Hyperbilirubinemia

NICU Initial Management for ≥ 35 Week Gestation Newborns

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

Center for Clinical Excellence

Maternal or Infant DAT(+) [#] or Concerns for hemolysis?
[If maternal DAT(+) or not done, collect infant blood type and DAT upon admission]

Yes → Measure TcB or TSB immediately, then
- Every 4 hours 2 times, then
- Every 12 hours 3 times

No → Visual jaundice?

- **No** → Obtain TcB* (if available) or TSB within 24-hours postnatal
- **Yes** → Measure TcB or TSB immediately

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

One or more Neurotoxicity risk factors?[β]

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

Abbreviations:
DAT = Direct Antiglobulin Test
TSB = Total Serum bilirubin
*** TcB = Transcutaneous bilirubin**
If the TcB exceeds or is within 3 mg/dL of the phototherapy treatment threshold or if the TcB is ≥20 mg/dL, always obtain a TSB

Does Infant meet threshold to begin phototherapy?

- **No** → Recheck bilirubin level within the next 12-24 hours
- **Yes** → Phototherapy

TSB ≤ 2mg/dL of exchange transfusion threshold?

- **Yes** → **Continue to Escalation of Care Algorithm**
- **No** → TSB should be measured within 12- 24 hours after starting phototherapy

TSB is 2 mg/dL below the Phototherapy level at initiation?

- **No** → Phototherapy
- **Yes** → Discontinue phototherapy

[#]Exception:
May collect routine TcB/TSB within 24h postnatal if all these criteria are met:
(1) infant DAT only positive to anti-Rh(D)
(2) mother received RhIG during pregnancy
(3) mother was anti-Rh(D) negative before RhIG,
(4) infant has no jaundice or hemolysis

Risk factors for Rebound Hyperbilirubinemia
Consider a longer period of Phototherapy to decrease TSB level further below threshold (*or* f/u in ≤24hrs)

- Discontinue phototherapy when TSB is ≥ 2 mg/dL below the hour-specific threshold at the initiation of phototherapy if discharge is planned within 24-hours of discontinuation.
- Discontinue phototherapy when TSB is ≥ 2 mg/dL below the hour-specific threshold for the date/time TSB was obtained if the infant will be monitored in the NICU for >24 hours post-discontinuation.

Monitor after discontinuation of Phototherapy:
- Consider rebound bilirubin 6-12 hours of discontinuation of phototherapy if DAT(+) or concerns for hemolysis
- If no risk factors, consider rebound bilirubin in 12-24 hour

Hyperbilirubinemia
NICU Escalation of Care

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

Center for Clinical Excellence

TSB ≤ 2mg/dL of exchange transfusion threshold?[∞]

No → Return to Initial Management Algorithm

Yes

- STAT labs: total & direct serum bilirubin; CBC + retic; albumin[α]; chemistry; type and crossmatch
- If not already started, Start Intensive Phototherapy Immediately
- Measure TSB at least q2hrs from the start of the escalation-of-care period until the escalation-of-care period ends
- Start IV hydration

[∞] When to Transfer to Main Campus NICU:

- When TSB reaches or exceeds Escalation of care threshold= Bilirubin level within 2mg/dL exchange transfusion level
- Consider transfer to Main Campus NICU prior to reaching the escalation of care threshold in the following scenarios:
  - Known ABO, Rh, or other antibody incompatibility requiring Intravenous immune globulin treatment
  - High rate of rise despite intensive phototherapy
  - GA < 35 weeks

[β] Neurotoxicity Risk Factors

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

[α]The Bilirubin to Albumin Ratio can be used in conjunction with the TSB level in determining the need for exchange transfusion

Infants with isoimmune hemolytic disease (DAT+) whose TSB ≤ 2mg/dL of exchange transfusion threshold?

Yes → Intravenous immune globulin can be administered. A repeat dose can be considered as clinically indicated.

