



Kernicterus and the healthy term newborn

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The evaluation and management of the jaundiced term newborn has changed significantly over the past several years and continues to present a challenge for practitioners, who must balance the risk of bilirubin toxicity leading to kernicterus, with the risk of over-investigating and treating healthy infants. Recent reports of increasing kernicterus have led to further discussion regarding the level of bilirubin considered detrimental to the otherwise healthy term neonate, whose jaundice is not attributable to hemolysis.

Sixty percent of term infants will become clinically jaundiced in the first week of life, with a higher incidence occurring in breastfed infants. Most neonatal jaundice is physiologic, occurring as the result of accelerated red blood cell breakdown, transient immaturity of the hepatic enzyme systems and increased enterohepatic circulation. Following extensive reviews, Newman & Maisels (1992) concluded that healthy term newborns with physiologic jaundice have a low risk of bilirubin toxicity. Based on these findings they recommended a less aggressive approach in managing these infants. Guidelines from the Fetus and Newborn Committee of the Canadian Paediatric Society (1999) and the American Academy of Pediatrics (1994) for the initiation of phototherapy in the healthy, term infant support this approach.

Traditional guidelines for the evaluation and management of the jaundiced newborn were based on a population of infants who spent 3–5 days in hospital and were predominantly formula fed. Significant jaundice was almost always recognized and treated before discharge. Today, with shortened hospital stays of 24–48 hours and the increased rate of breastfeeding, bilirubin levels peak after discharge. Several reviews of early hospital discharge programs have found an increase in readmission of infants to hospital primarily for dehydration and jaundice requiring phototherapy. Of great concern are reports that cases of kernicterus are increasing. It is therefore important to consider identification of infants at risk, appropriate treatment and adequate follow-up.

RESOURCES



Kernicterus and bilirubin encephalopathy

Kernicterus describes the neuropathologic changes resulting from deposits of unconjugated bilirubin in the basal ganglia nuclei. This is identified at autopsy by deep yellow staining of this region, and clinically, by severe disabling brain damage or death. Kernicterus is preventable. Although hyperbilirubinemia is common, extreme hyperbilirubinemia resulting in kernicterus is rare (Joint Commission on Accreditation of Healthcare Organizations (JCAHO), 2001). The bilirubin concentration causing kernicterus varies depending on the brain's vulnerability to bilirubin's neurotoxic effects. Predisposing factors for the development of kernicterus include acidosis, prematurity, hypoglycemia, sepsis and ethnicity.

Bilirubin encephalopathy is the clinical manifestation of the effects of bilirubin on the central nervous system. Symptoms of encephalopathy include lethargy, irritability, weak suck and hypertonia. With early recognition and intervention, bilirubin encephalopathy may be reversible (Reiser, 2001). Symptoms of kernicterus include opisthotonos, hypotonia and seizures. When these symptoms are apparent, permanent brain damage has already occurred. Long-term sequelae include hearing and speech deficits, motor and perceptual function deficits, delayed motor development, athetoid cerebral palsy, dental dysplasia, sensorineural hearing loss, and ataxia (Fetus and Newborn Committee, 1999; Reiser, 2001).

There have been approximately 90 cases of kernicterus reported in the USA from 1984 to 2001. Three of the newborns died and all others sustained brain damage. For these cases, risk assessments were reported to be inadequate and unreliable, and bilirubin levels were either not measured, or not measured in a timely manner (JCAHO, 2001). Table 1 summarizes the factors related to non-identification of recent cases of kernicterus in the USA.

Risk factors

Risk factors for recent cases of severe hyperbilirubinemia included:

- jaundice appearing in the first 24 hours after birth;
- inadequate nutrition/hydration through sub-optimal breastfeeding;
- near-term newborns (35–37 weeks) particularly if they were breastfed;
- birth weight less than 2500 g;
- bruising and cephalohematomas;
- hemolysis due to maternal isoimmunization, glucose-6-phosphate dehydrogenase deficiency, spherocytosis or other causes;
- genetic or ethnic risk factors in East Asian or Mediterranean descent, including siblings with jaundice;
- clinical symptoms suggestive of sepsis/metabolic disorder;
- need for resuscitation at birth.

