Hyperbilirubinemia

Inpatient

Nationwide Children's — When your child needs a hospital, everything matters.

Center for Clinical Excellence

[Verify that patient is appropriate for this pathway]

[Bilirubin Assessment Tool TRL Education]

[Link to BiliTool™]

One or more Neurotoxicity Risk Factors, other than GA?

Neurotoxicity Risk Factors
- Albumin <3 g/dL
- DAT positive, G6PD or other hemolytic conditions
- Sepsis
- Clinical instability in previous 24 hours

No → Use [No Neurotoxicity Risk Factors nomogram] in Epic "**Bilirubin Assessment Tools**" (or BiliTool™) to determine need for phototherapy

Yes → If clinical instability or not well appearing, [diagnostic timeout] to evaluate for acute illness

Use [One or More Neurotoxicity Risk Factors nomogram] in Epic "**Bilirubin Assessment Tools**" (or BiliTool™) to determine need for phototherapy

If elevated **direct (conjugated)** bilirubin, consult GI for urgent evaluation of cholestasis

TSB at or above phototherapy threshold?

No → **Off Pathway**

Yes →

Does patient reach or exceed the [Escalation of Care Threshold?] Use "**Bilirubin Assessment Tools**"

Yes →

Escalation of Care
- Page NICU Fellow for emergent consult
- **Start emergent phototherapy**
- Place IV and start IVFs + continue PO feeds
- Order [labs]
- Monitor for [acute bilirubin encephalopathy]
- **NBP Q2H**
- [IVIG] – should be done in **NICU** to ensure optimal monitoring and timely access to higher level care

No →

Initiate phototherapy on arrival to the floor

Testing
- **Neonatal Bilirubin panel (NBP)**: on admission then **every 12 hours after initiation of phototherapy**. Consider earlier or more frequent NBP checks if DAT positive, TSB is within 2 mg/dL of exchange transfusion threshold or rise >0.2 mg/dL/hr
- **CBC** (unless already obtained)
- **DAT** if not previously obtained
- [G6PD if risk factors]

Decision to transfer to NICU for possible IVIG and/or exchange transfusion?

No →

Yes →

Arrange transfer to NICU

Fluids/Electrolytes/Nutrition
- PO feeding ad lib with minimum intake defined
- IVF only if:
  - Dehydration with significant weight loss [(NEWT)] that cannot be corrected with PO feeding
  - TSB meeting [criteria for Escalation of Care]
- Consult to lactation if human milk feeding ***AND/OR*** Consult OT if concern for dysphagia

[Risk factors for rebound hyperbilirubinemia?]

Yes →
- Consider a longer period of phototherapy to decrease TSB level further below threshold (*or* f/u in ≤24hrs)
- Consider rebound bilirubin 6-12 hours of discontinuation of phototherapy if DAT positive or otherwise concerned for hemolysis

No →

Discontinue phototherapy when TSB is ≥ 2 mg/dL below the hour-specific threshold at the **initiation** of phototherapy

Discharge Planning
- PCP f/u and/**OR outpatient** TSB:
  - **≤24 hours if** Phototherapy at birth hospital **OR** Concern for hemolysis with or without positive DAT
  - **1-2 days** for other patients
- If appropriate follow-up cannot be arranged discharge may be delayed

Discharge patient when meeting criteria:
- Tolerating PO without significant weight loss (NEWT)
- Follow up arranged

Pre-Pathway Validation

Is this Neonatal Hyperbilirubinemia?

Diagnostic criteria for neonatal hyperbilirubinemia requiring phototherapy:

- Bilirubin level above the hour-specific level based on phototherapy thresholds.

Typical presentation:

- **Jaundice** is a yellow color produced by the deposition of bilirubin in the skin and subcutaneous tissues and progresses in a cephalocaudal direction. ***The presence or absence of jaundice is not a reliable method to assess total serum bilirubin (TSB), especially in infants with dark skin.***
- **Conjunctival icterus** is due to the deposition in in the conjunctiva and observed on the sclerae.
- **Other exam findings which may illustrate an increased risk for neonatal hyperbilirubinemia:**
  - Pallor (due to hemolysis)
  - Cephalohematoma
  - Bruising
  - Hepatosplenomegaly

Consider a **diagnostic timeout** ("What else could this be?")

