Newborn Critical Care Center (NCCC) Clinical Guidelines

Management of Non-Hemolytic Hyperbilirubinemia

GOALS

- Prevent bilirubin induced neurological dysfunction, including bilirubin encephalopathy or kernicterus
- Avoid exchange transfusion
- Minimize the risk of unintended harm such as decreased breastfeeding or unnecessary treatment for the general population

Who should be screened and timing of screening:

- All newborns prior to discharge
- Any neonate <24 hours age with clinically apparent jaundice
- Any clinically ill neonate with jaundice
- Infants with significant cephalohematoma, subgaleal, subarachnoid hemorrhage
- Any neonate with risk factors for jaundice (ABO/ Rh incompatibility, sepsis, acidosis, asphyxia, hypoalbuminemia, G6PD, extreme prematurity) obtain a serum bilirubin level at 12 hours of life

Measurement of bilirubin level:

- The transcutaneous bilirubin meter is indicated for use in infants born >35 weeks gestation who have not undergone exchange transfusion or phototherapy treatment. The device is indicated only for use before phototherapy treatment.

Considerations based on TcB meter results that prompt the need for a serum bilirubin to be ordered immediately:

- If the measured value is out of the measuring range (0 to 20 mg/dL or 0 to 340 µmol/L), a blinking value appears. This indicates that the measurement is out of range.
- TcB >15 - the transcutaneous bilimeter can underestimate total serum bili or if TCB results are 75th percentile on the TB nomogram for phototherapy.

MANAGEMENT STRATEGIES

Phototherapy

The response to phototherapy depends on the light wavelength and intensity, the surface area exposed and the rate at which isomerized bilirubin is removed from the bloodstream. To ensure maximal benefit from phototherapy one must ensure maximal wavelength, maximal light intensity and maximal surface area exposed.

Microwatts

- Spectral irradiance is measured in watts per centimeter or microwatts per square centimeter per nanometer (mW/cm^2 per nm) over a wavelength band.
- The American Academy of Pediatrics defines standard phototherapy as 8-10 mW/cm^2 per nm and intensive phototherapy as more than 30 mW/cm^2 per nm in the 430-490 nm bandwidth.
- Bilimeters should be used to ensure and document adequate mW/cm^2 per nm. This should be measured routinely to ensure adequate and safe phototherapy administration.

Light Source

- Include: blue light, white light and phototherapy blankets.
- Blue light carries a narrow spectrum of wavelengths at approximately 450 nm and is therefore most effective for use during phototherapy.
- Phototherapy blankets are advisable to increase surface area exposed to treatment – particularly as an addition to single overhead phototherapy.

Exposure

- Infants need to be **fully exposed**. This can be accomplished by eliminating blankets or clothing, minimizing diaper coverage and surrounding the infant with white sheeting for its reflective capabilities. All infants should have their eyes and gonads shielded while under phototherapy.

Continuous Phototherapy

- It is recommended that the infant not be out from under the lights for greater than 3 hours. Removal from phototherapy should be limited to those infants who are stable and not close to exchange transfusion level. Infants approaching exchange level should not be off phototherapy.

Phototherapy Morbidities

- Bronze baby syndrome, eye damage and insensible water loss with some heat sources.

Double Volume Exchange Transfusion

Exchange transfusions are rarely required for non-hemolytic hyperbilirubinemia. Morbidities and mortality from double volume exchange include: mortality 3-5/1000, hypoglycemia, electrolyte imbalances, thrombocytopenia, acidosis, volume overload, dysrhythmias, NEC, hypothermia, infections, graft vs host disease. *See Exchange Transfusion Guidelines for further details.*

RISK IN PRETERM INFANTS

- A large multi-center study suggests that infants 501 - 1000g with measured bilirubin peak values greater than 5 mg/dL had an increased risk of profound impairment, specifically a mental developmental score of 50 or less on a Bayley exam at 18 - 22 months. Of note, there is an equivalent increase in risk of death for infants 501-750g with aggressive phototherapy.
- Other studies suggested that infants < 1500g may have:
  1. Lower bilirubin binding capacity
  2. Increase in total serum bilirubin
  3. Increased risk of neurodevelopmental sequelae if infants are also acidotic

MANAGEMENT IN ALL INFANTS

Risk factors include: <37 weeks gestation, hemolytic disease, asphyxia, lethargy, temperature instability, sepsis, acidosis, albumin <3.0g/dL

- Evaluate for blood group incompatibility in all infants
- Determine bilirubin level at which phototherapy should be initiated based on age, weight and risk factors – see Appendix A for management of infants with ***non-hemolytic*** **hyperbilirubinemia**.
- If phototherapy is indicated, maintain enteral feeds whenever possible and ensure adequate hydration. Breast milk (or formula) supplementation is preferable to IV fluids.
- Discontinue phototherapy when bilirubin levels are below phototherapy threshold and assess for rebound hyperbilirubinemia following discontinuation of phototherapy.

