

# Neonatal Hyperbilirubinemia Pathway

This pathway is intended for patients ≥ 35 weeks gestation, ≤ 2 weeks of age with unconjugated (indirect) hyperbilirubinemia or parental concern for jaundice.

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#### **Glossary of Terms**

#### TSB – total serum bilirubin

- Ordered as "Bilirubin, Total, Newborn" in Fox Valley (FV) Epic
- Ordered as "Bilirubin Total" in MKE/CMG Epic

#### Direct bilirubin

- Ordered as "Bilirubin, Direct" in Fox Valley (FV) Epic
- Ordered as "Bilirubin Conjugated and Unconjugated" in MKE/CMG Epic

#### Order sets or Smart sets

- Inpatient: Gen Peds Neonatal Hyperbilirubinemia Admission
- Outpatient: Jaundice Hyperbilirubinemia Smartset

## TRANSFER/DISCHARGE FROM NEWBORN NURSERY

#### NEONATAL HYPERBILIRUBINEMIA PATHWAY

This pathway is intended for patients ≥ 35 weeks gestation, ≤ 2 weeks of age with unconjugated (indirect) hyperbilirubinemia or parental concern for jaundice

#### Exclusion criteria:

- Conjugated hyperbilirubinemia (direct) bilirubin ≥ 1 mg/dL
- Suspected sepsis or ill appearing
- < 35 weeks gestation
- > 2 weeks of age

Neurotoxicity Risk Factors

- Gestational age < 38 wk</li>
  Albumin < 3 g/dL</li>
- Isoimmune hemolytic disease (positive DAT), G6PD deficiency or other known hemolytic condition
- Sepsis
- Significant clinical instability in previous 24 h

FH Birth Center Newborn Nursery is staffed by MCW-CSG pediatricians in addition to private pediatrician groups and FH Family Medicine providers. Therefore, standardization of hyperbilirubinemia management according to CMG protocols is not applicable and will vary based on provider group. However, there are three meaningful dispositions that interface with the Children's enterprise:



No phototherapy required during birth	Follow-up with PCP in the recommended interval below based
hospitalization	on how far bilirubin level is below threshold

Phototherapy Threshold (See Figure 1 - Slides 9 and 10) minus TSB	Follow-Up Recommendations
2.0 – 3.4 mg/dl	TSB or TcB in 4 to 24 hours
3.5 – 5.4 mg/dl	TSB or TcB in 1 to 2 days
5.5 – 6.9 mg/dl	If discharging <72 HOL, then follow up within 2 days with TSB or TcB according to clinical judgement. If discharging ≥72 hours, clinical judgement.
≥ 7.0 mg/dl	If discharging <72 HOL, follow up within 3 days with TSB or TcB according to clinical judgement. If discharging <72 HOL, use clinical judgement.









### ANNOTATIONS

ANNOTATION A: Risk factors for developing significant hyperbilirubinemia that should be identified in the newborn nursery and prompt closer observation and follow-up include:

- Lower gestational age (risk increases with each additional week < 40 weeks)
- Jaundice in the first 24h after birth
- Predischarge transcutaneous bilirubin (TcB) or total serum bilirubin (TSB) close to phototherapy threshold
- Hemolysis from any cause, known or suspected, based on rate of rise > 0.2 mg/dL/hr after first 24h of life
- Phototherapy before discharge from nursery
- 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
- Macrosomic infant of a diabetic mother

<u>Risk factors for developing neurotoxicity (Acute bilirubin encephalopathy) that lower the threshold for initiating treatment</u> <u>include:</u>

- Gestational age < 38 weeks (and increasing with degree of prematurity)</p>
- ➢ Albumin < 3.0 g/dL</p>
- ➢ Isoimmune hemolytic disease (+DAT), G6PD deficiency, etc.
- Sepsis
- > Significant clinical instability in the previous 24 hours

Note: many of the conditions above are considered risk factors because they have negative effects on albumin binding of bilirubin, the blood-brain barrier, or the susceptibility of the brain cells to damage by bilirubin.

