

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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For more information on phototherapy, including educational resources for families, see the [Phototherapy page](#) in the Connect Primary Care team room under Clinical Resources

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

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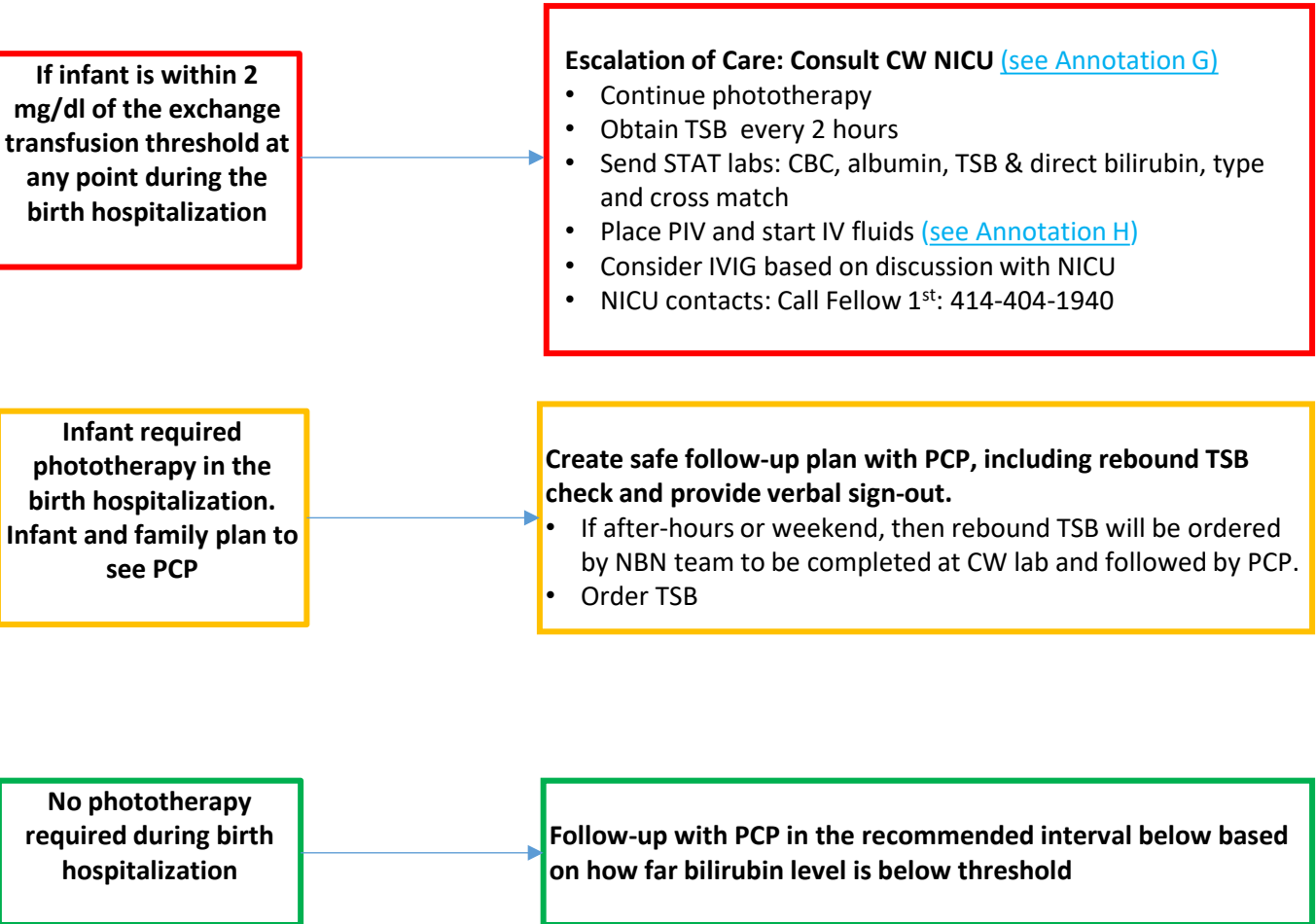
Exclusion criteria:

- 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
- Albumin < 3 g/dL
- 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:



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.

