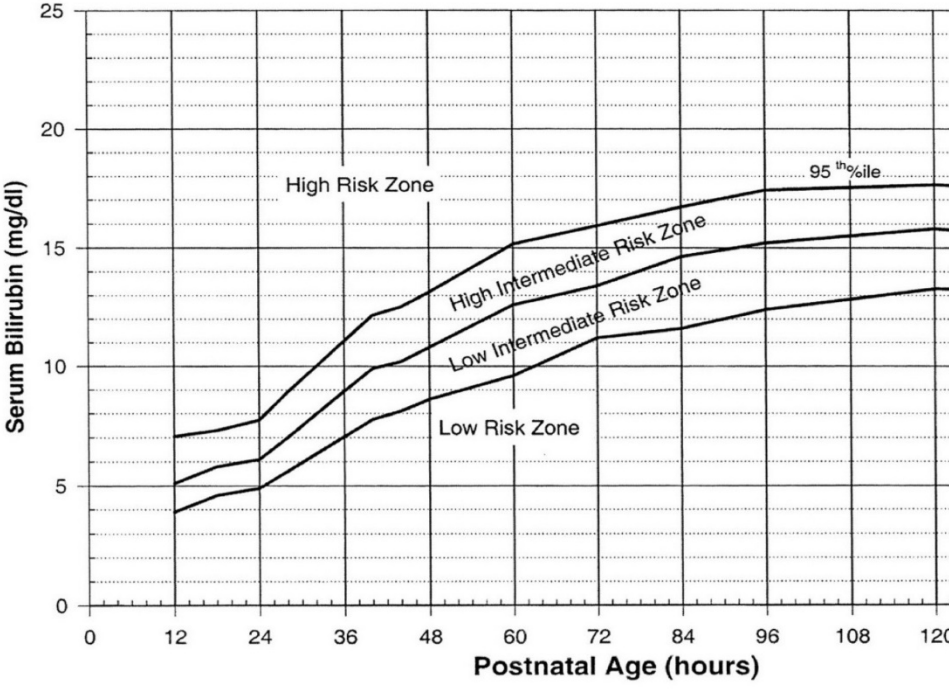
Neonatal hyperbilirubinemia is common and occurs in up to 80% of all newborns. Approximately 5-10% of newborns will require phototherapy, while a much smaller percentage will require more intensive therapies such as exchange transfusion. It is important to understand the risk factors for developing severe hyperbilirubinemia and the treatment guidelines based on these risk factors.

Risk Factors for Severe Hyperbilirubinemia in Infants ≥ 35 Weeks' Gestation

- Major risk factors
  - Pre-discharge TSB level in the high-risk zone (Fig 2)
  - Jaundice observed in the first 24 hours
  - Blood group incompatibility with positive direct Coombs test
  - Other known familial hemolytic disease (G6PD, spherocytosis, etc.)
  - Gestational age 35-36 wk.
  - Previous sibling received phototherapy
  - Cephalohematoma or significant bruising
  - Exclusive breastfeeding, particularly with poor feeding or excessive weight loss
  - Asian race
- Minor risk factors
  - Pre-discharge TSB or TcB level in the high intermediate-risk zone
  - Gestational age 37-38 weeks
  - Macrosomic infant
  - Male gender
- Low risk group
  - TSB or TcB level in the low-risk zone
  - Gestational age ≥ 41 wk.
  - Exclusive bottle feeding
  - Discharge from hospital after 72 hours

Risk Zone as a Predictor of Hyperbilirubinemia		
TSB Before Discharge	Newborns Total = 2840 n (%)	Newborns Who Subsequently Developed a TSB Level > 95th Percentile, n (%)
High-risk zone (>95th percentile)	172 (6.0)	68 (39.5)
High intermediate-risk zone	356 (12.5)	46 (12.9)
Low intermediate-risk zone	556 (19. 6)	12 (2.26)
Low-risk zone	1756 (61.8)	0

Nomogram for designation of risk in 2840 well newborns at 36 or more weeks' gest
weight of 2000g or more or 35 or more weeks' gestational age and birth weight of 250
hour-specific serum bilirubin values.



