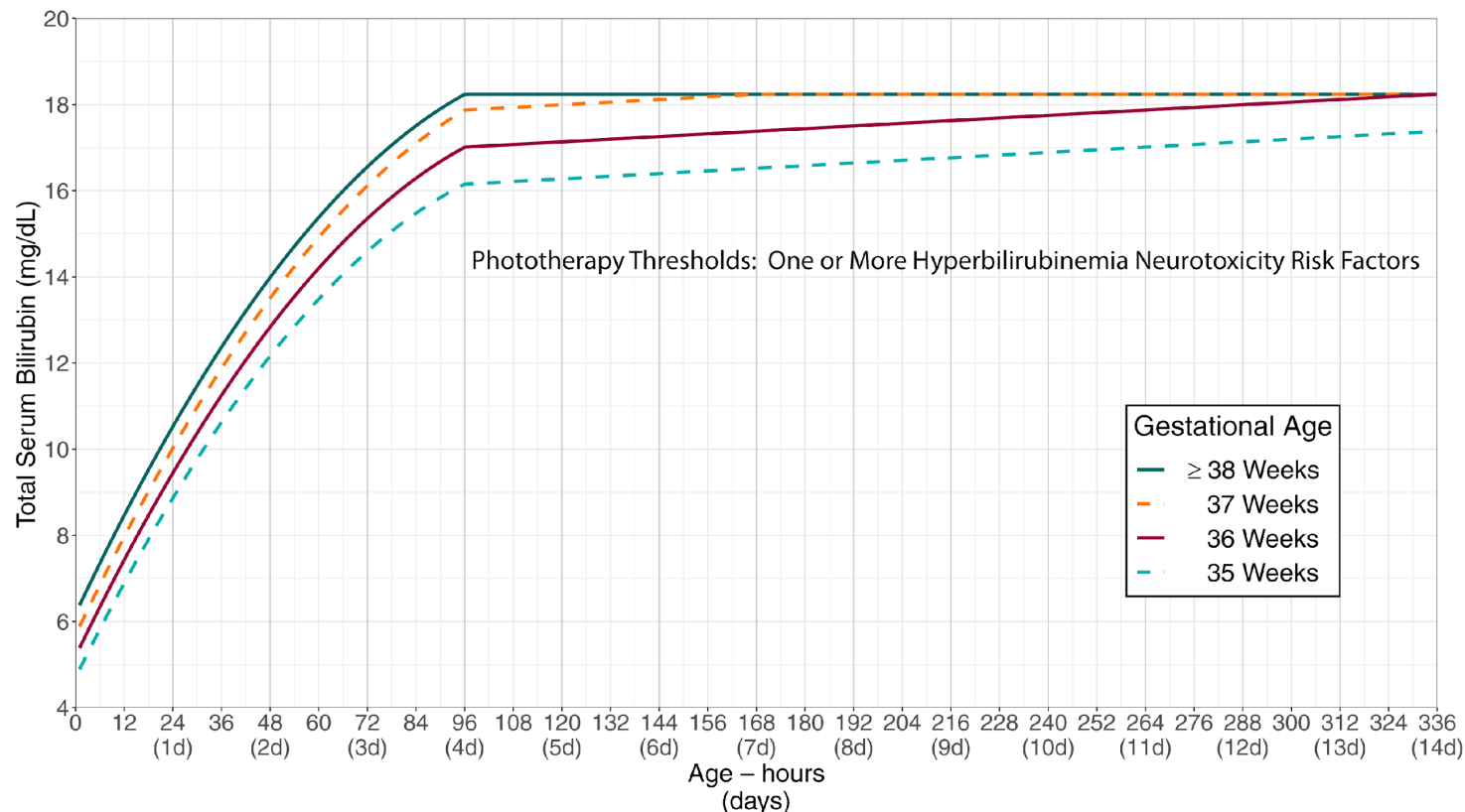


Figure Legend: Phototherapy thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract 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.