No

Infant's TSB rising despite therapy?
or
Infant has neurotoxicity risk factors?[β]

No → Return to Initial Management algorithm

Yes

Use Exchange Transfusion thresholds by GA: 1 or more Neurotoxicity risk factors to identify exchange transfusion levels

Use Exchange Transfusion thresholds by GA No Neurotoxicity risk factors to identify exchange transfusion levels

TSB at or above exchange transfusion threshold or Infant with signs of Acute Bilirubin Encephalopathy?

Yes → Perform Urgent Exchange Transfusion as per protocol

No → Continue current Management until TSB ≤ exchange transfusion threshold

Hyperbilirubinemia
NICU Exchange Transfusion

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

Center for Clinical Excellence

TSB ≤ 2mg/dL of exchange transfusion threshold? √ — No → Return to Initial Management Algorithm

Yes

Patient at NCH Main Campus NICU for exchange transfusion? — No →

Patients at Referral Hospital
1. Call NCH NICU via PCTC for urgent direct admission
2. Continue intensive phototherapy + IV hydration – obtain IV access if not already done✗
3. Make NPO if not already done

Transfer to Main Campus NCH

Yes

Patients at NCH Main Campus
1. STAT labs: total & direct serum bilirubin; CBC + retic; albumin; chemistry; type and crossmatch; G6PD testing
2. Notify blood bank
3. Measure TSB Q2hr
4. Continue intensive phototherapy + IV hydration – obtain IV access if not already done✗
5. Make NPO if not already done

TSB at or above exchange transfusion threshold or Infant with signs of Acute Bilirubin Encephalopathy? — Yes → Perform Urgent Exchange Transfusion as per protocol

No

Continue intensive phototherapy + IV hydration + check TSB Q2hr

TSB below 2mg/dL of exchange transfusion threshold level? — No → (back to Continue intensive phototherapy + IV hydration + check TSB Q2hr)

Yes → Return to Initial Management Algorithm

√
- Exchange Transfusion thresholds by GA No Neurotoxicity risk factors
- Exchange Transfusion thresholds by GA: 1 or more Neurotoxicity risk factors

✗
Umbilical line placement: venous and arterial recommended if possible

Escalation of Care Algorithm

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**

Neurotoxicity Risk Factors

- Gestational age <38 wk and this risk increases with the degree of prematurity
- Albumin <3.0 g/dL. However, albumin does not need to be routinely measured in all infants and should only be obtained if there is a clinical reason to obtain the lab
- Isoimmune hemolytic disease (ie, positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 h

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:

