

### RPPC Annotated Bibliography

**Bhutani, V.K. & Johnson, L.H. (2004).** *Urgent Clinical Need for Accurate and Precise Bilirubin Measurements in the United States to Prevent Kernicterus.* *Clinical Chemistry*, 50 (3): 1-4.

Kernicterus, a preventable brain injury resulting from severe neonatal jaundice has reemerged. Severe hyperbilirubinemia may be treated with phototherapy during the hospital stay, but some newborns discharged as healthy have developed severe hyperbilirubinemia after discharge and succumbed to serious sequelae. Implementation of preventive solutions is dependent on accurate, precise, and universally available measures of hyperbilirubinemia. Care of the vulnerable and sick infant could be optimized by better techniques to assess neurotoxic potential of bilirubin, such as measures of bilirubin-binding reserve of albumin.

**Bhutani, V.K., Johnson, L.H., & Keren, R. (2004).** *Diagnosis and management of hyperbilirubinemia in the term neonate: for a safer first week.* *Pediatric Clinics of North America*, 51: 843-861.

Newborn jaundice due to severe hyperbilirubinemia, with its potential for producing brain damage remains a continuing problem in the United States. Kernicterus and its subsequent neurologic consequences are re-emerging due to the lack of concern regarding an otherwise benign process of newborn jaundice. Recent reports have demonstrated that visual assessment of jaundice is unreliable and unsafe as an indicator to initiate further testing. Several predischarge screening strategies have been suggested as ways to identify an at-risk group of infants to be followed more closely. These safety recommendations are amenable to a system-based approach in which babies who are most likely have a benign experience with jaundice are identified early from those in which newborn jaundice is a potentially unsafe condition. Structural practice changes that would facilitate a system-based approach include: predischarge bilirubin management, follow-up bilirubin management and lactation support and nutritional management.

**Chou, S., Palmer, H., Ezhuthachan, S., Newman, C., Pradell-Boyd, B., Maisels, M.J. & Testa, M. (2003).** *Management of Hyperbilirubinemia in Newborns: Measuring Performance by Using a Benchmarking Model.* *Pediatrics*, 112 (6): 1264-1273.

Purpose: To provide standards for evaluation performance in prevention of serious newborn hyperbilirubinemia.

Results: Hospitals with access to newborns' inpatient and post discharge data can use the benchmarking model to compare their management of hyperbilirubinemia with a reference population that received rigorous care.

**Dennery, P.A., Seidman, D.S. & Stevenson, D.K. (2001).** *Neonatal Hyperbilirubinemia.* *The New England Journal of Medicine*, 344 (8): 581-590.

Earlier studies suggested that kernicterus from jaundice was rare and that too many infants were being treated unnecessarily. Newborn infants were being discharged from the hospital sooner after birth thus limiting the ability of physicians to detect jaundice during the period when serum bilirubin concentration is likely to rise. Physicians became less likely to treat jaundice in newborns which in turn led to an increase in reports of kernicterus. Changes in practice have since stimulated the development of new approaches to the prevention, detection and treatment of hyperbilirubinemia.

**Gartner, L. (2001). *Breastfeeding and Jaundice*. *Journal of Perinatology*, 21: S25-S29.**

Prolongation of unconjugated hyperbilirubinemia into the third and later weeks of life in the breastfed healthy newborn is a normal and regularly occurring extension of physiologic jaundice known as breastmilk jaundice. Breastfeeding jaundice occurs when insufficient caloric intake resulting from breastfeeding difficulties increases serum unconjugated bilirubin concentrations. Optimal breastfeeding practices resulting in minimal initial weight loss and early onset of weight gain are associated with both reduced breastfeeding jaundice and minimization of the intensity of breastmilk jaundice.

**Gartner, L., & Herschel, M. (2001). *Jaundice and Breastfeeding*. *Pediatric Clinics of North America*, 48 (2).**

Preventing toxicity from excessive jaundice and protecting and ensuring successful breastfeeding require an understanding of the normal and abnormal patterns and mechanisms of jaundice in the newborn period, particularly the mechanisms related to breastfeeding and human milk ingestion. Exaggerated jaundice can be a warning sign that breastfeeding is not going well for the infant and for entire populations of newborns. Optimal breastfeeding minimizes these exaggerations.

**Gartner, L., Herrarias, C.T. & Sebring, R.H. (1998). *Practice Patterns in Neonatal Hyperbilirubinemia*. *Pediatrics*, 101 (1): 25-31.**

Purpose: To determine practice patterns of office-based pediatricians and neonatologists in the treatment of neonatal hyperbilirubinemia in healthy, term newborns during 1992 before the publication of practice guideline for treatment of neonatal jaundice by the AAP.