ANNOTATION B: The early to intermediate phases of acute bilirubin encephalopathy are characterized by lethargy, hypotonia alternating with hypertonia, arching, retrocollis, opisthotonos, fever, and high-pitched crying. The late phase of acute bilirubin encephalopathy is characterized by the above symptoms, as well as deep stupor and seizures, and is more likely to result in irreversible CNS damage. "Kernicterus" is a term for the chronic central nervous system damage from elevated bilirubin levels, with symptoms that include cerebral palsy, deafness or diminished hearing, dental enamel dysplasia, paralysis of upward gaze, and developmental delay. A patient displaying any signs or symptoms of acute bilirubin encephalopathy is best placed in the neonatal intensive care unit.

**<u>ANNOTATION C:</u>** For newborn infants who have already been discharged and then develop a TSB above the phototherapy threshold treatment with a home LED-based phototherapy device rather than admission to the hospital is an option for infants who meet the following criteria:

- Gestational age ≥38 weeks
- ≥ 48 hours old
- Clinically well with adequate feeding
- No known hyperbilirubinemia neurotoxicity risk factors
- No previous phototherapy
- TSB concentration no more than 1 mg/dL above the phototherapy treatment threshold
- An LED-based phototherapy device will be available in the home without delay
- TSB can be measured daily
- Follow up plan set with family (provider is confident family will be able to follow up as needed)

\*Note: The effectiveness of home phototherapy varies with the quality of the device and the ability of the family to appropriately use it. This option should be used with caution and close follow up.

ANNOTATION D: Bilirubin is a product of red blood cell breakdown. Therefore, hemolysis will cause the TSB to rise faster than physiologic jaundice or breastfeeding (suboptimal intake) jaundice. Hemolysis is a risk factor for acute bilirubin encephalopathy and kernicterus. Hemolysis should be considered and evaluated for any time the TSB is rising at a rate greater than 0.2 mg/dL/hr or if the TSB does not fall or continues to rise despite intensive phototherapy. In cases in which a bili-blanket has been used at home prior to admission, the rate of rise may be falsely low and special consideration should be given to these patients when deciding whether to evaluate for hemolysis. Infants with known hemolytic disease should have their TSB levels monitored more closely than is recommended by this CPG.

ANNOTATION E: Measurement of the glucose-6-phosphate dehydrogenase (G6PD) level is recommended for infants receiving phototherapy whose family history or ethnic/geographic origin suggests the likelihood of G6PD deficiency, as well as infants whose TSB increases despite phototherapy, increases suddenly, or increases after an initial decline. G6PD should also be considered for formula fed infants readmitted for phototherapy, late onset hyperbilirubinemia, and infants who require escalation of care. G6PD deficiency is more common in Mediterranean, Middle Eastern, Southeast Asian, and African populations. G6PD deficiency occurs in about 13% of African American males and 4% of African American females. Clinicians should note that measuring the G6PD activity during or soon after what appears to be an acute hemolytic event or after an exchange transfusion can lead to a falsely normal result. If G6PD deficiency is strongly suspected, the G6PD activity should be measured at least 3 months later.<sup>1</sup>

## ANNOTATIONS (continued)

ANNOTATION F: Unsupplemented breastfed infants experience their maximum weight loss by day 3 of life and up to 10% loss of birth weight by this time is considered normal. Infants with more than 10% loss of birthweight should be evaluated for adequate intake. Evidence of adequate intake in breastfed infants includes 4 to 6 thoroughly wet diapers in 24 hours and 3 to 4 stools per day by the fourth day. By day 3 to 4 of life, stools should have transitioned from meconium to a mustard yellow, mushy or "seedy" stool.<sup>1</sup> Note: At CW, Current practice is to take the baby out of the incubator/bili lights and hold the baby for feeding with bili blanket in place. For all infants, feedings are not longer than 30 minutes. If a provider is concerned about a bili level, the provider may enter an order to feed the baby in the incubator until the bilirubin level comes down.

ANNOTATION G: Neonatology should be consulted for any infants that are at risk for requiring an exchange transfusion. If the TSB is rising rapidly (> 0.2 mg/dL/hr) or is within 2 mg/dL of exchange transfusion threshold, continue intensive phototherapy and initiate escalation of care while consulting the neonatologist. If the infant is requiring escalation of care, consider notifying the blood bank that an exchange transfusion may be necessary.