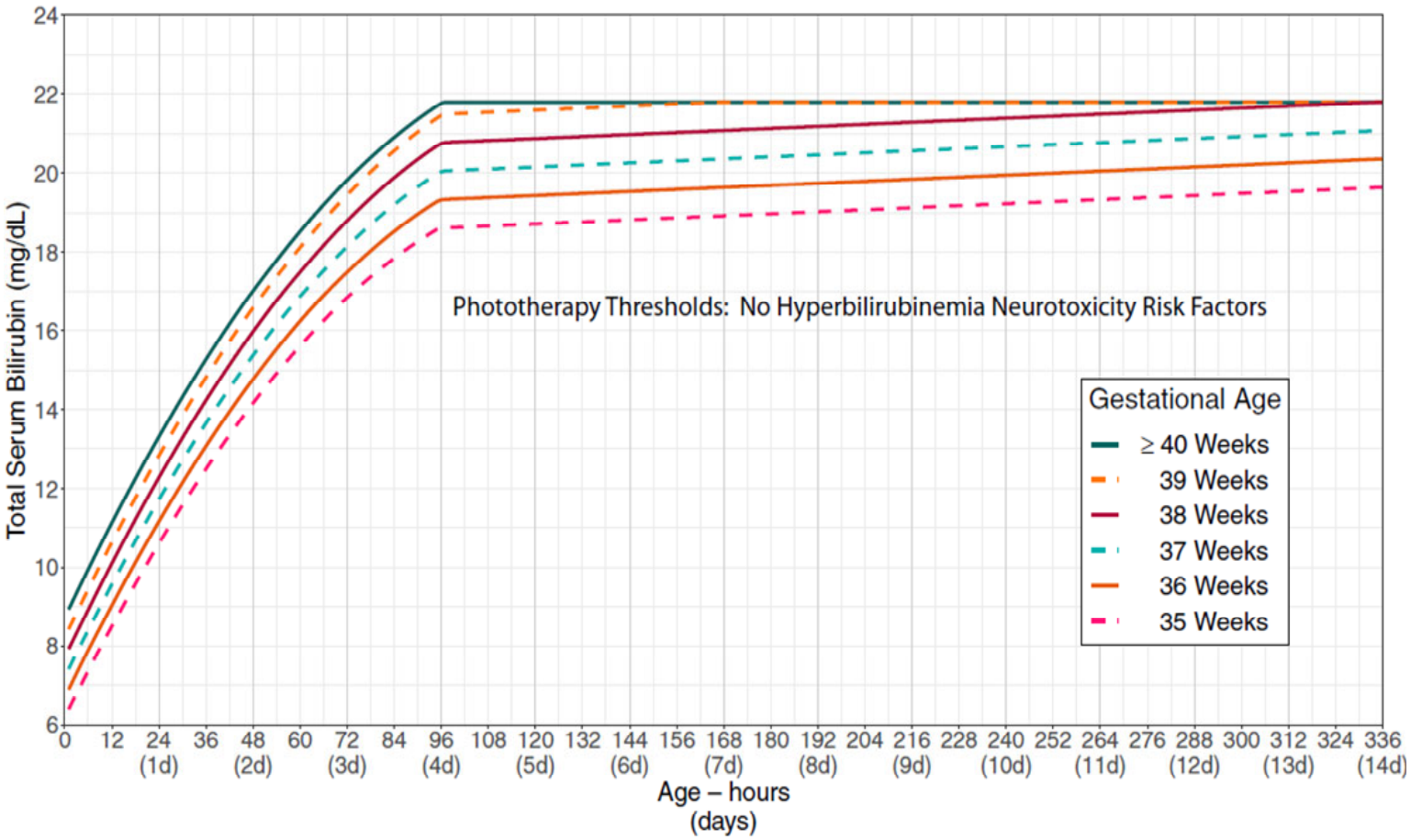
- Phototherapy required before discharge from newborn hospital
- Atypical development of hyperbilirubinemia (elevated TSB in formula fed infants or late-onset jaundice)

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.

Phototherapy Thresholds:
NO Hyperbilirubinemia Neurotoxicity Risk Factors

Use "**Bilirubin Assessment Tools**" in patient's chart
to view nomogram and
determine need for phototherapy



Neurotoxicity Risk Factors

- Gestational age < 38 weeks and this risk increases with the degree of prematurity
- Albumin < 3.0 g/dL
- Positive DAT, G6PD deficiency or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 hours