Pathway Inclusion Criteria

- Infants ≥ 35 weeks GA with hyperbilirubinemia up to and including 14 days

Pathway Exclusion Criteria

- Infant > 14 days of life

Red Flags

- **DAT positive**
- Abnormal vital signs
- Total bilirubin level within 2 mg/dL or above exchange transfusion
- If elevated **direct (conjugated)** bilirubin, consult GI for urgent evaluation of cholestasis

Link to Differential Diagnoses
for indirect (unconjugated) hyperbilirubinemia

Common causes of jaundice are suboptimal intake, "breast milk jaundice", or prematurity.

Consider uncommon etiologies when:

- Ill appearance or febrile, concerning for acute illness
- The bilirubin level is within 2 mg/dL or above exchange transfusion level
- The **direct bilirubin** level is greater than 1 mg/dL
- Abnormal newborn screen
- Microphallus, midline defects, abnormal brain MRI
- Age less than 3 days or greater than 7 days of life
- Patient is not responding to phototherapy as expected
- Family history of hematologic disease such as hereditary spherocytosis, G6PD deficiency, etc.
- Hypopituitarism (ACTH/TSH deficiency) and congenital hypothyroidism

Admission Criteria

- Total serum bilirubin level at or above phototherapy threshold
- **Home phototherapy criteria** not met or unavailable

Home Phototherapy Criteria ("bili blanket")

- Gestational age ≥38 weeks
- ≥48 hours old
- Clinically well with adequate feeding
- No known Neurotoxicity Risk Factors
- No previous phototherapy
- "Bili blanket" available in the home without delay
- TSB can be measured daily
- TSB no more than 1 mg/dL above phototherapy threshold

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Risk Factors for Hyperbilirubinemia

- **Gestational age** 35-36 weeks
- **Jaundice** in the first 24 h after birth
- Predischarge TCB or TSB 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.
- **Phototherapy** before birth hospital discharge
- **Family history**: Parent or sibling requiring phototherapy or exchange transfusion
- Family history or genetic ancestry suggestive of inherited **RBC disorders**, including glucose-6-phosphate dehydrogenase (**G6PD**) deficiency
- Exclusive breastfeeding with **suboptimal intake**
- **Scalp hematoma**
- **Significant bruising**
- **Down syndrome**
- **Macrosomic infant of a diabetic mother**

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Risk Factors for G6PD

Glucose-6-phosphate dehydrogenase (G6PD) deficiency

- G6PD is an X-linked recessive enzymopathy that decreases protection against oxidative stress and is one of the most important causes of significant and severe neonatal hyperbilirubinemia.
- **An infant with G6PD deficiency can develop a sudden and extreme increase in TSB that may be hard to anticipate or prevent.**

Genetic risk factor:

- Genetic ancestry from Sub-Saharan Africa, Middle East, Mediterranean, Arabian Peninsula and Southeast Asia
- Overall 13% of African American males and 4% African American females have G6PD deficiency.

Clinical events that should raise suspicion for G6PD deficiency:

- Phototherapy required before discharge from newborn hospital
- Atypical development of hyperbilirubinemia (elevated TSB in formula fed infants or late-onset jaundice)

G6PD activity should be measured in any infant:

- With jaundice of unknown cause
- Whose TSB increases despite intensive phototherapy (unless delta TSB is less than when initially starting phototherapy)
- Whose TSB increases after an initial decline
- Who requires escalation of care