(Dennery, Seidman & Stevenson, 2001).



Kernicterus and the healthy term newborn (continued)

Evaluation of jaundice

The first step in evaluating the jaundiced newborn is to determine whether the jaundice is physiologic or pathologic. Physiologic jaundice is a diagnosis of exclusion. The infant with risk factors for pathologic jaundice must be identified prior to discharge. Any infant who becomes jaundiced in the first 24 hours of life should be thoroughly assessed because the cause is likely pathologic. The peak total serum bilirubin level alone is an insufficient measure of bilirubin's toxic potential (Reiser, 2001). For infants with prolonged jaundice (lasting longer than seven days) or with conjugated hyperbilirubinemia (greater than 30 $\mu\text{mol/L}$), additional investigation and management (Table 2) may be required.

Management

It is important to establish a management plan that will minimize the risk of kernicterus in all term infants. Over 80% of newborns with conjugated bilirubin levels greater than 20 $\mu\text{mol/L}$ in the first four days of life are breastfed. This is likely related to a combination of decreased caloric intake and active enterohepatic circulation. Supplementing with water or dextrose solutions does not lower the bilirubin level in jaundiced, healthy breastfed infants. More frequent breastfeeding during the first few days of life has been associated with lower bilirubin levels.

It is important to ensure detailed assessment of latch, position, suck, swallow and mother's milk supply while in hospital and in the community. If the milk supply is adequate and the infant is latched appropriately, then increasing the frequency of breastfeeding (i.e., 10–12 times every 24 hours) and close monitoring of the infant may be sufficient. A weight loss of 7% is average for breastfed infants, but when this occurs in the first 72 hours of life, the clinician should be alert to breastfeeding problems and review the process. A weight loss of 10% is maximum for the breastfed infant (Lawrence and Lawrence, 1999). Parents must be aware of the signs of ineffective breastfeeding (Table 3) and when to seek help.

Signs of dehydration include: weight loss greater than 10%, decreased skin turgor, flat or sunken fontanelle, dry to parched mucous membranes, increased tachycardia, irritability, lethargy and decreased voiding or stools (Hazinski, 1992; Roberts, 2001). If dehydration is confirmed, supplementation is required to ensure adequate rehydration.

The Fetus and Newborn Committee of the Canadian Paediatric Society's guidelines for phototherapy in healthy term infants and in those with risk factors (Figure 1) are more conservative than the current American Academy of Pediatrics' guidelines (1994). "If the infant is a healthy term newborn, phototherapy should be started as indicated in the upper curve of the figure. If the infant has one or more risk factors, a clinical decision should be made to initiate phototherapy at the concentration indicated by the lower curve" (Fetus and Newborn Committee, 1991, p. 3).



If phototherapy fails to control the rising bilirubin levels, exchange transfusion is indicated to lower serum bilirubin concentrations.

Risk reduction strategies

Implementing the following strategies will help to decrease the incidence of kernicterus in healthy term newborns:

- evaluate all cases of jaundice appearing in the first 24 hours;
- assess maternal and infant blood types;
- develop policies for assessing the risk of severe hyperbilirubinemia in all infants (by history, clinical evaluation and, if necessary, laboratory measurement);
- develop detailed treatment strategies for specific levels of bilirubin at different ages (e.g., Canadian Paediatric Society's practice guidelines);
- allow early discharge (< 48 hours) only if a healthy status is confirmed for each baby and appropriate follow-up is provided within 24–48 hours;
- provide appropriate parental education about feeding, signs of dehydration and jaundice, and give the parents a handout to take home with the same information;
- ensure testing for serum bilirubin concentration is readily available for newborns on an outpatient basis;
- provide breastfeeding support before and after discharge from hospital, encourage frequent feeding, good latch and positioning, and assessment of maternal milk supply;
- provide adequate equipment (bilirubin lights and blankets, non-invasive transcutaneous bilirubin measurement device or lab services for timely total serum bilirubin testing);
- encourage families to accept the public health home visits, where available;
- consider checking bilirubin at least once before early discharge using a transcutaneous bilirubin measuring device or serum bilirubin levels;