For Infants Approaching Exchange Level

- Use *"intensive phototherapy"* - irradiance in the blue-green spectrum (wavelengths of approximately 430–490 nm) of at least 30 μW/cm^2 per nm (measured at the infant's skin directly below the center of the phototherapy unit) and delivered to as much of the infant's surface area as possible. Note that irradiance measured below the center of the light source is much greater than that measured at the periphery. Measurements should be made with a radiometer specified by the manufacturer of the phototherapy system.
- The sides of the bassinet, incubator, or warmer should be lined with white material. This will increase the surface area of the infant exposed and increase the efficacy of phototherapy.
- If bilirubin continues to rise and is nearing exchange transfusion level, one should consider a possible hemolytic etiology as a cause progressive hyperbilirubinemia and thus consider the use of IVIG and/or albumin.
- See Appendix B for exchange transfusion nomogram.

References:

1. Advances Neonatal Care. 2011 Oct;11(5 Suppl):S3-9. doi: 10.1097/ANC.0b013e31822efd64. Prevention of acute bilirubin encephalopathy and kernicterus in newborns: position statement #3049.
2. American Academy of Pediatrics. (2004). Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*, *114*(1), 297-316.
3. Cashore, W. J., & Oh, W. (1982). Unbound bilirubin and kernicterus in low birth weight infants. *Pediatrics, 69,* 481-485.
4. Clinical Guidelines for Non-invasive Bilirubin measurement using Transcutaneous Bilirubin. Dr. R Roy and Dr. S Mula 23/02: Risk factors include: <37 weeks gestation, hemolytic disease, asphyxia, lethargy, temperature instability, sepsis, acidosis, albumin <3.0g/dL ***I*20.**
5. Keren, R., and V. K. Bhutani. "Predischarge Risk Assessment for Severe Neonatal Hyperbilirubinemia." *NeoReviews*, vol. 8, no. 2, 2007, doi:10.1542/neo.8-2-e68.
6. Maisels, M.J., & McDonagh, A.D. (2008). Phototherapy for neonatal jaundice. *The New England Journal of Medicine, 358,* 920-928.Morris, B.H., Oh, W., Tyson, J.T., Stevenson, D.K., Phelps, D.L., O'Shea, T.M., Higgins, R. (2008).
7. Oh, W., Tyson, J.E., Fanaroff, A.A., Vohr, B.R., Perritt, R. (2003). Association between peak serum bilirubin and neurodevelopmental outcomes in extremely low birth weight infants, *Pediatrics, 112,* 773-779.
8. Keren, R., and V. K. Bhutani. "Predischarge Risk Assessment for Severe Neonatal Hyperbilirubinemia." *NeoReviews*, vol. 8, no. 2, 2007, doi:10.1542/neo.8-2-e68.

