
Management of Hyperbilirubinemia: Review of the Revised Guidelines

The American Academy of Pediatrics (AAP) published a guideline for the management of hyperbilirubinemia in 1994. An extensive revision of this clinical practice guideline was recently published, *Management of Hyperbilirubinemia in the Newborn Infant \geq 35 Weeks of Gestation* (*Pediatrics*. 2004; 114:297-316). <http://aappolicy.aappublications.org/cgi/content/full/pediatrics;114/1/297>

Why revise the guidelines?

The primary trigger for revision of the guidelines was a disturbing increase in the incidence of kernicterus. In 2001, both the CDC and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) issued reports warning of kernicterus in previously healthy newborns.

What is Kernicterus?

Pathologically, kernicterus refers to the yellow staining and damage of the brainstem nuclei and cerebellum. Kernicterus is also used to describe the clinical effects of severe hyperbilirubinemia. These effects are more precisely described as "bilirubin encephalopathy". Acute bilirubin encephalopathy occurs in three phases. Early phase (reversible): lethargy, hypotonia, poor feeding. Intermediate phase (possibly reversible): moderate stupor, irritability, hypertonia, fever and high-pitched cry, alternating with drowsiness and hypotonia. The hypertonia is classically manifested by backward arching of the neck (retrocollis) and trunk (opisthotonos). Advanced phase (probably non-reversible): pronounced retrocollis-opisthotonos, shrill cry, no feeding, apnea, fever, deep stupor to coma, seizures, and death.

The chronic form of bilirubin encephalopathy is characterized by athetoid cerebral palsy (often severe), hearing loss, dental-enamel dysplasia, and paralysis of upward gaze. These children usually have normal intelligence.

History of the Treatment of Hyperbilirubinemia

In 1945 exchange transfusions were introduced for the treatment of Rh hemolytic disease. By 1952 the association of kernicterus with high bilirubin levels was established, with a serum bilirubin greater than 20 mg/dL considered dangerous. Treatment with phototherapy emerged in 1956 and Rhogam was developed for the treatment of Rh hemolytic disease by 1964.

Fear of Kernicterus Was Lost

By the mid-1980s to early 90s, the widespread use of Rhogam and phototherapy had virtually eradicated kernicterus. A backlash developed against "excessive and unnecessary treatment of jaundice" and "fear of bilirubin levels above 20" (termed vigintiphobia). Kernicterus was thought not to occur unless a hemolytic condition was present.

Other contributing factors during this time included changes in breastfeeding and the duration of hospitalization for newborns. Breastfeeding increased significantly, without the benefit of optimal lactation support services. Hospital stays for mothers and newborns decreased from four or more days to as short as 24 hours, resulting in discharge before the normal bilirubin peak at ~3-5 days of age.

The Return of Kernicterus

The previously mentioned factors all contributed to a re-emergence of kernicterus among term and near-term breastfed infants who had been discharged from the nursery as healthy newborns. The alerts in 2001 from the CDC and JCAHO heightened awareness of kernicterus. Parent advocacy groups, most notably "Parents of Infants and Children with Kernicterus" (www.pickonline.org), have sought to increase awareness of this problem and promote universal bilirubin screening. The National Quality Forum declared kernicterus as one of the "never events," the only pediatric condition on this list. The AAP

responded with the revised practice guideline in July, 2004.

Focus of the Revised Guideline

The overall aim of the guideline is to promote an approach that will reduce the frequency of severe neonatal hyperbilirubinemia and bilirubin encephalopathy. An additional goal was to minimize the risk of unintended harm such as increased anxiety, decreased breastfeeding, or unnecessary treatment and cost. It also emphasized that kernicterus is largely preventable if appropriate steps are taken.

Summary of AAP Recommendations

The AAP considers the following as the 10 key recommendations provided by the guideline. Clinicians should:

1. Promote and support successful breastfeeding.
2. Establish nursery protocols for the identification and evaluation of hyperbilirubinemia.
3. Measure the total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) level on infants jaundiced in the first 24 hours.
4. Recognize that visual estimation of the degree of jaundice can lead to errors, particularly in darkly pigmented infants.
5. Interpret all bilirubin levels according to the infant's age in hours.
6. Recognize that infants at less than 38 weeks' gestation, particularly those who are breastfed, are at higher risk of developing hyperbilirubinemia and require closer surveillance and monitoring.
7. Perform a systematic assessment on all infants before discharge for the risk of severe hyperbilirubinemia.
8. Provide parents with written and verbal information about newborn jaundice.
9. Provide appropriate follow-up based on the time of discharge and the risk assessment.
10. Treat newborns, when indicated, with phototherapy or exchange transfusion.

Breastfeeding

Clinicians should advise mothers to nurse their infants at least 8 to 12 times per day for the first several days. The AAP recommends against routine supplementation of non-dehydrated breastfed infants with water or dextrose water.

Blood Typing

All pregnant women should be tested for ABO and Rh (D) blood types and have a serum screen for unusual isoimmune antibodies. If a mother has not had prenatal blood grouping or is Rh-negative, a direct antibody test (Coombs' test), blood type, and an Rh (D)

type on the infant's (cord) blood are strongly recommended.