CHILDREN'S MEDICAL GROUP (CMG)

NEONATAL HYPERBILIRUBINEMIA PATHWAY

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Consider Epic "Jaundice Hyperbilirubinemia SmartSet" for orders

First Newborn Visit

Does baby meet any of the below criteria?

- Received phototherapy in newborn nursery
- Jaundice within the first 24 hours of life
- Two bilirubin checks with a rate of rise > 0.2 mg/dL/hr
- Discharge TSB within 5.4mg/dL of phototherapy threshold

Does baby appear significantly jaundiced on exam?

Yes

Check TSB

See [Provider Weekend Bilirubin Process](#) for lab locations, hours, and scheduling instructions

No

Does patient require phototherapy?

Confirm through [Epic bilirubin navigator](#) or [BiliTool.org](#)TM

Is rate of rise > 0.2 mg/dL/hr or does infant have poor feeding/excessive weight loss?

No

No

Yes

Yes

Re-check TSB in 24 hours

Discontinue hyperbilirubinemia monitoring

- Stop checking TSB when unlikely to exceed phototherapy threshold based on rate of rise < 0.2 mg/dL/hr
- Routine Infant Care

Does patient meet home phototherapy requirements? (See [Annotation C](#))

Yes

Yes

Start home phototherapy per clinic process – order to be placed by provider. See [CMG Phototherapy and Bilirubin Resources](#)

Are any of the following present at 2 week and 1-month visits:

1. Is the patient still jaundiced at:
 - 2 weeks for formula fed infants?
 - 3-4 weeks for breastfed infants? (See [Annotation M](#))
2. Stools pale, gray, or white by inspection or report?
3. Prior direct bilirubin level available and above reference range?

Yes to any

No

Proceed with Mission Control Process (414-266-2470) for next steps/direct admit

(See [Annotation L](#) for admission criteria)

Check TSB daily while on home phototherapy

(See [Annotation K](#) and [Annotation L](#))

Evaluate for cholestasis:

- Obtain TSB & direct bilirubin
- Transition out of pathway for further management

Is TSB falling?

No

Yes

Proceed with Mission Control Process (414-266-2470) for next steps/direct admit

(See [Annotation L](#))

Discontinue home phototherapy when TSB level is ≥ 2 mg/dL below the treatment threshold at which phototherapy was started, with consideration of risk factors

(See [Annotation I](#))

For questions concerning this work: Contact clinicalguidelines@childrenswi.org

URGENT CARE

NEONATAL HYPERBILIRUBINEMIA PATHWAY

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Neurotoxicity Risk Factors

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- Isoimmune hemolytic disease (positive DAT), G6PD deficiency or other known hemolytic condition
- Sepsis
- Significant clinical instability in previous 24 h

Are any of the following present?

- Ill-appearing
- Neurological dysfunction (signs of acute bilirubin encephalopathy such as lethargy, abnormal tone, opisthotonos)

Yes

Transfer to Emergency Room

No

Patient meets pathway inclusion criteria

Send to appropriate lab for STAT TSB

[Lab locations and hours](#)

Use Urgent Care lab process for after-hours lab draws

Does patient require phototherapy?

Confirm through [Epic bilirubin navigator](#) or [BiliTool.org](#)TM

Yes

Proceed with direct admission process

Hospital Mission Control (414-266-2470)
(See [Annotation L](#))

No

Discharge Criteria

- TSB below phototherapy threshold
- Feeding adequately
- **Close follow-up with PCP 1-2 days**
- If rate of rise is >0.2 mg/dL/hr, arrange for recheck TSB in 24 hours (either weekend lab or in PMD office)

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EMERGENCY DEPARTMENT TRAUMA CENTER (EDTC) NEONATAL HYPERBILIRUBINEMIA PATHWAY

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- Suspected sepsis or ill appearing
- < 35 weeks gestation
- > 2 weeks of age

Neurotoxicity Risk Factors

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

Patient meets inclusion criteria

Yes

- Assign triage ESI Level 2
- Nursing notifies provider to order TSB STAT
- Start biliblanket while awaiting results

Does patient require phototherapy?
Confirm through [Epic bilirubin navigator](#) or [BiliTool.org™](#)

Yes

No

Discharge Criteria

- TSB below phototherapy threshold
- Feeding adequately
- Close follow-up with PCP 1-2 days
- If rate of rise is >0.2 mg/dL/hr, arrange for recheck TSB in 24 hrs through PCP (if weekend/holiday and PCP cannot arrange outpatient lab, recommend return to EDTC)

Is TSB within 2mg/dL of exchange transfusion threshold?