(Adapted from Fetus and Newborn Committee, 1999; JCAHO, 2001)

Conclusion

Recent reports of kernicterus are an important reminder that hyperbilirubinemia in the healthy, term infant has the potential to cause bilirubin encephalopathy. To ensure optimal management of jaundice in otherwise healthy term infants, neonatal caregivers must recognize the risk factors for kernicterus, review current patient care processes with regard to the identification and management of hyperbilirubinemia in newborns, and identify strategies for risk reduction that could enhance the effectiveness of these processes. The devastating effects of kernicterus are preventable. All health care providers should ensure that appropriate screening and intervention occurs in a timely manner.

References

American Academy of Pediatrics. Management of hyperbilirubinemia in the healthy term newborn. *Pediatrics* 1994; 94(4 Pt 1): 558-65. www.aap.org/policy/hyperb.htm



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Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. *N Engl J Med* 2001; 344(8): 581-90.

Fetus and Newborn Committee of the Canadian Paediatric Society. Approach to the management of hyperbilirubinemia in term newborn infants. A joint statement with the College of Family Physicians of Canada. *Paediatr Child Health* 1999; 4(2): 161-4 (reaffirmed February 2001). Ottawa, ON: Canadian Paediatric Society. www.cps.ca/english/statements/FN/fn98-02.htm

Hazinski MF. *Nursing care of the critically ill child*. St. Louis: Mosby, 1992.

International Lactation Consultant Association. *Evidence-based guidelines for breastfeeding management during the first fourteen days*. United States Maternal-Child Health Bureau, 1999.

Joint Commission on Accreditation of Healthcare Organizations. Kernicterus threatens healthy newborns. *Sentinel Event Alert* 2001; 18. www.jcaho.org/search_frm.html

Lawrence RA, Lawrence RM. *Breastfeeding: A guide for the medical profession (5th ed.)*. St. Louis: Mosby Book Company 1999.

Newman TB, Maisels MJ. Evaluation and treatment of jaundice in the term newborn: A kinder, gentler approach. *Pediatrics* 1992; 89(5 Pt 1): 809-18.

Reiser D. Hyperbilirubinemia: Exploring neonatal conditions related to bilirubin production. *AWHONN Lifelines* 2001; 5(3): 55-61.

Roberts K. Fluid and electrolyte regulation. In: Curley M, Moloney-Harmon P (eds.). *Critical care nursing of infants and children*. Philadelphia: W.B. Saunders Company, 2001.

RESOURCES

Table 1: Factors related to non-identification of recent kernicterus cases

1. Newborn assessment:
 - unreliability of visual assessment of jaundice in newborns with dark skin
 - failure to recognize jaundice in an infant, or its severity (based on visual assessment, and measure of bilirubin level before the infant's discharge from the hospital or during a follow-up visit)
 - failure to measure the bilirubin level in an infant who is jaundiced in the first 24 hours
2. Continuum of care:
 - early discharge (before 48 hours) with no follow-up within 1–2 days of discharge (this is particularly important for infants less than 38 weeks' gestation)
 - failure to provide early follow-up with physical assessment for infants who are jaundiced before discharge
 - failure to provide ongoing lactation support to ensure adequacy of intake for breastfed newborns
3. Parent and family education:
 - failure to provide appropriate information to parents about jaundice and failure to respond appropriately to parental concerns about a jaundiced newborn, poor feeding, lactation difficulties and change in newborn behavior and activity
4. Treatment:
 - failure to recognize, address or treat rapidly rising bilirubin
 - failure to aggressively treat severe hyperbilirubinemia in a timely manner with intensive phototherapy or exchange transfusion

(JCAHO, 2001)

**Table 2: Laboratory investigation for hyperbilirubinemia in term newborns**

Indicated (if bilirubin concentrations reach phototherapy levels)

- serum bilirubin total and direct

Optional (in specific clinical circumstances)

- direct Coombs test (use cord blood if available)
- complete blood count
- blood smear for red cell morphology
- reticulocyte count
- Glucose-6-phosphate dehydrogenase screen
- serum electrolytes and albumin or protein concentrations

Adapted from Fetus and Newborn Committee, 1999.