If the maternal blood is group O, Rh-positive, it is an option to test the cord blood for the infant's blood type and direct antibody test, but it is not required provided that there is appropriate surveillance, risk assessment before discharge, and follow-up.

Clinical Assessment

Clinicians should ensure that all infants are routinely monitored for the development of jaundice, and nurseries should have established protocols for the assessment of jaundice. Jaundice should be assessed whenever the infant's vital signs are measured but no less than every 8 to 12 hours. Protocols should include the circumstances in which nursing staff can routinely obtain a transcutaneous bilirubin (TcB) level or order a total serum bilirubin (TSB) measurement. Visual estimation of the bilirubin level from the degree of jaundice should be recognized as unreliable, especially in darkly pigmented infants.

Laboratory Evaluation

A TcB and/or TSB measurement should be performed on every infant who is jaundiced in the first 24 hours after birth. The need for and timing of a repeat TcB or TSB measurement will depend on the zone in which the TSB falls, the age of the infant, and the evolution of the hyperbilirubinemia. All bilirubin levels should be interpreted according to the infant's age in hours.

Causes of Jaundice

The possible cause of jaundice should be sought in an infant receiving treatment or whose TSB is rising rapidly without obvious explanation. Measurement of glucose-6-phosphate dehydrogenase (G6PD) level is recommended in infants receiving phototherapy whose family history, ethnic background or geographic origins suggest a risk of G6PD deficiency. It should also be considered in any infant with a poor response to phototherapy. G6PD deficiency has been reported to present in one third of infants with kernicterus.

Risk Assessment Before Discharge

Before discharge, every newborn should be assessed for the risk of developing severe hyperbilirubinemia, and all nurseries should establish protocols for assessing this risk. Such assessment is particularly important in infants who are discharged before the age of 72 hours.

The AAP recommends 2 clinical options used individually or in combination for the systematic assessment of risk: predischarge measurement of the bilirubin level using TSB or TcB and/or assessment of clinical risk factors. Whether either or both options are used, appropriate follow-up after discharge is essential.

Parent Information

Hospitals should provide both written and verbal information on jaundice to parents prior to discharge. Examples in English, Spanish, Chinese, and Italian are available from the AAP at <http://www.aap.org/family/jaundicefeature.htm>

Follow-up

Follow-up should, in general, be scheduled for approximately 48 hours after discharge. The goal is to have the infant evaluated during the time period when the bilirubin level should be at its peak, which is generally at 3 to 5 days of age. Lack of early post-discharge follow-up has been a common finding in infants with kernicterus.

Treatment

Treatment thresholds depend on TSB, gestational age, and risk factors such as hemolytic disease, asphyxia, G6PD, lethargy, temperature instability, sepsis, acidosis, or albumin level < 3 gm/dL.

If a hemolytic process is occurring, intravenous immunoglobulin (0.5-1 gram/kg over 2 hours) may be a valuable supplementary treatment.

Immediate exchange transfusion is recommended in any infant who demonstrates intermediate or advanced bilirubin encephalopathy, even if the TSB is falling.

Implementation Strategies

A systematic approach is recommended, including:

1. Establishment of standing protocols for nursery assessment of jaundice, including testing TcB and TSB levels without requiring a physician order.
2. Checklists or reminders associated with risk factors, age at discharge, and laboratory test results that provide guidance for appropriate follow-up.
3. Explicit educational materials for parents.

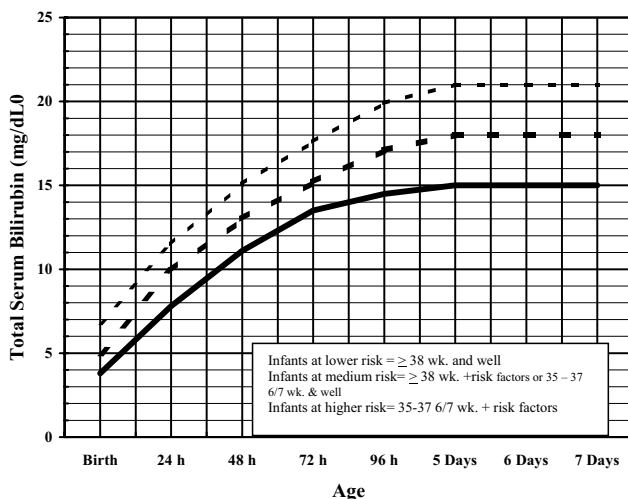
Conclusion

Kernicterus is cause of severe brain injury. With the systematic approach described in these guidelines, emphasizing universal assessment of risk factors, appropriate screening and treatment and timely post-discharge follow-up, kernicterus should be largely preventable.

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Phototherapy Guidelines for Infants ≥ 35 wks Gestation



*The risk factors listed above are conditions that might affect the likelihood of brain damage at different bilirubin levels. These factors increase the risk of brain damage because of their negative effects on albumin binding of bilirubin, the integrity of the blood brain barrier, and the susceptibility of the brain cells to damage by bilirubin.

- Guidelines refer to use of intensive phototherapy.
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- Risk factors* = isoimmune hemolytic disease, G6PD deficiency, asphyxia, respiratory distress, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0 g/dL (if measured)
- For well infants 35-36 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 wks.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL below those shown but home phototherapy should not be used in any infant with risk factors.