Yes

No

Consult NICU

- Admit to acute care vs NICU based on NICU consult recommendations
- Place PIV and start Maintenance IVF (See [Annotation H](#))
- Send STAT labs: CBC, albumin, direct bilirubin, type & cross match
- Continue biliblanket
- NICU RNs bring down overhead lights to start intensive phototherapy if being admitted to NICU

Admit to Acute Care

- Continue biliblanket
- PIV not routinely recommended. Discuss with admitting provider if hydration concerns

ACUTE CARE (Fox Valley & Milwaukee)

NEONATAL HYPERBILIRUBINEMIA PATHWAY

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

Pre-Hospital Evaluation:

- History and physical to determine neurotoxicity risk factors (see [Annotation A](#)) and assess for signs of infection or encephalopathy (see [Annotation B](#))
- Obtain TSB

Does patient reach phototherapy threshold?

No

Outpatient management per PCP

Yes

Is TSB within 2mg/dL of exchange transfusion threshold?

Yes

Consult Neonatology

NICU required?

Yes

Admit to NICU

Admit to Acute Care (see [Annotation N](#))

Admit to Acute Care

- **Start Intensive Phototherapy:** Expose as much skin surface area as possible.
- Use "Gen Peds Neonatal Hyperbilirubinemia Admission" order set
- **Admission labs**
- Obtain TSB on arrival if initial labs were >5 hours prior to admission
- If maternal blood type is Rh negative or unknown, obtain infant blood type and DAT/Coombs (if not previously done)
- If TSB is rising rapidly (>0.2 mg/dL/hour) OR jaundice is unexplained by history and exam OR infant had jaundice in the first 24 hours of life, evaluate for hemolysis (see [Annotation D](#))
 - Obtain CBC no diff, as well as blood type and DAT/Coombs if not previously done
- Consider G6PD level if unexplained hemolysis, rising TSB on phototherapy, or indicated by family history or ethnicity (see [Annotation E](#))
- **Breast milk or formula feed a minimum of every 3 hours, monitor voids and stools** (see [Annotation F](#))
- Lactation consult if desired by caregiver
- If milk supply allows, expressed breast milk is preferred over formula for breastfed infants requiring supplementation

Is TSB within 2mg/dL of exchange transfusion threshold?

Yes

Escalation Of Care – Consult Neonatology (see [Annotation G](#))

- Continue phototherapy
- Obtain TSB every 2 hours
- Send STAT labs: CBC, albumin, Direct bilirubin, type & cross match
- Place PIV and start IV fluids (See [Annotation H](#))
- Consider IVIG based on discussion with NICU
- **Consider transfer to NICU**

No

Continue Intensive Phototherapy

- Obtain repeat TSB within 12 hours or with next AM lab draw (whichever comes first) until meeting discharge criteria
- Consider repeat TSB sooner if concern for hemolysis or if expected to meet discharge criteria (see below)

Discharge Criteria

- TSB level is ≥ 2 mg/dL below the treatment threshold at which phototherapy was started, with consideration of risk factors (see [Annotation I](#))
- Tolerating PO, feeding issues resolved
- Follow-up with PCP within 24-48 hours of discharge
 - Outpatient TSB level in 24 hours for infants ≤ 4 days of age at discharge, with known hemolysis, gestational age <38 weeks, or history of phototherapy during the birth hospitalization (see [Annotation J](#))

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

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

- Gestational age < 38 weeks (and increasing with degree of prematurity)
- Albumin < 3.0 g/dL
- 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.