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Figure 5:

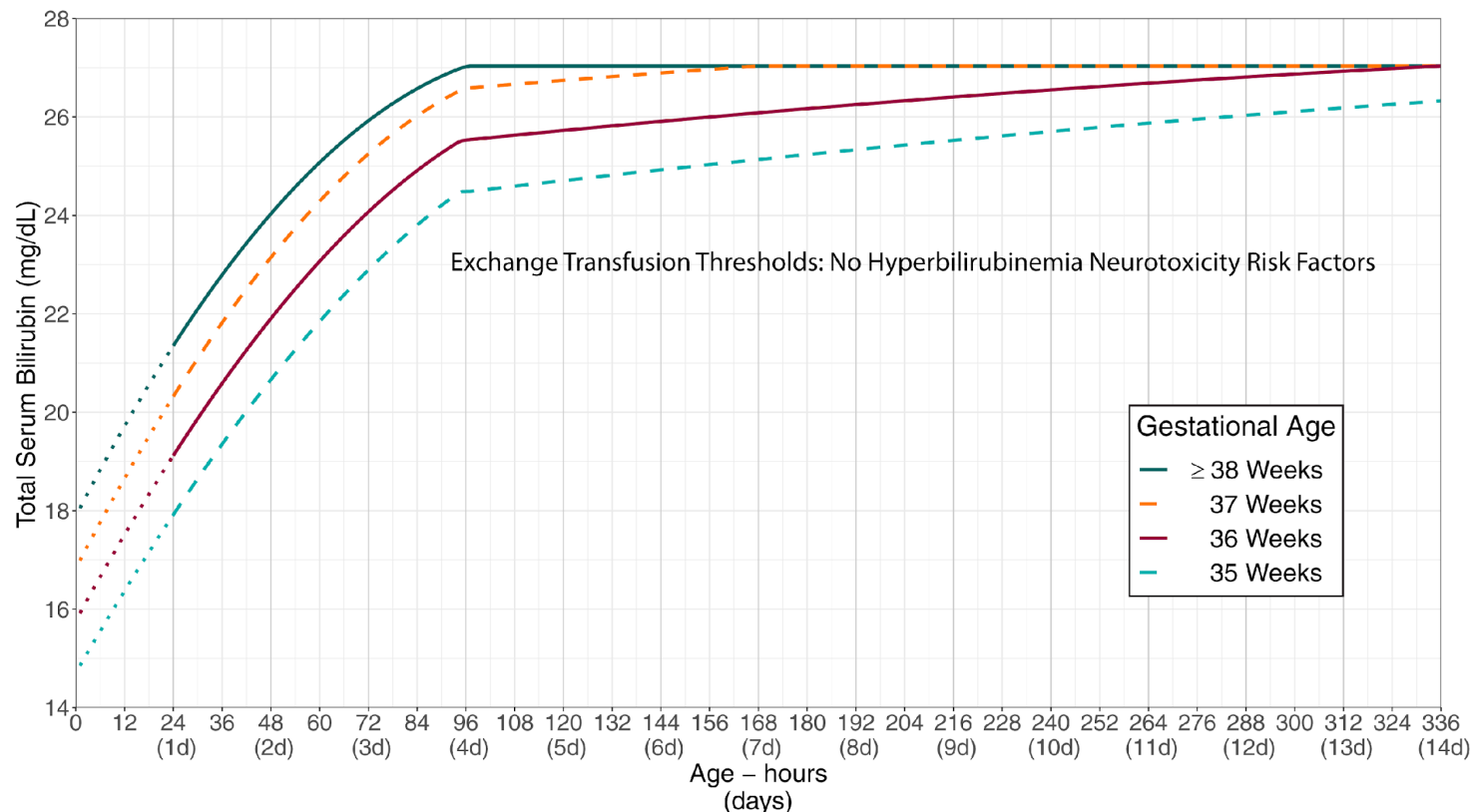


Figure Legend:

Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. See Fig 2, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct 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 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.