Results: There was a tendency for neonatologists to initiate both phototherapy and exchange transfusions at lower serum bilirubin concentrations than office-based general pediatricians. Only a small percentage of both pediatricians and neonatologists indicated they would interrupt breastfeeding at 8-13 mg/dL. Physicians with the fewest years in practice (5 years or less) differed greatly in initiating exchange transfusions at higher serum bilirubin concentrations.

**Gourley, G.R. (2002). *Breastfeeding, neonatal jaundice and kernicterus*. *Seminars in Neonatology*, 7: 135-141.**

Despite the many advantages of breastfeeding, there is documentation of the strong association between breastfeeding and an increase in the risk of neonatal hyperbilirubinemia. Breast-fed infants have higher bilirubin levels than formula-fed infants. Suggested mechanisms for these findings include poor fluid and caloric intake, inhibition of hepatic excretion of bilirubin, and intestinal absorption of bilirubin. Appropriate support and advice must be provided to the lactating mother so that successful breastfeeding can be established and the risk of severe hyperbilirubinemia reduced.

**Harris, M.C., Bernbaum, J.C., Polin, J.R., Zimmerman, R. & Polin, R.A. (2001).** *Developmental Follow-Up of Breastfed Term and Near-Term Infants with Marked Hyperbilirubinemia. Pediatrics, 107 (5): 1075-1081.*

Purpose: To identify all infants > 36 weeks gestational age with bilirubin levels > 25 mg/dL and evaluate them for early and late evidence of bilirubin brain injury.

Results: Transient neurologic abnormalities were observed in 5 of the 6 infants readmitted to the hospital during the first week of life with marked hyperbilirubinemia. The abnormalities resolved with aggressive management using hydration, phototherapy, and exchange transfusion. Less aggressive therapy may be associated with residual neurologic abnormalities. Inadequate establishment of breastfeeding coupled with early discharge practices may play a role in the development of marked hyperbilirubinemia in these infants.

**International Lactation Consultant Association. (1999).** *Evidence-Based Guidelines for Breastfeeding Management during the First Fourteen Days. Funded by a contract from the US Maternal-Child Health Bureau, April.*

Management strategies presented include both clinical and educational components. To effectively facilitate breastfeeding, the health care professional must determine an appropriate clinical strategy and discern the mother's need for specific information relative to its implementation. Often, commonly held beliefs and misconceptions need to be addressed before an appropriate clinical strategy can be implemented.

**Johnson, L.H., Bhutani, V.K. & Brown, A.K. (2002).** *System-based approach to management of neonatal jaundice and prevention of kernicterus. Journal of Pediatrics, 140 (4).*

Analysis of 90 cases enrolled in the Pilot Kernicterus Registry for Term (37 weeks) and Near-Term (35-36 weeks) infants discharged as healthy. The focus of the analysis was on the 61 infants who required hospital readmission and/or medical intervention during the first postnatal week. The analysis was structured to evaluate the data available in hospital charts, reports from colleagues, and medical legal records for possible oversights in pre and post discharge care that may have contributed to CNS damage. The data reported suggest opportunities and protocols for a system-based approach to management that would minimize the potential for lapses in care and the risk for kernicterus.

**Madden, J.M., Soumerai, S.B., Lieu, T.A. Mandl, K.D., Zhang, F., & Ross-Degnan, D. (2004). Length-of-Stay Policies and Ascertainment of Post-discharge Problems in Newborns. *Pediatrics*, 113 (1): 42-49.**

Purpose: Evaluate the effects of an early postpartum discharge program and a subsequent legislative mandate for 48 hours of hospital coverage on incidence of newborn jaundice and feeding problems.

Results: Jaundice diagnoses were 8% of newborns during the baseline, then rose to 11% throughout the program and post mandate periods. Bilirubin testing rose by 3.4% and the proportion of tested newborns with results calling for consideration of phototherapy rose by 6%. Phototherapy use also rose from 1.8% to 2.4% of newborns. Feeding problem diagnoses doubled. Re-hospitalizations for jaundice were constant and ER visits dropped from .3% of newborns to 0. Sudden increases in jaundice-related measures and identification of infant feeding problems were not associated with changes in length of stay. These increases seem to be the results of more frequent evaluation of newborns during the critical day 3 to 4 period and may also have been elevated by a new climate of concern about neonatal vulnerability.

**Maisels, M.J. & Watchko, J.F. (2003). *Treatment of Jaundice in Low Birth weight Infants. Arch Dis Child Fetal Neonatal Ed*, 88: F459-F463.**

Exchange transfusion and phototherapy remain the staples of intervention for the jaundiced newborn. Clinical management of the jaundiced low birth weight infant is discussed.

