Children's Hospital and Health System, Inc.
Patient Care Treatment Guideline
CW Urgent Care (UC)

SUBJECT: Neonatal Jaundice

Purpose/inclusion criteria/exclusion criteria: To evaluate and initiate treatment of neonatal jaundice in neonates with documented or history of elevated **unconjugated (indirect)** bilirubin or jaundice who are **≥ 24 hour**s and **≤ 14 days** old who were born at **≥ 35 weeks** gestation.

> Premature babies < 35 weeks gestation and babies presenting with jaundice after 2 weeks of age may have another etiology for their hyperbilirubinemia that likely would not respond to phototherapy so would fall out of the recommendations of this guideline. Additionally those with conjugated hyperbilirubinemia (direct bilirubin > 2 mg/dL or > 20% of TSB) would fall outside of this guideline.

Definition: Jaundice refers to the yellow coloration of the skin and the sclera caused by the accumulation of bilirubin in the skin and mucous membranes. Jaundice is caused by a raised level of bilirubin in the body, a condition known as hyperbilirubinemia. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life. For most babies, jaundice is not an indication of an underlying disease, and this early jaundice (termed "physiological jaundice") is generally harmless. *Total serum bilirubin (TSB) generally peaks at 3-5 days of life.*

Breastfed infants regularly have unconjugated hyperbilirubinemia that extends into the second and third weeks of life and often up to 8-12 weeks of life. Approximately 10% of breastfed babies are still jaundiced at 1 month. This prolongation of physiologic jaundice due to breastfeeding is known as "breast milk jaundice". The mechanism of breast milk jaundice in humans is unknown. Breastfeeding should continue during this time.

Jaundice has many possible causes including blood group incompatibility, hemolytic disease, sepsis, metabolic and endocrine disorders, and anatomic abnormalities of the liver. If left untreated, hyperbilirubinemia can lead to acute bilirubin encephalopathy and kernicterus. Kernicterus describes the chronic and permanent clinical sequelae of bilirubin toxicity including cerebral palsy, high frequency hearing loss, dental dysplasia and mild mental retardation. A total bilirubin > 25 mg/dL is associated with an increased risk of these problems.

Etiology: Bilirubin is mainly produced from the breakdown of red blood cells. Red blood cell breakdown produces **unconjugated (indirect)** bilirubin, which circulates mostly bound to albumin although some is free and thus able to enter the brain. Unconjugated bilirubin is metabolized in the liver to produce **conjugated (direct)** bilirubin which then passes into the gut and is largely excreted in stool. Unconjugated bilirubin is potentially toxic to neural tissue.

Differential Diagnosis:

- Pathologic Jaundice, defined as:
  - Present in first 24 hours of life
  - Total Serum bilirubin (TSB) level > age-specific 95th percentile
  - TSB rising by > 0.2 mg/dL per hour
  - Conjugated bilirubin > 2 mg/dL or > 20% of TSB
- Infections including TORCH infections and/or sepsis
  - Consider UTI with elevated conjugated bilirubin and/or late onset (after the fourth or fifth day) of jaundice
- Hemolysis such as ABO or Rh incompatibility
  - G6PD which occurs in 11-13% of African Americans
- Normal skin pigmentation variant
- Birth trauma
- Anatomic or metabolic liver abnormalities
- Metabolic and endocrine disorders (including maternal diabetes)
- Polycythemia

Guideline

Subjective Data/History

- Birth History
  - Gestational age
  - Date and time of birth
  - Birth weight
  - Delivery details (forceps, vacuum, etc.)
  - Maternal blood type
  - Maternal or infant infections
- HPI
  - Feeding: breast/formula, duration & frequency of feed, intake in past 24 hours
  - Urine output in past 24 hours
  - Pattern of stooling; color of stool
  - Presence of fever, method of temperature measurement, acetaminophen use
  - Signs of bilirubin encephalopathy:
    - Early: lethargy, hypotonia, high-pitched cry, poor feeding
    - Intermediate: irritability, retrocollis (spasmodic torticollis), opisthotonos (muscle spasms causing backward arching of head, neck and spine), fever
    - Advanced: apnea, stupor, coma
- Family History
  - Sibling received phototherapy
  - Hematological disorders (i.e. G6PD-deficiency, hereditary spherocytosis, known blood group incompatibility)

