

## **Management of Indirect Hyperbilirubinemia in Preterm Neonates**

### **What is the current practice?**

To reduce the bilirubin load and use of exchange transfusion in preterm infants.

### **Current practices include the following:**

- Early onset of enteral feeding
- Proactive use of effective phototherapy
- Clinical reliance on TB levels to assess bilirubin load
- Identification of vulnerable infants with hemolysis, sepsis, or hypoalbuminemia

### **Best practice recommendations**

- Use consensus and expert recommendations for initiation and use of phototherapy until predictive evidence is validated in prospective studies
- Minimize, based on clinical judgment, exposure to phototherapy in ELBW infants who may be more vulnerable to side effects of photo-oxidant injury, yet more at risk for developing bilirubin-related neurotoxicity if left untreated
- Aggressive reduction of bilirubin load if there is onset of any neurologic signs
- Be informed of hypoalbuminemia or any concurrent conditions that may alter bilirubin binding to albumin and increase the potential risk of BIND

**Historic clinical risk factors for bilirubin neurotoxicity in preterm neonates.**

*Clinical Risk Factors for Neurotoxicity*

1. Birthweight <1000 g
2. Apgar Score <3 at 5 min of age
3. Arterial oxygen tension <40 mm Hg for >2 h
4. Arterial pH <7.15 for >1 h
5. Core temperature <35°C for >4 h
6. Serum albumin <2.5 g/dL
7. Sepsis
8. Clinical deterioration

Data from Brown AK, Kim MH, Wu PY, et al. Efficacy of phototherapy in prevention and management of neonatal hyperbilirubinemia. *Pediatrics* 1985;75:393-400.

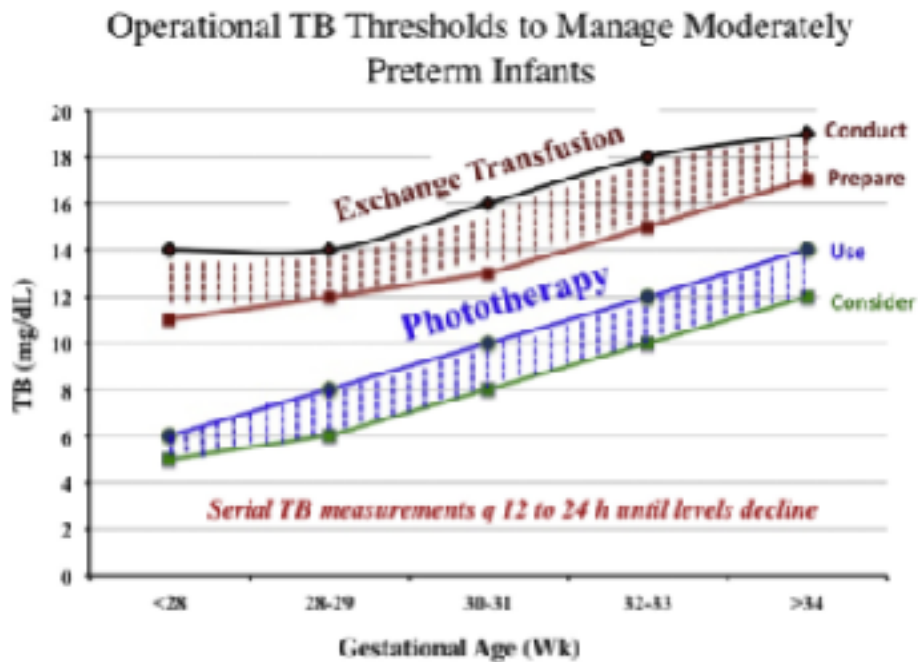


Fig.1 Suggested use of phototherapy and exchange transfusion in preterm infants less than 35 weeks GA. The operational thresholds have been demarcated by recommendations of an expert panel. The shaded bands represent the degree of uncertainty. (Adapted from Maisels MJ, Watchko JF, Bhutani VK, et al. An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation. *J Perinatol* 2012;32:660-4)

**Table 1** Suggested use of phototherapy and exchange transfusion in preterm infants <35 weeks gestational age

	<i>Phototherapy</i>	<i>Exchange transfusion</i>
<i>Gestational age (week)</i>	<i>Initiate phototherapy total serum bilirubin (mg dl<sup>-1</sup>)</i>	<i>Total serum bilirubin (mg dl<sup>-1</sup>)</i>
<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

**Table 2.** This table reflects the authors' recommendations for operational or therapeutic TSB thresholds for bilirubin levels at, or above which, treatment is likely to do more good than harm.

- Use the lower range of the listed TSB levels for infants at greater risk for bilirubin toxicity, for example, (1) lower gestational age, (2) serum albumin levels <2.5 g/dl, (3) rapidly rising TSB levels, suggesting hemolytic disease and (4) those who are clinically unstable.
- When a decision is being made about the initiation of phototherapy or exchange transfusion, infants are considered to be clinically unstable if they have one or more of the following conditions: (a) blood pH <7.15; (b) blood culture positive sepsis in the prior 24 h; (c) apnea and bradycardia requiring cardio-respiratory resuscitation (bagging and or intubation) during the previous 24 h; (d) hypotension requiring pressor treatment during the previous 24 h; and (e) mechanical ventilation at the time of blood sampling.
- Recommendations for exchange transfusion apply to infants who are receiving intensive phototherapy to the maximal surface area but whose TSB levels continue to increase to the levels listed.

- For all infants, an exchange transfusion is recommended if the infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, high pitched cry) although it is recognized that these signs rarely occur in VLBW infants.
- Use total bilirubin. Do not subtract direct-reacting or conjugated bilirubin from the total.
- Use postmenstrual age for phototherapy for example, when a 29 0/7 week infant is 7 days old, use the TSB level for 30 0/7 weeks.
- Discontinue phototherapy when TSB is 1–2 mg/dl below the initiation level for the infant's postmenstrual age. Discontinue TSB measurements when TSB is declining and phototherapy is no longer required.
- Measure the serum albumin level in all infants. Measure irradiance at regular intervals with an appropriate spectroradiometer.
- The increased mortality observed in infants  $\leq 1000$  g who are receiving phototherapy suggests that it is prudent to use less intensive levels of irradiance in these infants. In such infants, phototherapy is almost always prophylactic - it is used to prevent a further increase in the TSB and intensive phototherapy with high irradiance levels usually is not needed.
- In infants  $\leq 1000$  g, it is reasonable to start phototherapy at lower irradiance levels. If the TSB continues to rise, additional phototherapy should be provided by increasing the surface area exposed (phototherapy above and below the infant, reflecting material around the incubator).
- If the TSB, nevertheless, continues to rise, the irradiance should be increased by switching to a higher intensity setting on the device or by bringing the overhead light closer to the infant. Fluorescent and LED light sources can be brought closer to the infant, but this cannot be done with halogen or tungsten lamps because of the danger of a burn.