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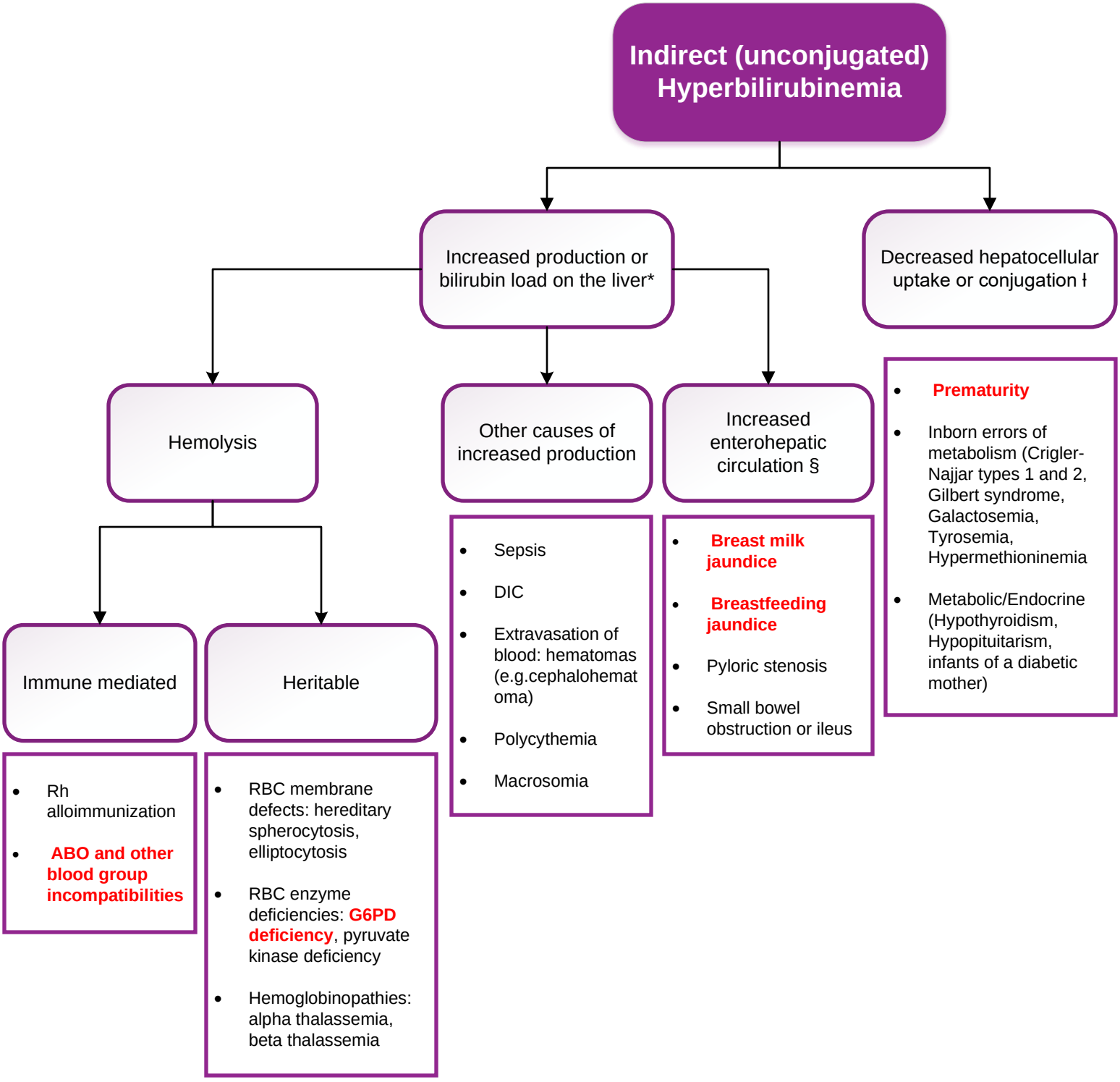
Differential Diagnoses

This is an inclusive list of the differential diagnoses for the etiology of neonatal hyperbilirubinemia. However, the most **common causes of jaundice** that will be seen are highlighted in **red** and should be included as the top differentials for *most* well appearing patients admitted with this diagnosis.



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[Return to Pre-Pathway Validation]

Severity

Benign neonatal hyperbilirubinemia (AKA “physiologic jaundice”) is a transient and normal increase in total serum bilirubin (TSB) occurring in almost all newborn infants.

Significant hyperbilirubinemia in infants ≥ 35 weeks gestational age is defined as TSB > 95th % on Bhutani nomogram.

Severe neonatal hyperbilirubinemia is a TSB > 25 mg/dL and is associated with and increased risk for developing bilirubin-induced neurologic dysfunction.

Extreme hyperbilirubinemia is TSB > 30 mg/dL and is associated with high risk for bilirubin-induced neurologic dysfunction.

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Direct Antiglobulin Test

If the maternal antibody screen is positive or unknown, the infant should have a direct antiglobulin test (DAT) and the infant's blood type should be determined as soon as possible.

The DAT helps to identify infants at risk for hyperbilirubinemia due to hemolysis.