Clinical decision support tool: <https://peditools.org/bili2022/>

Figure 6:

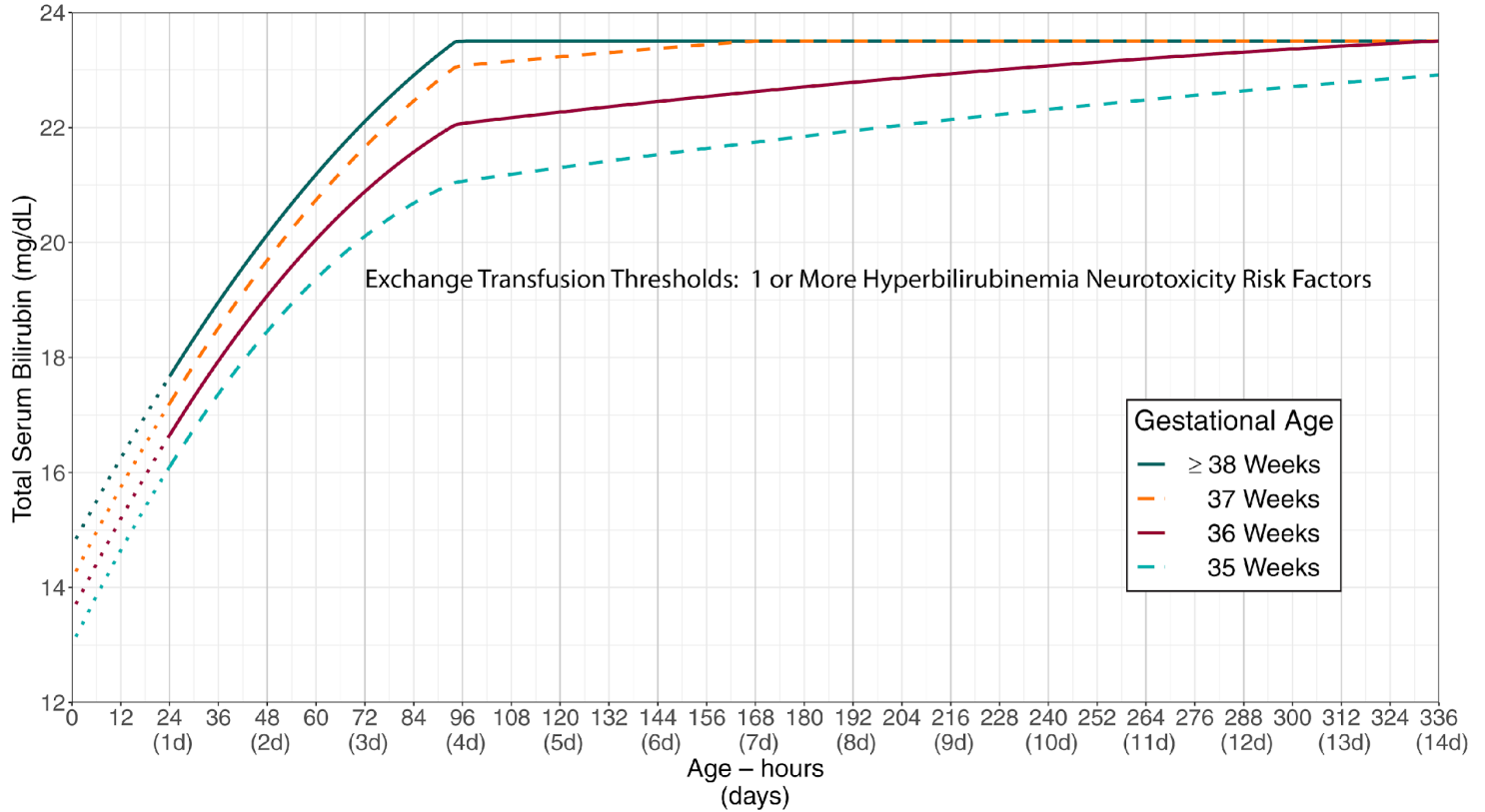


Figure Legend:

Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. See Fig 2, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct 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 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.

Clinical decision support tool: <https://peditools.org/bili2022/>

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Revision History

Original Date Approved: February 2, 2021

2024 Update: Guideline and Algorithm revised to align to the VIP Pediatric Acute Care Quality Network project LIGHT.

May 2024: Algorithm title change: LIGHT Algorithm for Breastfeeding Infants 5-Days-Old with Hyperbilirubinemia. Added callout to the algorithm page titled LIGHT Phototherapy Algorithm for Infants >35 Weeks Gestational Age.

* If weight < 2.7 kg discuss NICU placement for infant warmer to prevent hypothermia. Added the same to Guideline Admissions section.

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