- Inherited conditions leading to decreased hepatic bilirubin clearance such as Crigler-Najjar syndrome and Gilbert syndrome

Objective Data/Physical Exam

- Vital signs, weight
  - For febrile infants (history of or current rectal temperature ≥ 38°C or 100.4°F), follow the Urgent Care Febrile Neonate evidence-based guideline.
- General appearance
- Hydration status
- Abdominal exam: hepatomegaly, splenomegaly
- Neurologic exam: tone, retrocollis, opisthotonus, nuchal rigidity
- Skin exam: bruising, petechiae, pallor, hematoma, rash
- Assess for jaundice (*visual estimation of bilirubin levels from the degree of jaundice can lead to errors)*
  - Cephalocaudal progression
    - Infants whose jaundice is limited to the face have a lower bilirubin level than those with jaundice below the nipple line
  - Scleral icterus
  - Apply gentle pressure with 1 finger to reveal color of skin and subcutaneous tissue

Diagnostic Studies

- See Appendix A: Treatment of Neonatal Jaundice in Urgent Care; Appendix B: Nomograms
- All bilirubin levels should be interpreted based on infant's age in hours

Treatment

- Ill-appearing infants with concerns of hemolysis, infection, acute bilirubin encephalopathy etc. should be evaluated in the ED
- See Appendix C: Factors that increase or decrease the risk of severe hyperbilirubinemia
- See Appendix A: Treatment of Neonatal Jaundice in Urgent Care
  - Use www.bilitool.org to access an hour specific nomogram to determine your patient's risk stratification (See Appendix B: Nomograms)
    - Must have the patient's date and time of birth and the TSB
    - Consider trend of bilirubin

Education of Patient/Family

- Assure adequate PO intake/hydration
  - Encourage frequent feedings
    - Breast fed infants, should be fed a minimum of 8-10 times/24 hours
    - Consider supplementation if infant has continued weight loss (>10% of birth weight), poor stooling or difficulty with breast feeding

- Supplement with expressed breast milk or, if not available, formula
- Early consultation with lactation consultant if needed
- Encourage frequent skin to skin contact between mother and baby
- Infant should be put to breast before onset of crying
- Ensure mother is hand expressing/pumping breast milk frequently to help establish milk supply
- Bottle fed infants should have at least 1-2 ounces of expressed breast milk or formula every 2-3 hours for the first week of life

- Recognize signs of increasing jaundice and dehydration

Follow-up

- See Appendix A: Treatment of Neonatal Jaundice in Urgent Care
- Call PMD or go to the ED if the infant develops fever, lethargy, hypotonia, irritability, arching, poor feeding, signs of infection, signs of dehydration or other concerns/questions.

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References

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Gartner, L. (2010). ABM clinical protocol #22: Guidelines for management of jaundice in the breastfeeding infant equal to or greater than 35 weeks' gestation. *Breastfeeding Medicine, 5*(2), 87-93.