ANNOTATION C: 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.¹

For questions concerning this work: Contact

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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.¹ **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.¹ 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.⁵ It is recommended to start IV fluids for infants requiring escalation of care.¹

ANNOTATION I: The 2022 AAP hyperbilirubinemia clinical practice guideline recommends stopping phototherapy once total serum bilirubin is ≥ 2 mg/dL below the phototherapy threshold at which phototherapy was initiated.¹ 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.⁶ 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.⁶ The 2022 AAP guideline recommends shared decision making with families when considering continuing phototherapy beyond the recommended discharge criteria of ≥ 2 mg/dL below the phototherapy threshold at which phototherapy was initiated.¹ 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.^{1,7,8} 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.¹ 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.¹ 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:

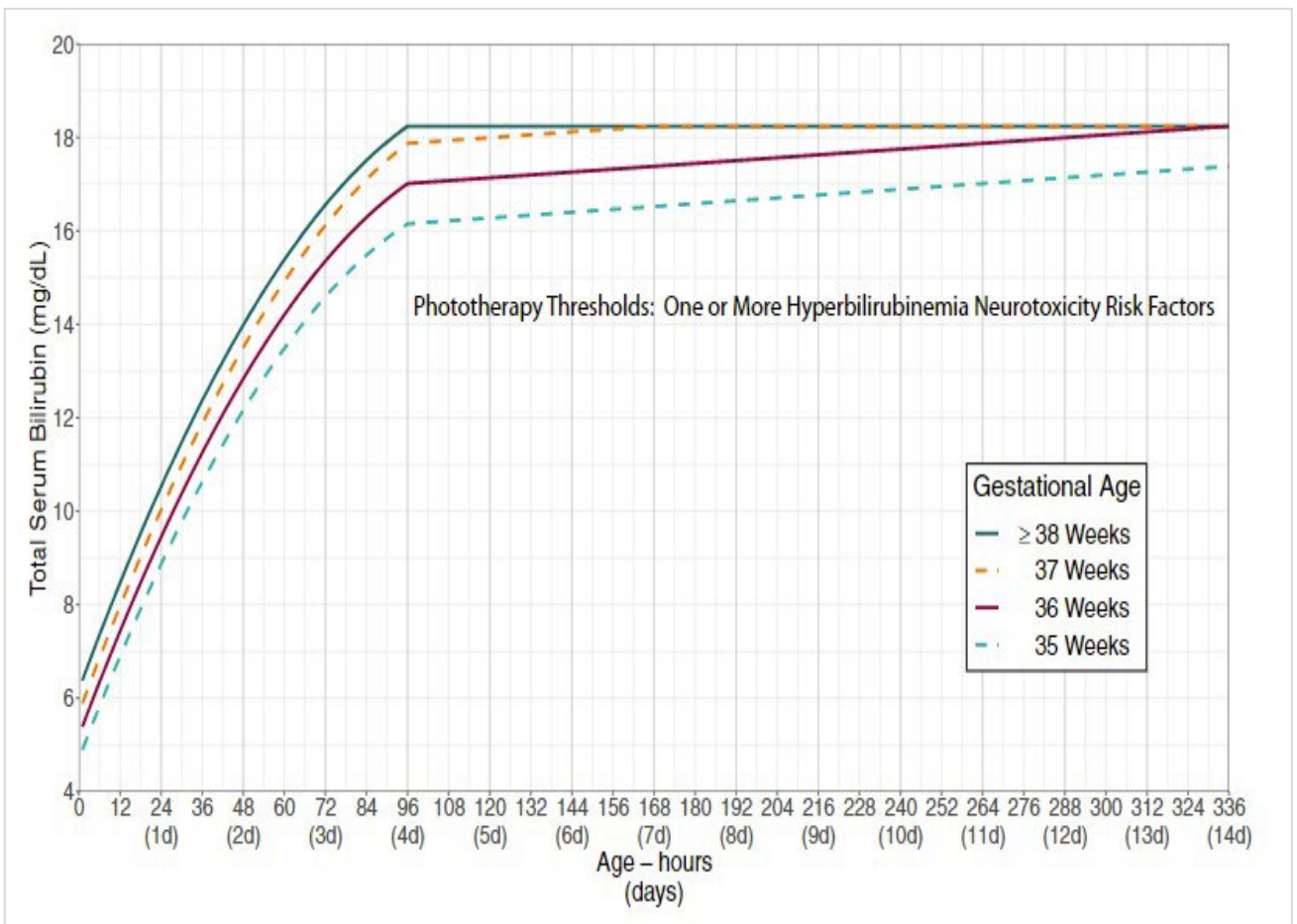
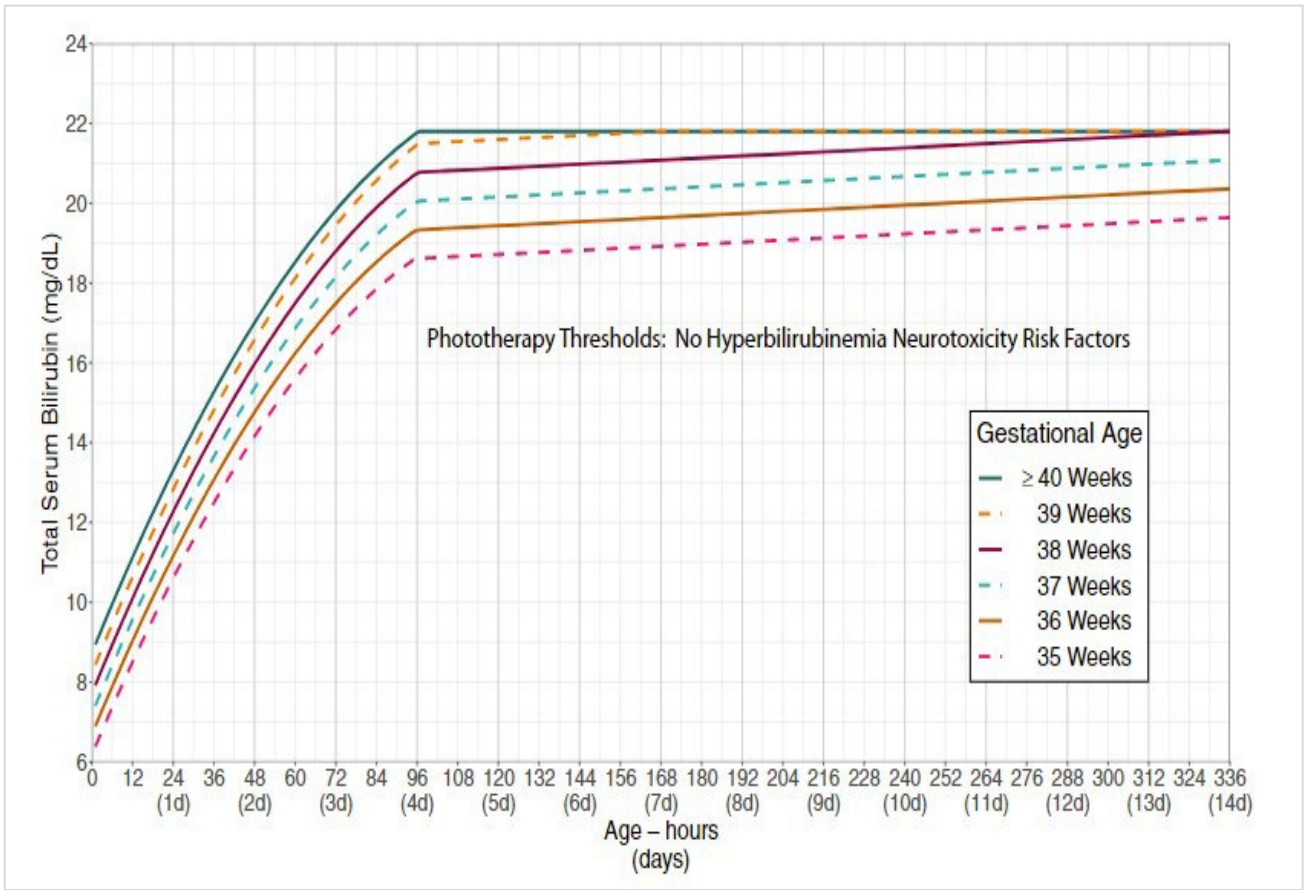
- **Infants currently or previously on home phototherapy** should be admitted for inpatient phototherapy if the TSB increases and the difference between the TSB and the phototherapy threshold narrows (or the TSB is > 1 mg/dL above the phototherapy threshold).
- **Infants that have not been on home phototherapy 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.