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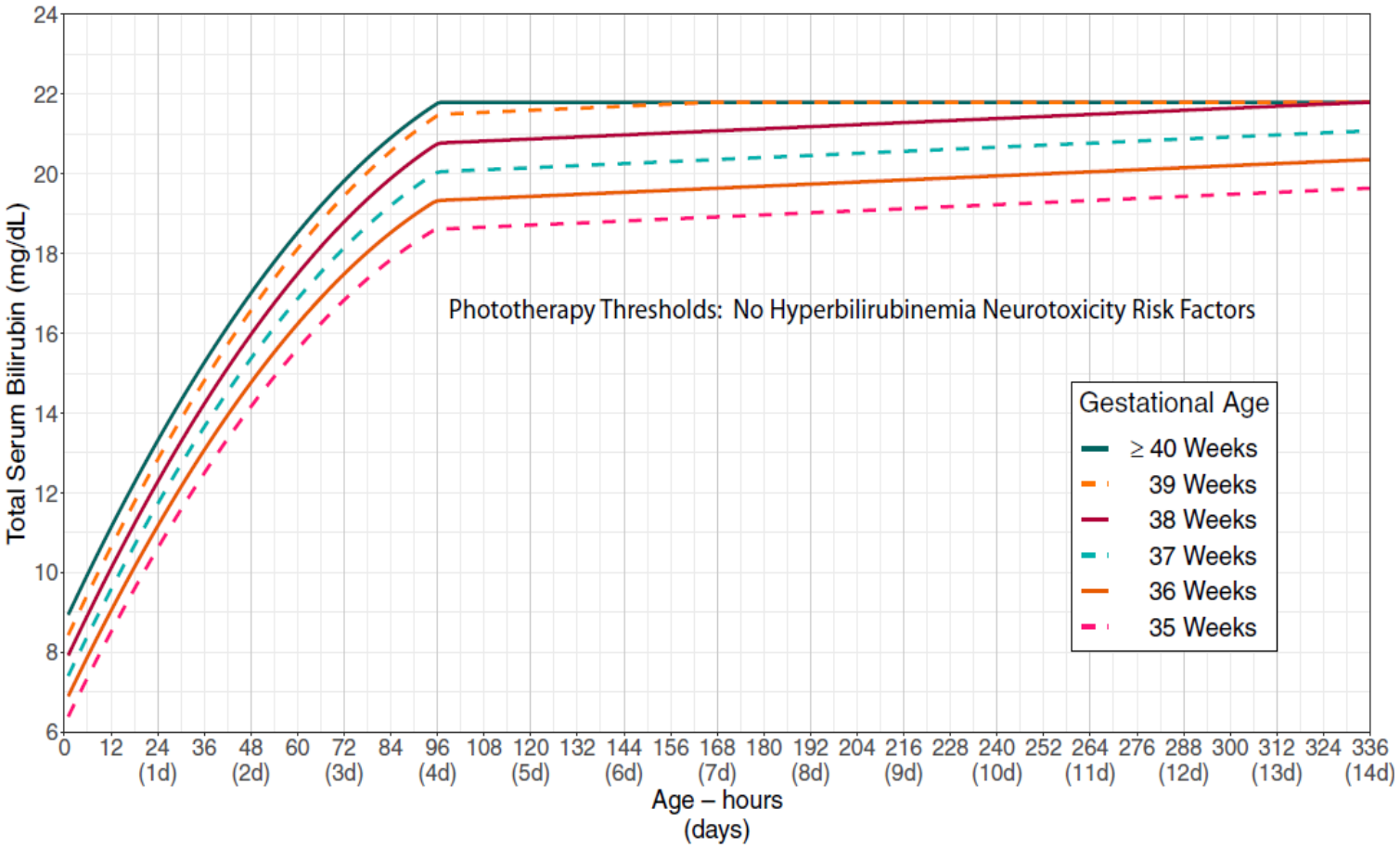
Return to Pre-Pathway Validation

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.

Phototherapy Thresholds:
No Hyperbilirubinemia Neurotoxicity Risk Factors



Hyperbilirubinemia Neurotoxicity Risk Factors

- Albumin < 3.0 g/dL
- Positive DAT, G6PD deficiency or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 hours
- Gestational age < 38 weeks is a neurotoxicity risk factors but may be accounted for in graphs and calculators such as the Bilitool™

(Kemper et al. 2022)

Use "**Bilirubin Assessment Tools**" in patient's chart (or BiliTool™) to view nomogram and determine need for phototherapy