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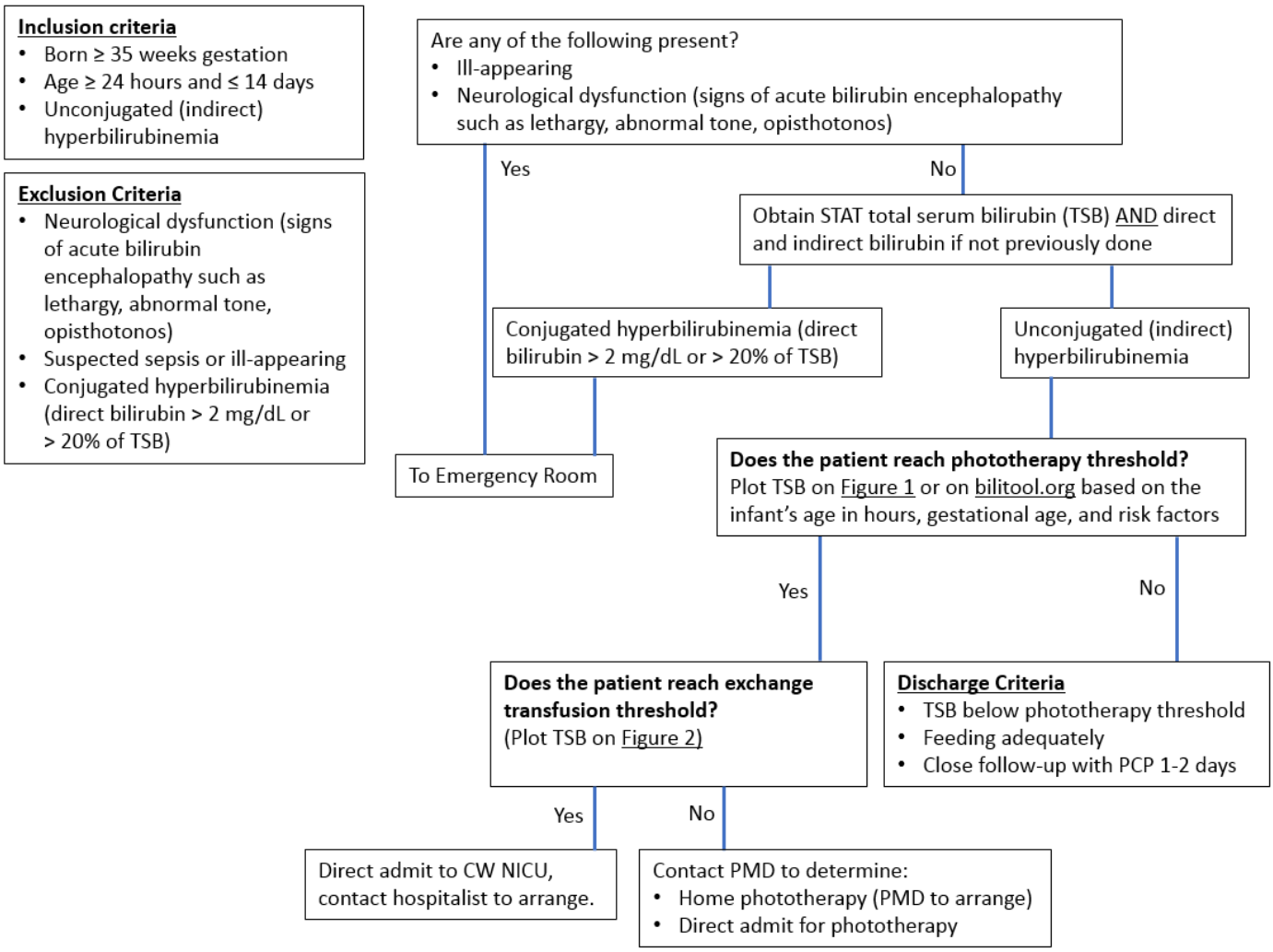
Maisels, M. J., Bhutani, V. K., Bogen, D., Newman, T. B., Stark, A. R., & Watchko, J. F. (2009). Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. *Pediatrics, 124*(4), 1193-1198.

Sardari, S., Mohammadizadeh, M., & Namnabati, M. (2019). Efficacy of home phototherapy in neonatal jaundice. *Journal of Comprehensive Pediatrics, 10*(1), 1-6.