ANNOTATION H: Intravenous (IV) fluids are not routinely required in infants receiving phototherapy.<sup>1</sup>Oral supplementation is only recommended for infants who are clinically dehydrated, and supplementation with formula or expressed breast milk is often sufficient for hydration in a breastfed infant. A 2017 Cochrane review of healthy, term infants requiring phototherapy for unconjugated hyperbilirubinemia concluded that there is no evidence that IV fluid supplementation affects important clinical outcomes such as bilirubin encephalopathy, kernicterus or cerebral palsy.<sup>5</sup> It is recommended to start IV fluids for infants requiring escalation of care.<sup>1</sup>

ANNOTATION I: The 2022 AAP hyperbilirubinemia clinical practice guideline recommends stopping phototherapy once total serum bilirubin is  $\geq 2 \text{ mg/dL}$  below the phototherapy threshold at which phototherapy was initiated.<sup>1</sup> Additionally, Barak et al conducted a small randomized controlled trial of 52 infants to better understand what cutoff to use for stopping phototherapy during the birth hospitalization.<sup>6</sup> They compared a TSB 1 mg/dL below the treatment threshold to a TSB 3 mg/dL below the treatment threshold and found that there was no difference in readmissions or need for repeat phototherapy. This study could not determine whether infants with risk factors, such as increased hemolysis by G6PD deficiency, should be treated for longer periods of time.<sup>6</sup> The 2022 AAP guideline recommends shared decision making with families when considering continuing phototherapy beyond the recommended discharge criteria of  $\geq 2 \text{ mg/dL}$  below the phototherapy was initiated.<sup>1</sup> In some circumstances, for infants who have met all discharge criteria, it may be appropriate to discharge overnight if desired by the family and approved by the attending physician.

ANNOTATION J: Significant rebound after stopping phototherapy is rare in infants who are readmitted after their birth hospitalization for hyperbilirubinemia, particularly after day 4 of life. Therefore, most infants do not require a rebound bilirubin level. <sup>1,7,8</sup> However, if an infant is less than 4 days old at time of discharge or has hemolytic disease, the risk of rebound is higher, and a follow-up bilirubin level is recommended within 24 hours of stopping phototherapy.<sup>1</sup> If the patient has met discharge criteria, discharge need not be delayed to check a rebound bilirubin level after stopping phototherapy, as long as follow-up with the primary care provider has been arranged.<sup>1</sup> Of note, Children's Wisconsin outpatient laboratory on the main campus has weekend hours by appointment. Discuss this option with case management when arranging weekend discharges for infants who need a level 24 hours after stopping phototherapy.

ANNOTATION K: 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. 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).

#### **ANNOTATION L:**

- Infants currently or previously on home phototherapy should be admitted for inpatient phototherapy if the TSB increases and the difference between the TSB and the phototherapy threshold narrows (or the TSB is >1 mg/dL above the phototherapy threshold).
- Infants that have not been on home phototherapy or are not eligible for home phototherapy (see Annotation C) should be admitted if their TSB meets or exceeds phototherapy threshold. Admission of a patient below phototherapy threshold may be considered based on clinical discretion after considering individual circumstances of a patient.

ANNOTATION M: For breastfed infants who are still jaundiced at 3 to 4 weeks of age, and for formula-fed infants who are still jaundiced at 2 weeks of age, the total and direct-reacting (or conjugated) bilirubin concentrations should be measured to identify possible pathologic cholestasis.

ANNOTATION N: In the scenario where TSB is within 2 mg/dL of exchange transfusion threshold prior to phototherapy, NICU consult is recommended. Additional laboratory workup and timing of repeat TSB will be dependent on clinical scenario. Considerations include: gestational age, neurotoxicity risk factors, and TSB value.

### **Phototherapy Threshold Diagram** Use EPIC Embedded Bilitool for patient specific results





### **Exchange Transfusion Threshold Diagram** Use EPIC Embedded Bilitool for patient specific results





# Epic Bilirubin Navigator

## If reviewing a Lab either from the chart > Labs or the InBasket, within the report will be a hyperlink to open up the Bilirubin Navigator that plots out the Bilirubin lab tests. This navigator can be found for infants 0-14 days.