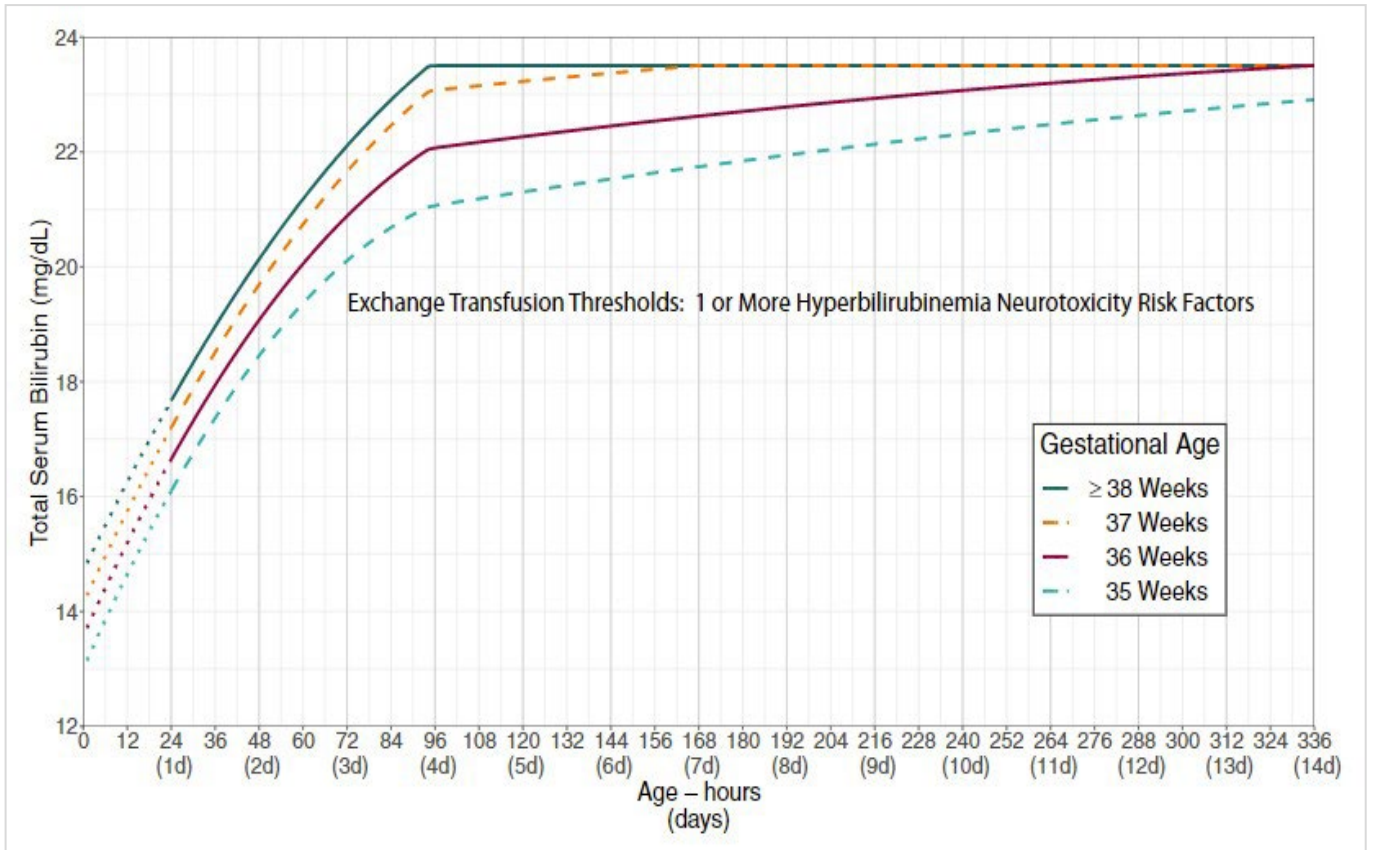
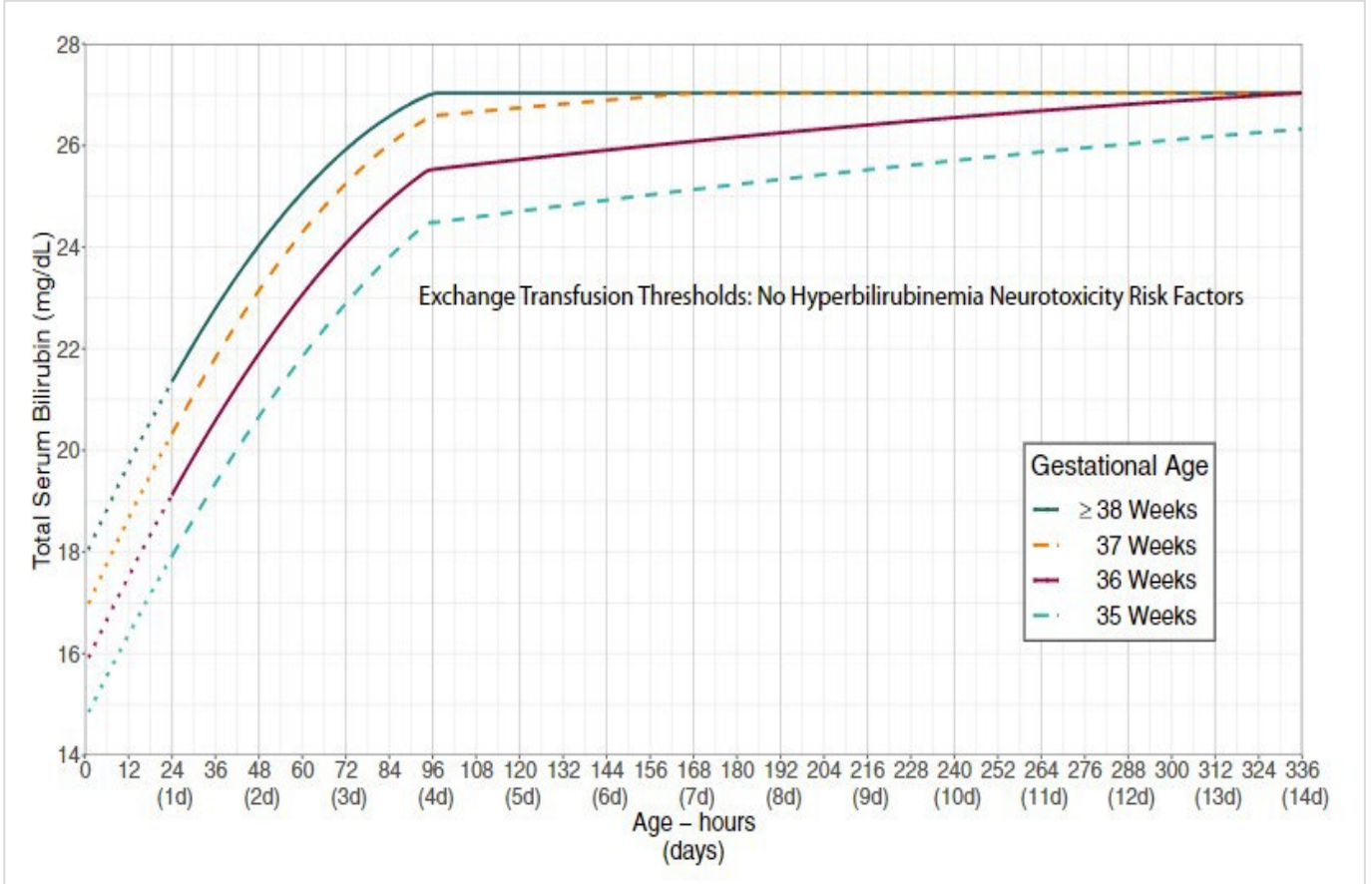
Phototherapy Threshold Diagram