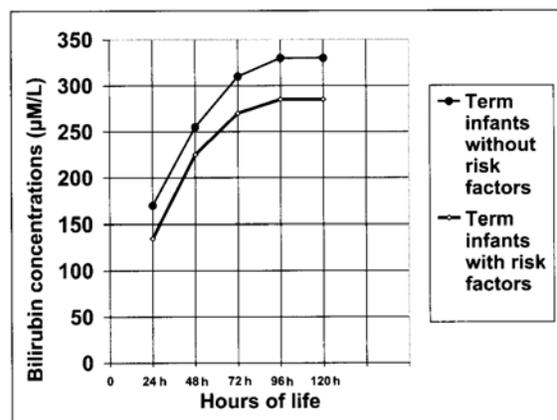
Table 3: Signs of ineffective breastfeeding

- ✓ infant weight loss greater than 7%
- ✓ continued weight loss after day 3
- ✓ less than 3 bowel movements in 24 hours
- ✓ meconium stools after day 4
- ✓ irritability, restlessness, sleepy or refusal to feed
- ✓ no audible swallowing during feedings
- ✓ no change in weight or size of breasts and no change in milk volume and composition by 3-5 days
- ✓ persistent or increasingly painful nipples
- ✓ engorgement unrelieved by feeding
- ✓ does not begin to gain weight by day 5
- ✓ does not return to birthweight by day 14

(International Lactation Consultant Association, 1999, p. 11)

Figure 1: Guidelines for initiation of phototherapy for hyperbilirubinemia in term infants with and without risk factors. Some risk factors include gestational age younger than 37 weeks, birth weight less than 2500 g, hemolysis, jaundice at younger than 24 h of age, sepsis and the need for resuscitation at birth.

(CPS, 1999, reaffirmed 2001)





Kernicterus and the healthy term newborn (continued)

Quiz

1. **The percentage of term infants clinically jaundiced in the first week of life is:**
 - a) 20%
 - b) 30%
 - c) 40%
 - d) 50%
 - e) 60%

2. **Important risk factors for severe hyperbilirubinemia are:**
 - a) Jaundice appearing in the first 24 hours of life
 - b) Near-term newborns (35-37 weeks)
 - c) Hemolysis secondary to maternal isoimmunization
 - d) Glucose-6-phosphate dehydrogenase deficiency
 - e) All of the above

3. **The maximum amount of weight loss permitted in breastfed babies is:**
 - a) 5%
 - b) 7%
 - c) 10%
 - d) 15%

4. **Laboratory investigations recommended in newborns with severe hyperbilirubinemia include:**
 - a) Blood group and Coomb's test
 - b) Complete blood count, smear and reticulocyte count
 - c) Glucose-6-phosphate dehydrogenase screen
 - d) Serum protein, albumin and electrolytes
 - e) All of the above

5. **All newborns have the same risk of hyperbilirubinemia secondary to G6PD deficiency:**
 - a) True
 - b) False

6. **Signs of inadequate breastfeeding include:**
 - a) Weight loss greater than 7%
 - b) Persistence of meconium stools beyond four days of age
 - c) Failure to gain weight by five days of age
 - d) Failure to regain birthweight by 14 days of age
 - e) All of the above

7. **Newborns discharged early from hospital need to be reassessed by an experienced health-care provider within:**
 - a) 48 hours after discharge
 - b) 72-96 hours after discharge
 - c) 7 days after discharge

Answers:
1-e, 2-e, 3-c, 4-e, 5-b, 6-e, 7-a

RESOURCES