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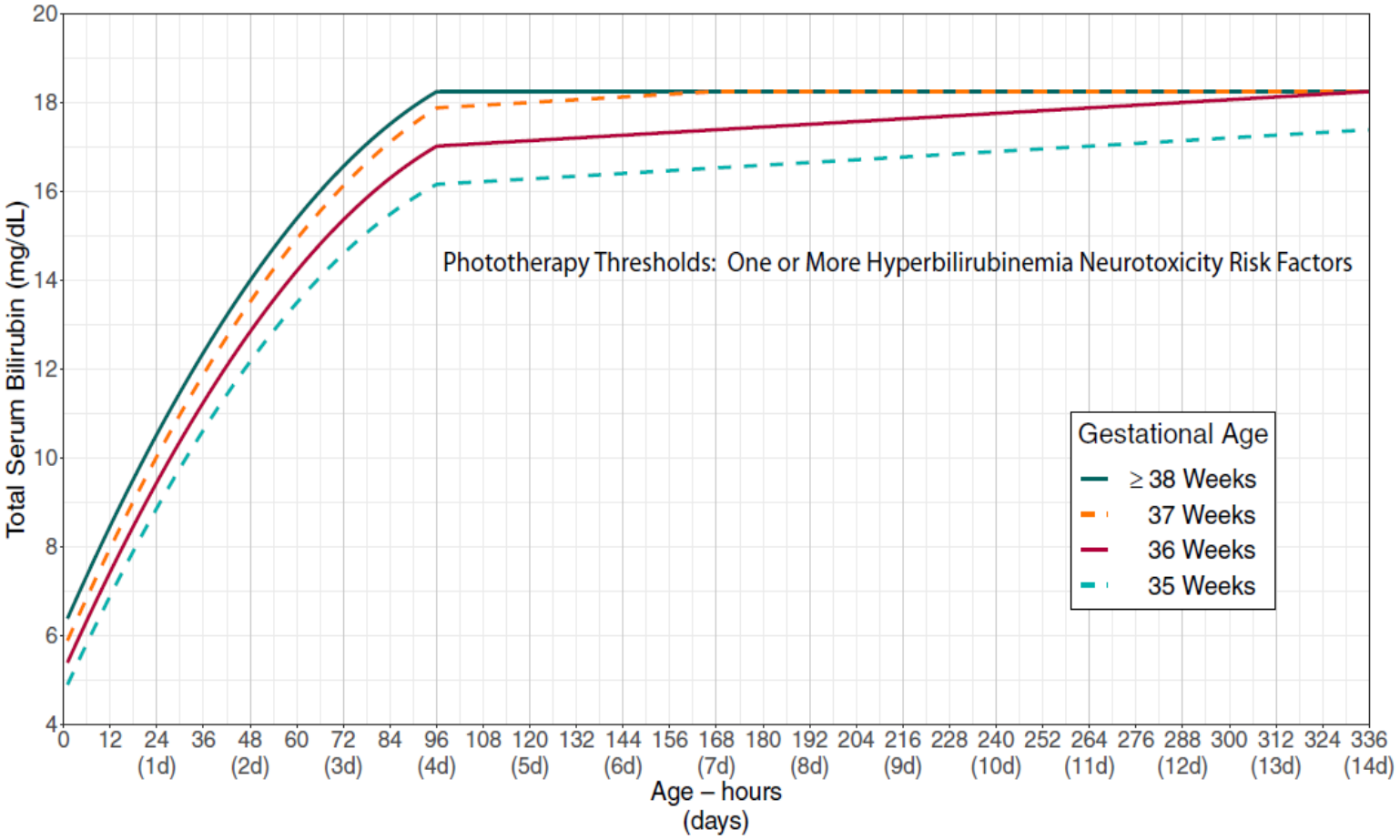
Phototherapy Thresholds:
One or More Hyperbilirubinemia Neurotoxicity Risk Factors



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(Kemper et al. 2022)

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Frequency of TSB Monitoring After Initiation of 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
- Presence of hyperbilirubinemia neurotoxicity risk factors
- TSB concentration. (TSB is within 2 mg/dL of exchange transfusion threshold)
- TSB trajectory. The rate of rise is >0.2 mg/dL/hr

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Acute Bilirubin Encephalopathy

Defined clinically based on the following signs and symptoms:

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

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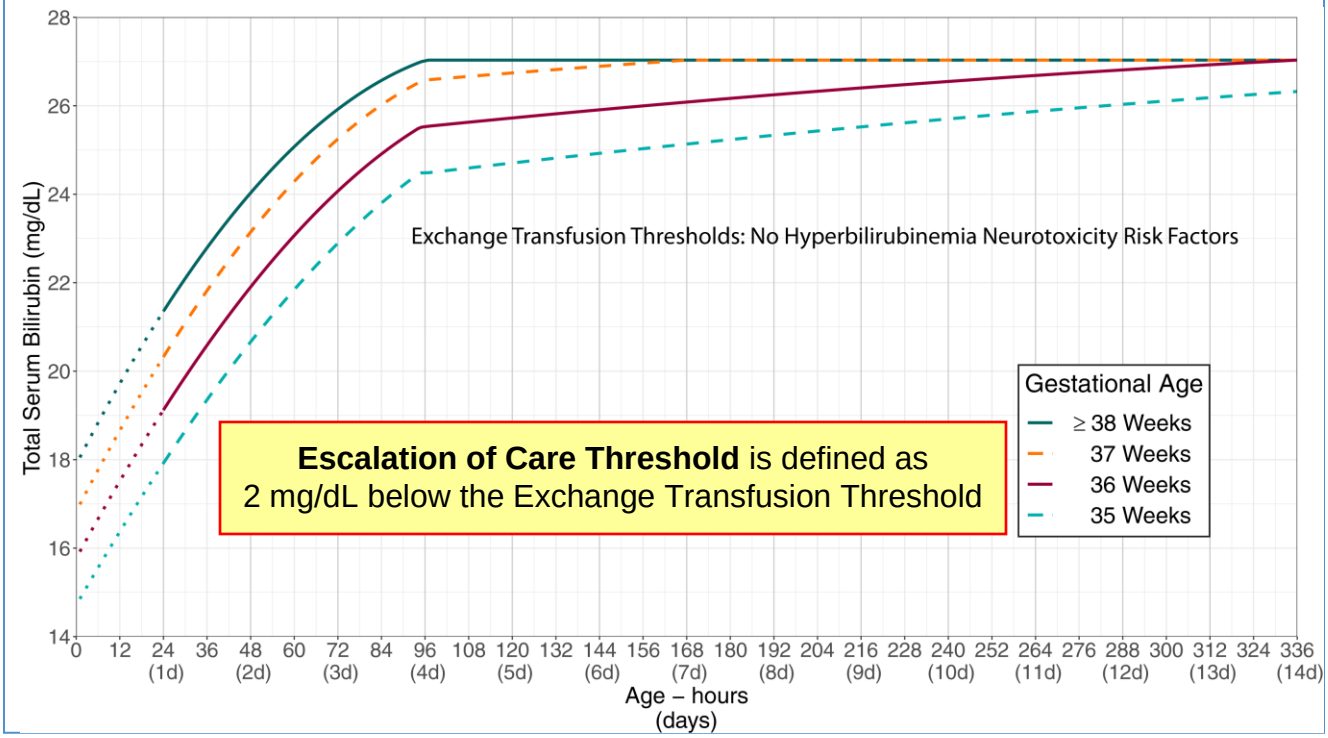
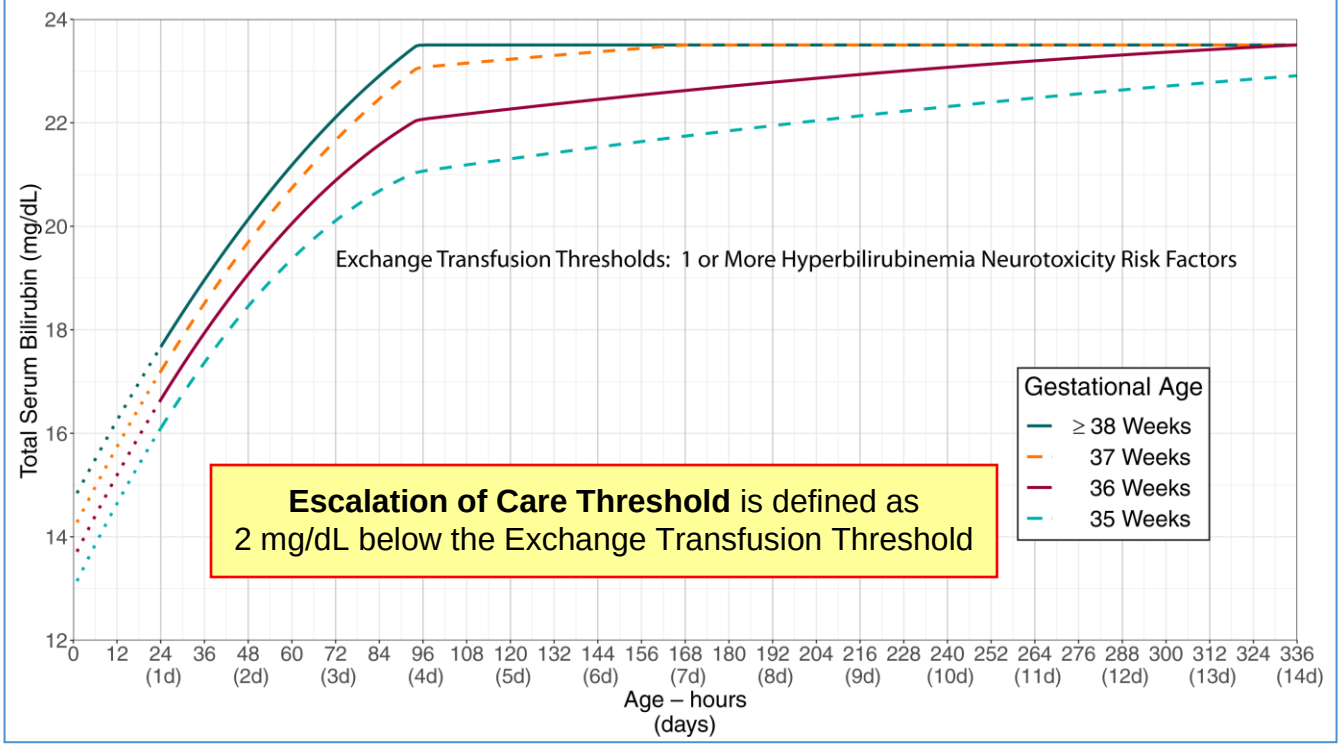
Exchange Transfusion Thresholds Based on Hours of Age