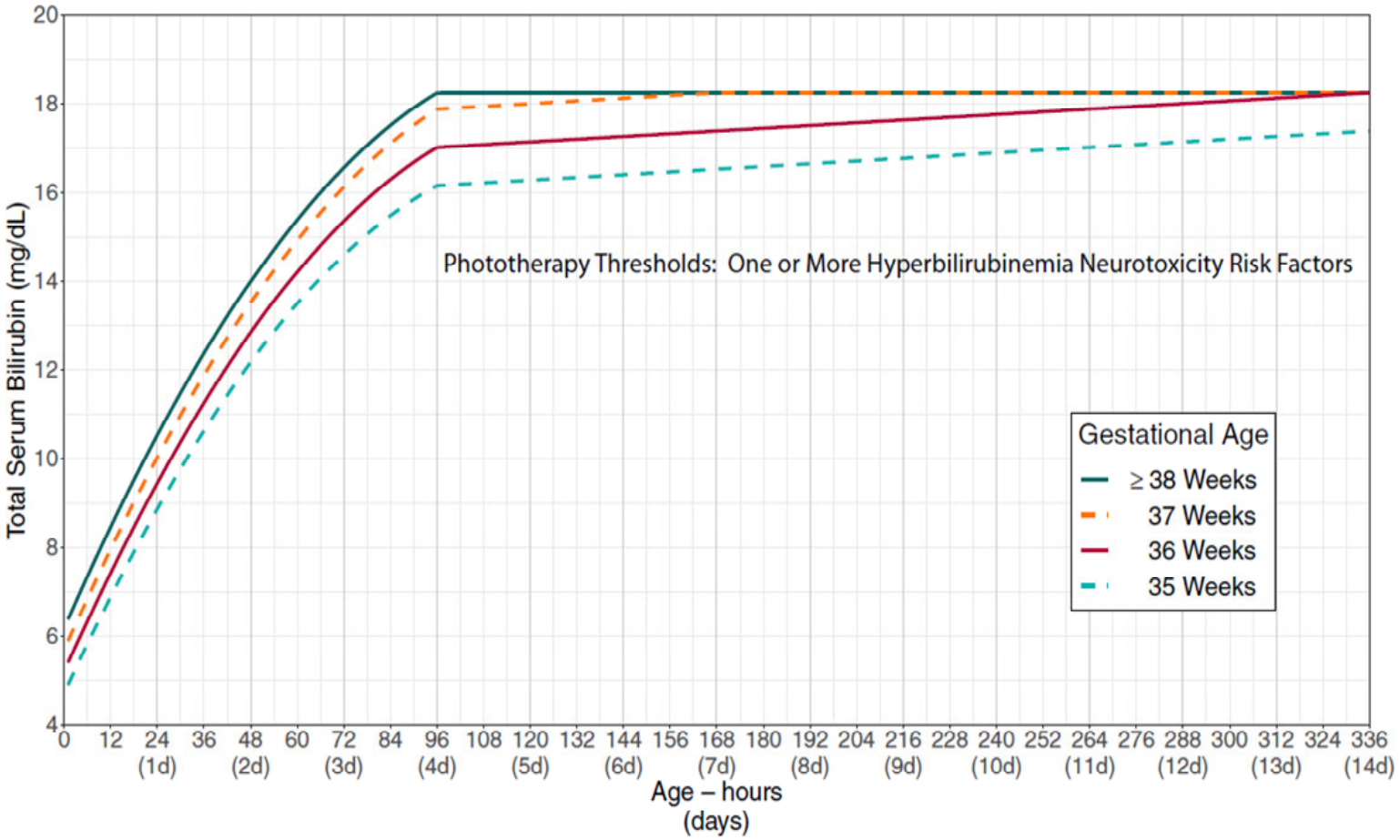
Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin

(Kemper et al. 2022)

Initial Management Algorithm

Phototherapy Thresholds:
One or More Hyperbilirubinemia Neurotoxicity Risk Factors

Use "**Bilirubin Assessment Tools**" in patient's chart
to view nomogram and
determine need for phototherapy



Neurotoxicity Risk Factors

- Gestational age < 38 weeks and this risk increases with the degree of prematurity
- Albumin < 3.0 g/dL
- Positive DAT, G6PD deficiency or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 hours