Use EPIC Embedded Bilitool for patient specific results



Exchange Transfusion Threshold Diagram

Use EPIC Embedded Bilitool for patient specific results



For questions concerning this work: Contact

clinicalguidelines@childrenswi.org

Original: 03.2025

Process Owner: Dr. Angela Baker-Franckowiak

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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.

Results

Bilirubin Neonatal (lab collect) (Order 5317151904)

Bilirubin Neonatal (lab collect)

Order: 5317151904

Status: Final result Visible to patient: Yes (seen) Next appt: 10/31/2024 at 10:00 AM in Pediatrics (John G Schimek, MD) Dx: Hyperbilirubinemia, neonatal

0 Result Notes | 1 Follow-up Encounter

Component Ref Range & Units 2 d ago

Bilirubin Neonatal 10.6 ^

0.0 - 9.9 mg/dL

Comment: Performed at CHW Clinics New Berlin, 4855 S Moorland Rd, New Berlin WI 53151

Resulting Agency CHW LAB

Specimen Collected: 10/22/24 14:34

Last Resulted: 10/22/24 14:54

Lab Flowsheet Order Details View Encounter Lab and Collection Details Routing Result History View All Conversations on this Encounter

Bilirubin Result

Bilirubin Graph: 37 wk (AAP, 2022)

Graph covers patient age range from 0d 0h to 14d 0h.