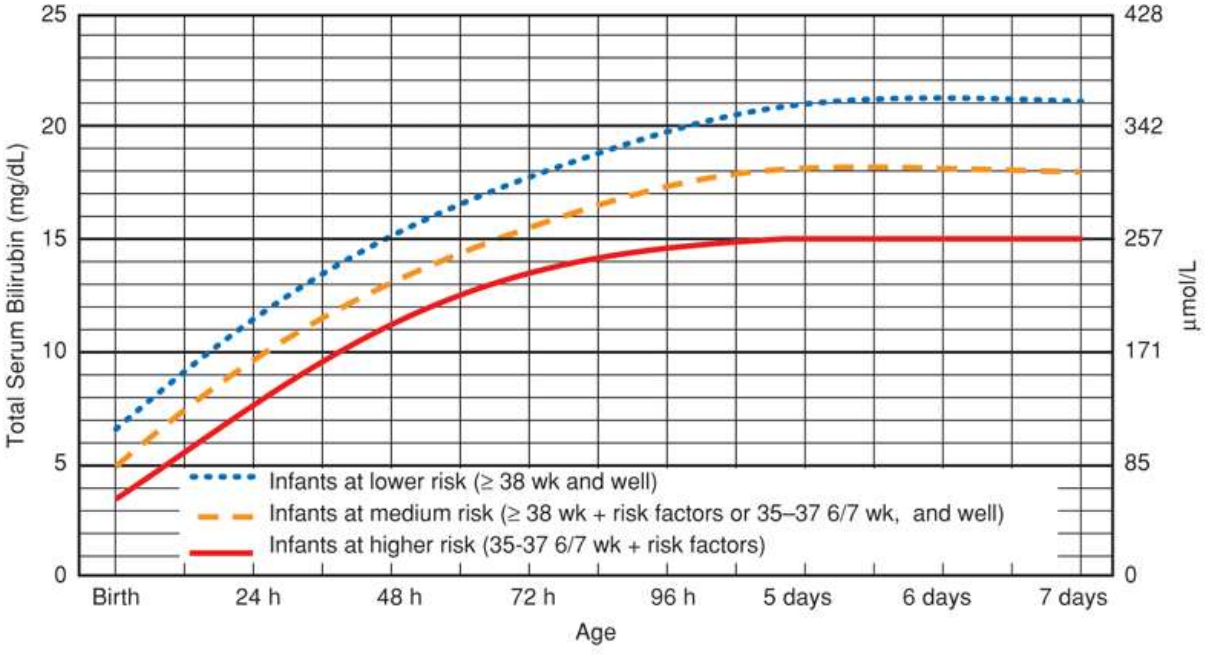
APPENDIX A

Table 1: Guidelines for treatment of NON-HEMOLYTIC hyperbilirubinemia in term and preterm infants

WEIGHT (grams)	PHOTOTHERAPY THRESHOLD *(TSB⁺ in mg/dL)*		EXCHANGE THRESHOLD * *(TSB⁺ in mg/dL)*	
	Age < 72 hours	Age > 72 hours	Age < 72 hours	Age > 72 hours
500 - 750	5	5	13	13
751 - 1000	5	5 (7 after 1 week)	15	15
1001 - 1250	5	10	13-15	15
1251 - 1500	6-8	12	15	17
1501 - 2000	8-10	13	17	18
2001 - 2500	10-13	15	18	19

⁺ *TSB: Total Serum Bilirubin* **Use intensive phototherapy*

Guidelines for Phototherapy in Hospitalized Infants of ≥ 35 Weeks Gestation

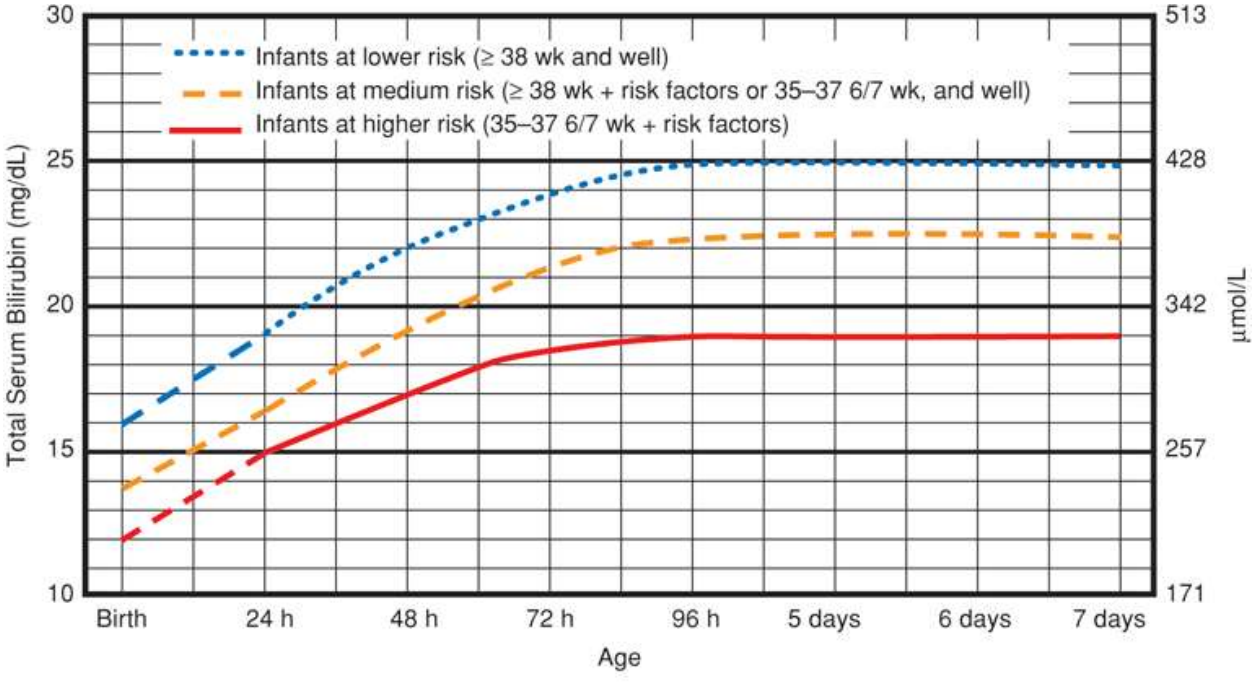


- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0 g/dL (if measured).
- For well infants 35–37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2–3 mg/dL (35-50 mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

Subcommittee on Hyperbilirubinemia. *Pediatrics* 2004; 114:297-316

APPENDIX B

Guidelines for Exchange Transfusion in Hospitalized Infants of ≥ 35 Weeks Gestation



- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥5 mg/dL (85 µmol/L) above these lines.
- Risk factors—isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (see legend).
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- If infant is well and 35–37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

Subcommittee on Hyperbilirubinemia. *Pediatrics* 2004; 114:297-316