		🕐 Bilirubin Neonatal (lab collect) (Order 5317151904
t)		Order: 5317151904
(seen) Next appt: 10/31/2024 at 1	10:00 AM in Pediatrics (John G S	chimek, MD) Dx: Hyperbilirubinemia, neonatal
Encounter		
2 d ago		
10.6 *		
ics New Berlin, 4855 5 Mc	orland Rd, New Berlin WI	53151
CHW LAB		
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		View All Conversations on this Encounter
	6d 13h.	
	🕹 Seen	Back to Top
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#### Clicking the hyperlink to go to the Bilirubin Graph reveals info below

Hours since birth														1.1
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Hyperbilirubinemia Neurotoxicity risk facto Albumin < 3 0 gidu Isoimmune hemolytic Sepsis Significant clinical ins	irs: : disease (I.e.	positive di	ect antiglob		) deficiency, (	¢ or other hen	nolytic condi	tions		37 wk w	ithout risk fac ith hyperbilin dolty risk fact	tors binemia ors		

## Addendum A: Weekend Process for Neonatal Bilirubin Checks

Day of planning:	Sign Out	Registration	Lab Order	Scheduling of labs
Friday discharge with Saturday labs	Birth Hospital contacts PCP office with weekend plan RN or MD accepts	Family contacts PCP office	PCP office is asked to place order Or Birth Hospital Faxes order 414-266-2597 Or Hospital sends paper order with family Or Hospital completes lab requisition Children's Website	Central Scheduling 414-607-5280 (7:30 – 5:30) on Friday
Saturday discharge with Sunday labs	Hospital contacts PCP on call provider through triage for peds	Family can call 414- 266-4950 (outpatient lab registration)	Birth Hospital Faxes order 414-266-2597 or Hospital sends paper order with family or Hospital completes lab requisition Children's Website	Schedule at time of registration
Saturday lab results requiring Sunday labs	N/A	N/A	PCP on call orders lab	Family can call 414-266-4950

Lab hours available at https://childrenswi.org/medical-care/laboratory-services. Contact lab at 414-266-2500 for holiday hours.

### • What if a family needs a phototherapy blanket on the weekend?

- 1. Place Epic order for phototherapy DME81
- 2. Call Home Care Medical: 262-786-9870 F: 262-957-5535
  - Speak with respiratory (x208) to order bili blanket or bed. They will take a verbal order but need to fax order to them on Monday, send message to triage pool to fax order on Monday.
  - $\circ~$  Expect delivery within 4 hrs. No insurance \$50/day. Return within 36 hrs of d/c or be billed late fee \$50.
- 3. Other options
  - Oxygen One P: 262-521-2202 F: 262-521-2249
  - Aurora At Home (only babies born at Aurora) P: 800-862-2001 F: 414-327-6965
  - Contact Children's Wisconsin Case Management at (414-266-3680) for assistance

### • Be prepared to provide the following information when ordering phototherapy:

- Patient's name, address, home phone number, email address, DOB and diagnosis
- Patient's insurance information (including group number and employer of policy holder)
- Name and DOB of policy holder
- Physician's name and email address
- They may ask for chart notes and/or patients last bili level
- D/C Bili Blanket: Phototherapy Discharge Fax order needs to be filled out, PCP signs and fax to DME Company

For more information on phototherapy, including educational resources for families, see the <u>Phototherapy page</u> in the Connect Primary Care team room under Clinical Resources.



# Neonatal Hyperbilirubinemia Pathway

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#### **Medical Disclaimer**

This Clinical Practice Guideline (CPG) is designed to provide a framework for evaluation and treatment. It is not intended to establish a protocol for all patients with this condition, nor is it intended to replace a clinician's judgement. Adherence to this CPG is voluntary. Decisions to adopt recommendations from this CPG must be made by the clinician in light of available resources and the individual circumstances of the patient. Medicine is a dynamic science; as research and clinical experience enhance and inform the practice of medicine, changes in treatment protocols and drug therapies are required. The authors have checked with sources believed to be reliable in their effort to provide information that is complete and generally in accord with standards accepted at the time of publication. However, because of the possibility of human error and changes in medical science, neither the authors nor Children's Hospital and Health System, Inc., nor any other party involved in the preparation of this work warrant that the information contained in this work is in every respect accurate or complete, and they are not responsible for any errors in, omissions from, or results obtained from the use of this information.

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