No neurotoxicity risk factors



1 or More neurotoxicity risk factors



(Kemper et al. 2022)

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[Go to Escalation of Care]

Escalation of Care

Escalation of Care STAT Labs:

- NBP
- CBC
- Reticulocyte count
- CMP (or albumin, chem7)
- Type and Cross match
- **DAT** if not previously obtained ***and*** mother was DAT pos, blood group O, Rh(D) neg ***OR*** status unknown

- **In consultation with NICU:**
  - **Notify blood bank** of preparation for potential exchange transfusion
  - If **positive DAT**, consider **IVIG**: 0.5 to 1 g/kg over 2 hours. Dose can be repeated in 12 hours.
  - An exchange transfusion may be considered if the **bilirubin to albumin ratio** is:
    - ≥ 8.0 if the gestational age is ≥38 weeks' gestation and there are no hyperbilirubinemia neuro-toxicity risk factors, or
    - ≥7.2 if the gestational age is≥38 weeks' gestation and there is at least 1 hyperbilirubinemia neurotoxicity risk factor, or
    - ≥7.2 if the gestational age is 35 through 37 weeks' gestation with no hyperbilirubinemia neurotoxicity risk factor, or
    - ≥6.8 if the gestational age is 35 through 37 weeks' gestation and at least 1 hyperbilirubinemia neurotoxicity risk factor

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Risk Factors for Rebound Hyperbilirubinemia

A longer period of phototherapy is an option if patient has one or more risk factor for rebound hyperbilirubinemia:

- GA <38 weeks GA
- Age <38 hours at the start of phototherapy
- Hemolytic disease

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Patient & Caregiver Education

IP DC INSTRUCTIONS - HYPERBILIRUBINEMIA

Your baby was in the hospital for jaundice (hyperbilirubinemia).

Facts

Jaundice is common in newborns. High bilirubin levels in the blood cause jaundice. It can make babies' skin look yellow or orange. It commonly happens on the second or third day of life. Bilirubin levels often peak at 5 to 6 days of life, and jaundice usually goes away by 2 weeks of life.

Treatment in the Hospital

Your baby received special light therapy (phototherapy) to decrease the level of bilirubin in the blood.

Treatment at Home

- Continue to breastfeed or bottle feed your baby as you have been doing
- Take care of your baby as you normally would
- Do NOT put your baby in the sunlight as a way to decrease jaundice. This can cause serious sunburn.

Please read Helping Hand, *Jaundice* for more information.

GO TO YOUR CHILD'S DOCTOR OR TO THE EMERGENCY ROOM IF YOUR BABY:

- Does not have at least 5 wet diapers each day
- Is not feeding at least 8-12 times each day or does not seem interested in human milk or formula
- Is looking more yellow
- Has a temperature of 100.4°F or higher
- Is sleepier than usual or is hard to wake up

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References

1. 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. doi:10.1542/peds.2022-058859

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Quality Measures

Inpatient

- TSB monitoring after inpatient intensive phototherapy initiation
  - Numerator: TSB within 12 hours of the start of phototherapy
  - Denominator: Hospitalized newborns receiving intensive phototherapy for a TSB concentration above the treatment threshold