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Ten Commandments for Preventing and Managing Hyperbilirubinemia:

1. Promote and support successful breastfeeding
2. Measure TSB if clinical jaundice before 24 hours
3. If TcB is elevated, must confirm with TSB
4. Recognize that visual diagnosis of jaundice is unreliable
5. Interpret all TSB levels according to infant's age in hours
6. Do not treat late preterm as a term infant; they are at a much higher risk.
7. Determine the need for repeat bilirubin levels and safety for hospital discharge based on the 24 hour screening bilirubin level
8. Provide parents with information about newborn jaundice
9. Plan follow-up based on time of discharge and the risk assessment
10. When indicated, treat the newborn with phototherapy or exchange transfusion

Indirect Hyperbilirubinemia
Etiology:

- Concentration from dehydration
- Increased production
    - Blood group incompatibility: Rh, ABO, minor subgroup
    - RBC defects: spherocytosis, elliptocytosis, pyruvate kinase or G6PD deficiency, thalassemia
    - Extravascular blood: cephalohematoma, bruises
    - Polycythemia
    - Sepsis or UTI
- Increased enterohepatic circulation
    - Bowel obstruction, ileus
    - Breast milk jaundice
- Decreased excretion
    - Prematurity
    - Hypothyroidism
    - Hepatocellular dysfunction
    - Galactosemia, tyrosinemia
    - Drugs (aspirin, sulfa)
    - Crigler-Najjar syndrome

Initial Work-up for bilirubin in high risk zone and/or requiring phototherapy:

- Total and Direct bilirubin
- Document maternal antibody status and send cord blood for infant's Type and Coombs
- Hematocrit and reticulocyte count: evidence of hemolysis
- Smear: Spherocytosis, fragmented RBCs with hemolysis (heel stick will be a false positive)
- Consider screen for sepsis and/or UTI
- Consider G6PD, thalassemia and pyruvate kinase screen
- If hyperbilirubinemia occurs after two weeks of age, obtain results of newborn screen and consider testing for thyroid dysfunction (TSH, free T4)

Management:

- Consider supplementing feeds to decrease enterohepatic circulation or starting IVFs to improve urine output and increase bilirubin excretion

Phototherapy

- First line of treatment for management of hyperbilirubinemia in a newborn
- Can be a high-intensity bilirubin blanket (for babies in the newborn nursery) to multiple banks of overhead lights depending on the bilirubin level
- Use total bilirubin. Do not subtract direct bilirubin from the total.
- For infants > 35wks: Follow AAP guidelines and bilirubin charts (see pages 69 & 70)
- For infants < 35wks and <7 days:

	Initiate Phototherapy	Exchange Transfusion for infants without neurologic findings
Gestational Age (Week)	**Total Serum Bilirubin (mg/dl)**	**Total Serum Bilirubin (mg/dl)**
<28 0/7	5-6	11-14
28 0/7-29 6/7	6-8	12-14
30 0/7-31 6/7	8-10	13-16
32 0/7-33 6/7	10-12	15-18
34 0/7-34 6/7	12-14	17-19

week infant is 7 days old, use the TSB level for 30 0/7 weeks.

- Use lower range of listed TSB levels for infants at greater risk of bilirubin toxicity:
  - Lower gestational age
  - Rapidly rising TSB (rate of rise $\geq$0.2 mg/dL/hour)
  - Significant bruising
  - Clinically unstable

IVIG & Albumin Infusions for Hypoalbuminemia:

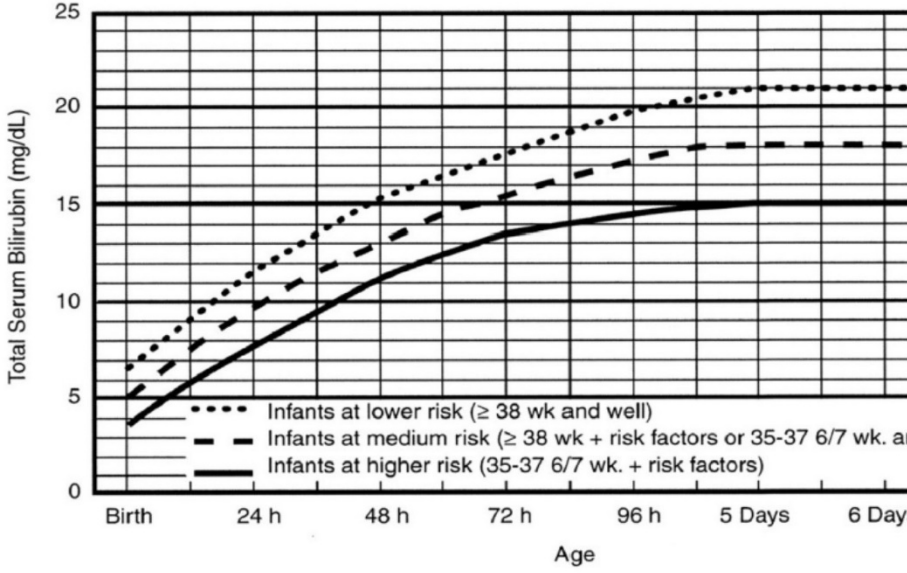
- IVIG: 1 gm/kg over 2-4 hours
  - May be useful for hyperbilirubinemia associated with hemolysis
- Albumin: 10-20 ml/kg of 5% Albumin
  - Studies have shown conflicting levels of efficacy but may be used on a case-by-case basis