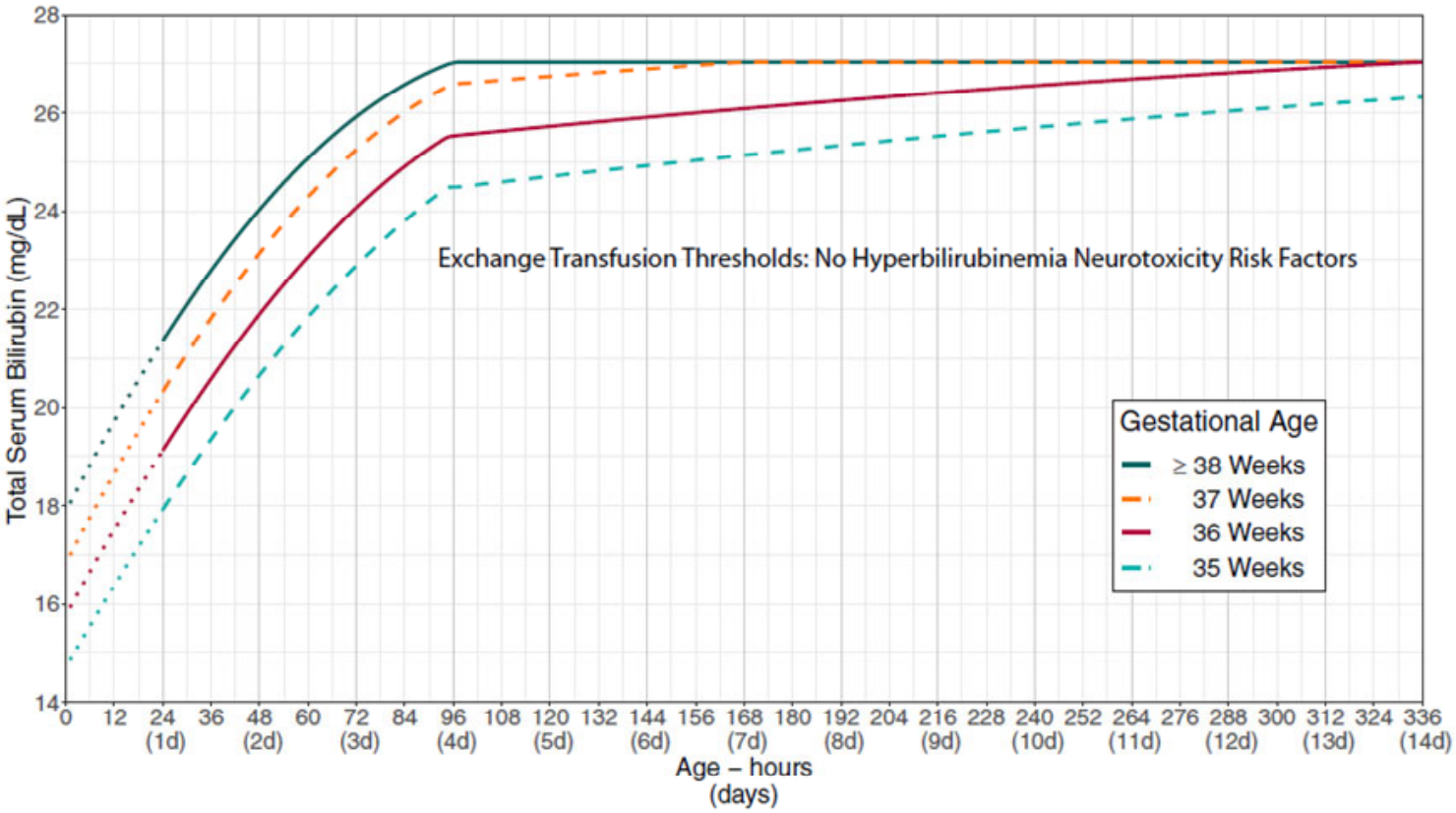
Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin

(Kemper et al. 2022)

Initial Management Algorithm

Exchange Transfusion Thresholds by Gestational age: No Neurotoxicity Risk Factors

Use "**Bilirubin Assessment Tools**" in patient's chart
to view nomogram and
determine need for exchange transfusion



Neurotoxicity Risk Factors

- Gestational age < 38 weeks and this risk increases with the degree of prematurity
- Albumin < 3.0 g/dL
- Positive DAT, G6PD deficiency or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 hours

Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin

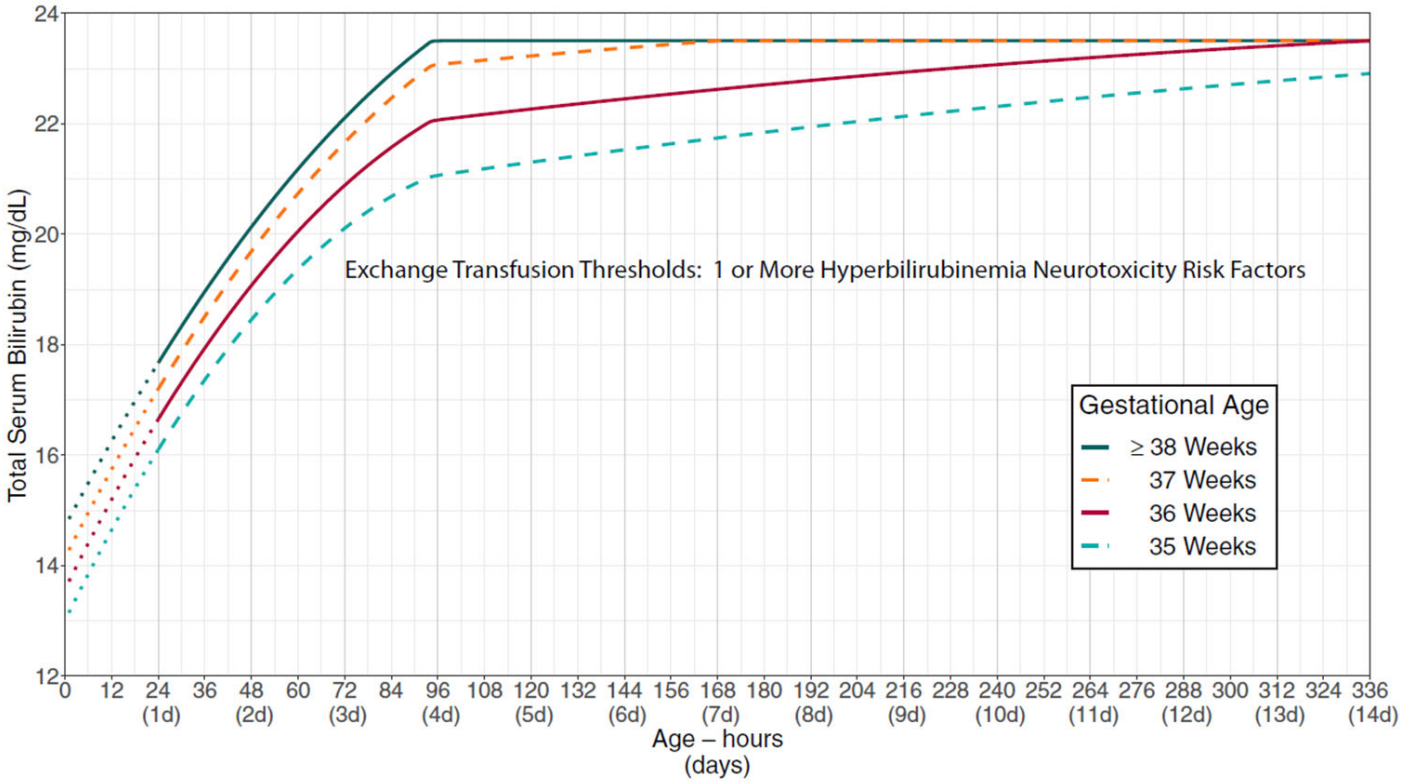
(Kemper et al. 2022)

Escalation of Care Algorithm

Exchange Transfusion Algorithm

Exchange Transfusion Thresholds by Gestational age: 1 or more Neurotoxicity Risk Factors

Use "**Bilirubin Assessment Tools**" in patient's chart
to view nomogram and
determine need for exchange transfusion



Neurotoxicity Risk Factors

- Gestational age < 38 weeks and this risk increases with the degree of prematurity
- Albumin < 3.0 g/dL
- Positive DAT, G6PD deficiency or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 hours

Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin

(Kemper et al. 2022)

Escalation of Care Algorithm

Exchange Transfusion Algorithm

Phototherapy in Neonatal Jaundice

Phototherapy Policy Document:
Phototherapy in Neonatal Jaundice

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.