- Providing phototherapy for elevated TSB
  - Numerator: Newborns treated with phototherapy
  - Denominator: Newborns exceeding the phototherapy threshold based on age in hours, gestational age, and neurotoxicity risk factors

- Avoiding unnecessary phototherapy
  - Numerator: Newborns not treated with phototherapy
  - Denominator: Newborns who never had a TSB higher than 3 mg/dL below the threshold based on age in hours, gestational age, and risk factors

- Escalation of care
  - Numerator: Receipt of IV hydration, emergent intensive phototherapy, and neonatologist consultation
  - Denominator: Newborns requiring escalation of care

- Evaluation for anemia for those requiring phototherapy
  - Numerator: Newborns in whom a hematocrit, hemoglobin concentration, or CBC was done
  - Denominator: Newborns receiving phototherapy for a TSB above the phototherapy threshold

- Family education
  - Numerator: Prior to discharge, family given information about jaundice, place and time of follow-up, and birth hospital information (last TcB or TSB, age at which it was done, any DAT results)
  - Denominator: All newborns discharged at <7 days of age

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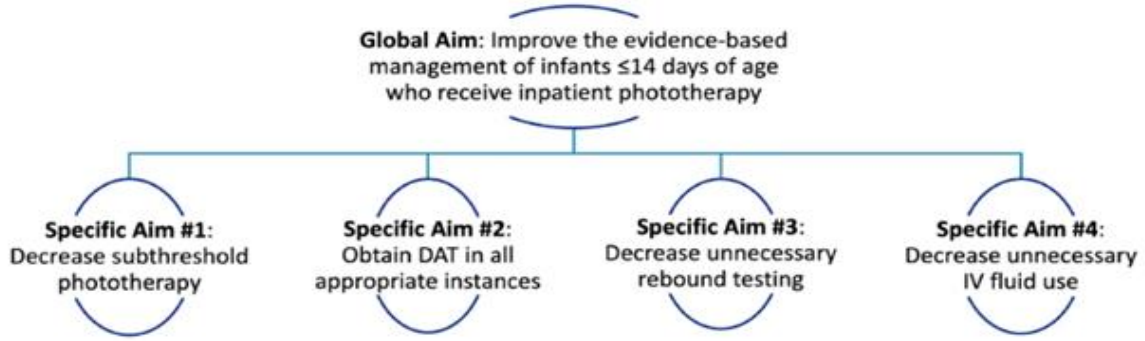
Metrics

VIP Quality Network: LIGHT (Learning & Implementing Guidelines for Hyperbilirubinemia Treatment)

Project Aims



Project Measures

Measure	Definition
Decrease initiation of subthreshold inpatient phototherapy	Proportion of infants who receive inpatient phototherapy for subthreshold TSB (≥0.3 mg/dL below phototherapy threshold) will be 10% or less
Increase appropriate obtainment of direct antiglobulin test (DAT)	DAT status will be assessed in 100% of infants with blood type O mothers who undergo inpatient phototherapy
Decrease unnecessary rebound bilirubin measurements in low-risk infants who undergo inpatient phototherapy	Proportion of infants who start inpatient phototherapy at ≥48 hours of age without hemolysis concerns (DAT negative and no other concerns) who have a bilirubin <18 hours after phototherapy discontinuation will be 10% or less
Decrease unnecessary IV fluid use	5% or less of well-appearing infants who receive inpatient phototherapy and do not meet escalation of care threshold (2 mg/dL below exchange transfusion threshold) will receive IV fluids

Balancing Measures

Measure	Definition
Incidence of reaching escalation of care threshold	% 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
Incidence of total serum bilirubin (TSB) >25 mg/dL	% of infants who have a TSB >25 mg/dL at the start of or during inpatient phototherapy
Phototherapy duration	Number of hours infants undergo inpatient phototherapy
Hospitalization duration	Numbers of hours infants are hospitalized during phototherapy admission
Readmission or re-initiation of phototherapy	% of infants who are reinitiated on or readmitted for inpatient phototherapy within 4 days of previous inpatient phototherapy discontinuation

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Team & Process

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Clinical Pathway Approved

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Ryan Bode, MD, MBOE

Advisory Committee Date: *June, 2023*

Origination Date: *June, 2023*

Next Revision Date: *June, 2026*

Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

For more information about our pathways and program please contact:
ClinicalPathways@NationwideChildrens.org

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Epic Bilirubin Assessment Tool Education

Epic "Bilirubin Assessment Tool" Education Document

On Anchor **"Technical Resource Library"** site

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