Exchange transfusion for Hyperbilirubinemia: Goal is to prevent kernicterus and bilirubin-induced neurologic dysfunction (BIND)

- For infant ≥ 35 weeks GA, follow AAP guidelines
  - Also indicated when infant has signs of kernicterus or BIND regardless of TSB level
- For infants < 35 weeks and without neurologic findings, use table above

Guidelines for phototherapy in infants of 35 or more weeks

Note: levels shown are approximations.



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, te 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 intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those clos
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg below those shown but home phototherapy should not be used in any infant with risk factors.

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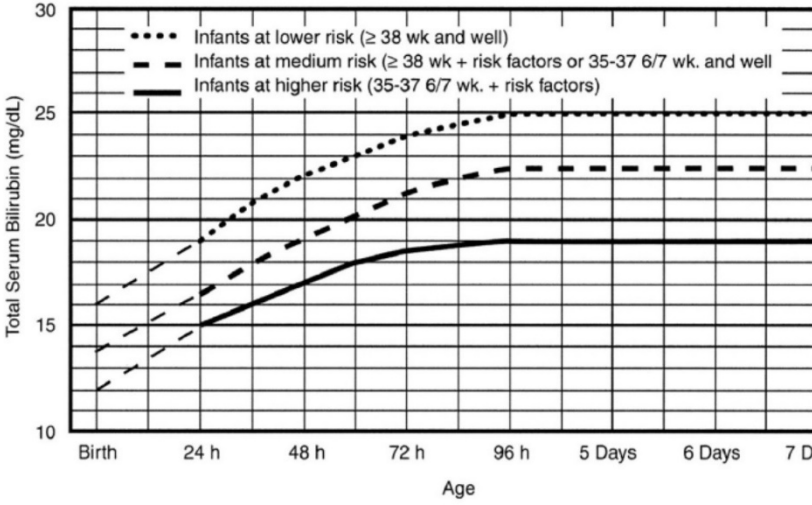
Guidelines for exchange transfusion in infants of 35 or more wee

Note: levels shown are approximations.



- 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 actua gestational age.

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Exchange transfusion

- Goal: To remove antibodies and bilirubin
  - –Before exchange, send baby's blood for metabolic screen, G6PD screen, and Hgb electrophoresis
  - –Request fresh blood (< 3 days)
  - –Should be double volume (removes 87% of baby's RBCs, infants ≥35 weeks have blood volume of 85 mL/kg)
  - –Aliquots should be no more than 5% of blood volume in a single pass
  - –Length of exchange procedure would be about 2 hours
- Complications of exchange
  - –Arrhythmia, cardiac arrest
  - –Hypoglycemia, hypocalcemia, hyperkalemia
  - –Necrotizing Enterocolitis
  - –Portal vein thrombosis or other thromboembolic events
  - –Thrombocytopenia
- Review detailed protocol for this procedure

Direct Hyperbilirubinemia (if TsB <5, any direct bilirubin ≥1 mg/dL. If TsB ≥5, any direct bilirubin >20% of total)

Etiology

- Prolonged TPN use
- Anatomic Obstruction
  - –Biliary atresia and/or choledochal cyst
  - –Alagille syndrome
  - –Biliary sludge in preterm infants
  - –Tumor/mass
- Infections
  - – CMV
  - – Enterovirus
  - – HSV
  - – Parvovirus
  - – UTI
  - – Sepsis
  - – Toxoplasmosis

- Genetic/Metabolic
  - Alpha-one antitrypsin deficiency
  - Cystic fibrosis
  - Galactosemia
  - Zellweger syndrome
  - GALD

Diagnosis & Management:

- Liver ultrasound
- LFTs, including GGT
- GI consult
- Consider HIDA scan
- Discuss with nutrition and pharmacy about reconstituting trace elements in TPN
- Consider ursodiol

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