(Kemper et al. 2022)

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 neonate
- 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

TSB should be measured if the TcB exceeds or is within 3 mg/dL of the phototherapy treatment threshold or if the TcB is ≥20 mg/dL.

Bilirubin Albumin Ratio

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

Escalation of Care Algorithm

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
- Age <48 hours at the start of phototherapy
- Hemolytic disease

Initial Management Algorithm

Special Considerations

Additional considerations for patients being treated for hyperbilirubinemia:

- Consider switching to bottle feeding if patient is exclusively breast feeding, if the baby cannot be taken off PTx during to concern for rising bilirubin.
- If escalating care, avoid time away from phototherapy for skin to skin or breast feeding
- Avoid use of medications that are potent bilirubin displacers (ie. Ceftriaxone) – discuss with pharmacy
- Intensive phototherapy is defined as use of two or more sources of phototherapy (ie. A biliblanket and an overhead light, or two overhead lights)
- Ensure that the phototherapy has maximum exposure to skin (minimal diaper coverage)

Additional considerations about Bilirubin Threshold for Discontinuation of Phototherapy:

The recommendation to discontinue phototherapy when TSB is ≥ 2 mg/dL below the hour-specific threshold at the initiation of phototherapy was devised to prevent rebound at home and kernicterus/readmission.

However, if there is no anticipated discharge within 24 hours of phototherapy discontinuation, clinical teams may discontinue phototherapy based on current day's threshold level.

Acute Bilirubin Encephalopathy

Defined clinically based on the following signs and symptoms:

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

Escalation of Care Algorithm

Exchange Transfusion Algorithm

References

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.

Quality Metrics

Pathway Goal

- Goal of the pathway is to increase compliance to 2022 AAP Clinical practice Guidelines for Mx of Hyperbilirubinemia in neonates

Quality Measures

- TSB monitoring after intensive phototherapy initiation
  - Numerator: TSB within 12 hours of the start of phototherapy
  - Denominator: Neonates in NICU receiving intensive phototherapy for a TSB concentration above the treatment threshold

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

- Avoiding unnecessary phototherapy
  - Numerator: Neonates not treated with phototherapy
  - Denominator: Neonates 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: Neonates requiring escalation of care

- Evaluation for anemia for those requiring phototherapy
  - Numerator: Neonates in whom a hematocrit, hemoglobin concentration, or CBC was done
  - Denominator: Neonates 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

Team & Process

Pathway Development Team:

Leaders:

Neonatology:

Roopali Bapat, MD, MSHQS
Maria Jebbia, MD
Jonathon Slaughter, MD, MPH

Members:

Neonatology:

Naik Apurwa, MD
Elizabeth Stafford, NNP, APRN
Nicole Cochran, NNP, APRN
Sheria Wilson, MD, MA
Audrey Miller, MD
Teresa Seto, MD
Jason Jackson, DO
Julia Taylor, NNP
Namrita Odackal, DO
Shama Patel, MD, MPH

Hospital Pediatrics:

Jana Erner, MD

Nursing Informatics:

Alexandria O'Connor, BSN, RN

Neonatal Nurse Educator:

Sarah Hastie
Kim Samson, MSN, RNC-NIC

Clinical Pathways Program:

Medical Director – Neonatology:

Roopali Bapat, MD, MSHQS

Medical Director – Quality:

Ryan Bode, MD, MBOE

Medical Director – Clinical Informatics & Emergency Medicine:

Laura Rust, MD, MPH

Business & Development Manager:

Rekha Voruganti, MBOE, LSSBB

Program Coordinators:

Tahje Brown, MBA

Tara Dinh, BS

Joaquin Serantes, BA

Guideline Approved:

Medical Director – Associate Chief Quality Officer, Center for Clinical Excellence:

Ryan Bode, MD, MBOE

Advisory Committee Date: *November, 2023*

Origination Date: *December, 2023*

Next Revision Date: *December, 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