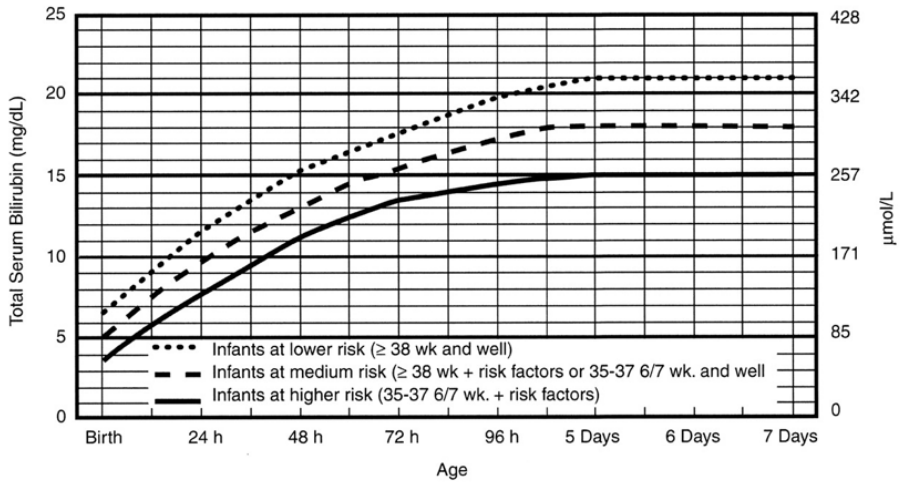
Treatment information also provided by Yan Zhan, Pediatric Emergency Medicine Fellow, Children's Wisconsin (personal communication, May 2020).

Appendix A: Treatment of Neonatal Jaundice in Urgent Care



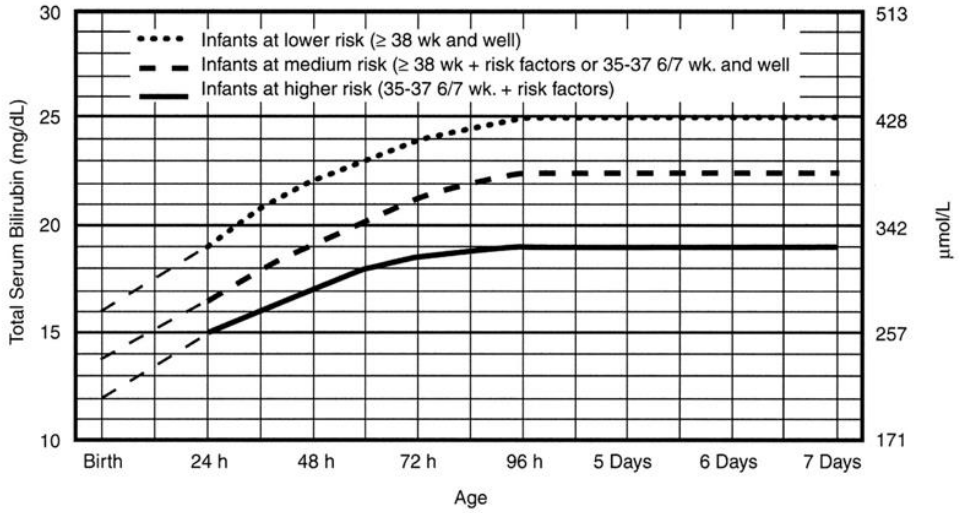
Appendix B: Nomograms

Figure 1: Threshold for Phototherapy Initiation



- 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 < 3.0g/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 (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

Figure 2: Threshold for Exchange Transfusion



- 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.

Appendix C: Factors that affect the risk of severe hyperbilirubinemia (AAP, 2004)

Major risk factors

- Jaundice in first 24 hours
- ABO incompatibility with positive direct Coombs
- Known hemolytic disease (e.g. G6PD deficiency)
- Gestational age 35-36 weeks
- Previous sibling required phototherapy
- Significant bruising or cephalohematoma
- Exclusive breastfeeding, esp. with poor feeding or weight loss
- East Asian Race

Minor risk factors

- Gestational age 37-38 weeks
- Jaundice observed before discharge
- Previous sibling with jaundice not requiring phototherapy
- Macrosomic infant of a diabetic mother
- Maternal age ≥ 25 years
- Male gender

Protective factors

- TSB or TcB in the low-risk zone
- Gestational age ≥ 41 weeks
- Exclusive bottle feeding
- Black race (based on mother's report)
- Discharge from hospital after 72 hours