Result from 10/22/2024 2:34 PM was taken when the patient's age was 6d 13h.

Result Care Coordination

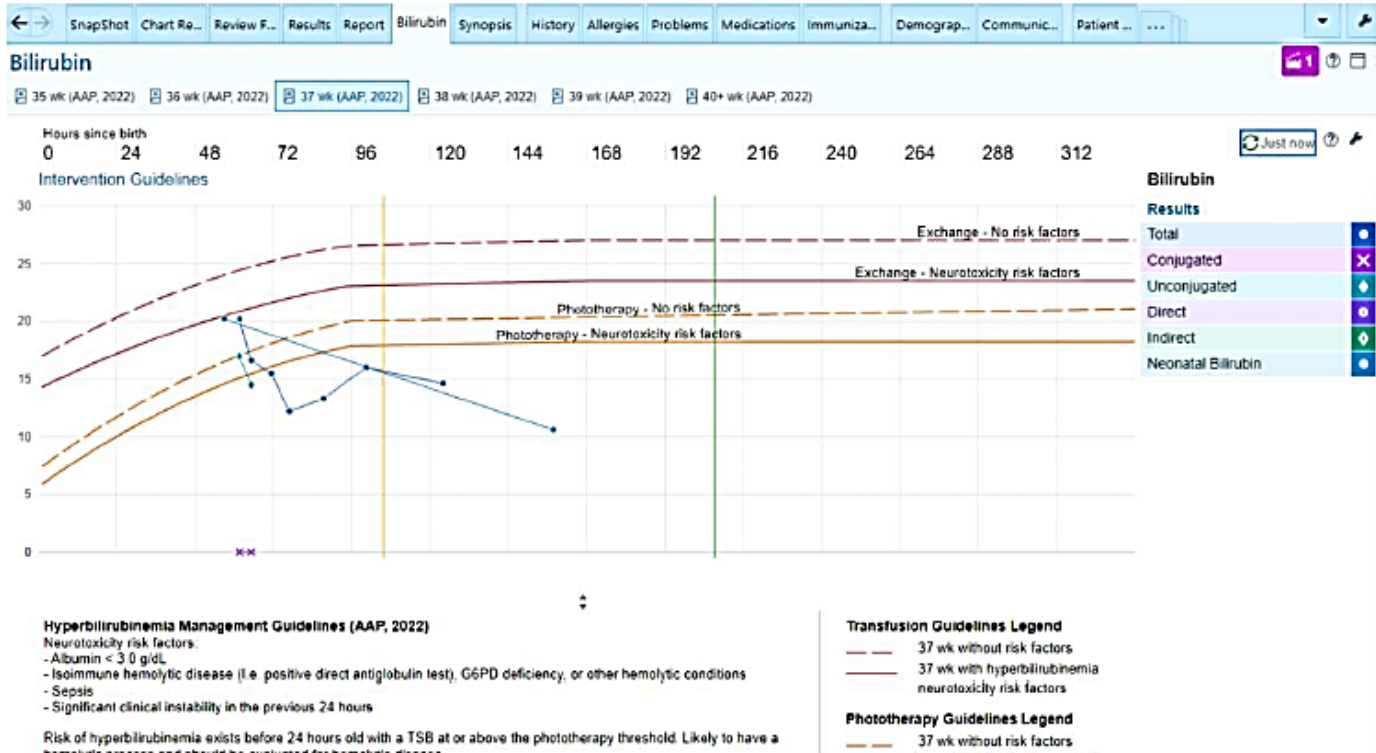
Patient Communication

Add Comments

Seen

Back to Top

Clicking the hyperlink to go to the Bilirubin Graph reveals info below



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Neonatal Hyperbilirubinemia Pathway

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Approved by: Hyperbilirubinemia Pathway Workgroup

Approved 03.28.2025 by UC, EDTC, CMG, NICU and Quality Department
04.23.2026: updated links

Original Pathway developed March 2025

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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