**MMWR Weekly (2001). *Kernicterus in Full-Term Infants --- United States, 1994-1998. June 15, 2001/ 50 (23): 491- 494.***

Kernicterus is not a reportable condition in the United States, and its prevalence is unknown; however, a pilot registry at a Pennsylvania hospital documented 90 cases in 21 states from 1984 to June 2001. This report summarizes case histories of four full-term, healthy infants who developed kernicterus and underscores that to prevent kernicterus, newborns must be screened and promptly treated for hyperbilirubinemia.

**Oh, W., Tyson, J., Fanaroff, A., Bohr, B., Perritt, R., Stoll, B., Ehrenkranz, R., Carlo, W., Shankaran, S., Poole, K. & Wright, K. (2003). Association between Peak Serum Bilirubin and Neurodevelopmental Outcomes in Extremely Low Birth Weight Infants. *Pediatrics*, 112: 773-779.**

Purpose: To assess the association between peak total serum bilirubin (PSB) levels during the first 2 weeks of life and neurodevelopmental outcomes of extremely low birth weight infants at 18-22 months' age.

Results: PSB concentrations during the first 2 weeks of life are directly correlated with death or neurodevelopmental impairment, hearing impairment, and Psychomotor Development Index < 70 in extremely low birth weight babies.

**Porter, M.D. & Beth, D.L. (2002). *Hyperbilirubinemia in the Term Newborn. American Family Physician, 65 (4).***

Hyperbilirubinemia is one of the most common problems encountered in term newborns. Recommendations support the use of less intensive therapy in healthy term newborns with jaundice. Phototherapy should be instituted when the total serum bilirubin level is at or above 15 mg/dL in infants 25-48 hours old. Jaundice is considered pathologic if it presents within the first 24 hours after birth, the total serum bilirubin level rises by more than 5 mg/dL per day or is higher than 17 mg/dL, or an infant has signs and symptoms suggestive of serious illness. The management goals are to exclude pathologic causes of hyperbilirubinemia and initiate treatment to prevent bilirubin neurotoxicity.

**Steffensrud, S. (2004). *Hyperbilirubinemia in Term and near-Term Infants: Kernicterus on the Rise? Newborn and Infant Nursing Reviews, 4 (4): 191-200.***

Jaundice in term and near-term infants is generally benign, however, concern has surfaced in recent years regarding reemergence of kernicterus in this patient population. An increasing number of litigation cases centering on kernicterus have arisen and increasingly apparent is the fact that otherwise healthy newborn infants may be at risk for this potentially devastating neurologic condition. An understanding of the historical perspective, bilirubin physiology, etiologies, clinical symptoms, potential sequale, evaluation, treatment and prevention is important to minimize the occurrence of kernicterus.

**Suresh, G.K. & Clark, Robin (2004). *Cost-Effectiveness of Strategies That Are Intended to Prevent Kernicterus in Newborn Infants. Pediatrics, 114 (4): 917-924.***

Purpose: To determine the direct costs to prevent a case of kernicterus using 3 strategies: (1) universal follow-up in the office or at home within 1-2 days of early newborn discharge, (2) routine pre-discharge serum bilirubin with selective follow-up and laboratory testing, and (3) routine pre-discharge transcutaneous bilirubin with selective follow-up and laboratory testing. Results: The cost to prevent 1 case of kernicterus was \$10,321,463, \$5,743,905, and \$9,191,352 respectively for strategies 1, 2, and 3. The cost per case depended on the population incidence of kernicterus and the relative risk reduction of each strategy. If the incidence of kernicterus and the relative risk reduction is high, annual cost savings of \$46,179,465 would result with strategy 2. If the incidence or risk is lower, then the cost per case prevented ranged from \$4,145,676 to as high as \$77,650,240.

**Wang, M.L., Dorer, D.J., Fleming, M.P. & Catlin, E.A. (2004). *Clinical Outcomes of Near-Term Infants. Pediatrics, 114: 372-376.***

Purpose: To test the hypothesis that near-term infants have more medical problems after birth than full-term infants and that hospital stays might be prolonged and costs increased. Results: Near-term infants had significantly more medical problems and increased hospital costs compared with full-term infants in rates of temperature instability, hypoglycemia, respiratory distress, and jaundice. Near-term infants were evaluated for possible sepsis more frequently than full-term infants and more often received intravenous infusions. Cost analysis revealed a relative increase in total costs for near-term infants resulting in a cost difference of \$2630 (mean) and \$429 (median) per near-term infant. Near-term infants may represent and unrecognized at-risk neonatal population.

**Watchko, J.F. & Maisels, M.J. (2003). *Jaundice in low birth weight infants: pathobiology and outcome. Archives of Disease in Childhood Fetal and Neonatal Edition, Vol. 88.***

Jaundice in preterm, as well as full term, infants results from an increased bilirubin load in the hepatocyte, decreased hepatic uptake of bilirubin from the plasma and defective bilirubin conjugation. Hyperbilirubinemia in preterm infants is more prevalent, more severe, and its course more protracted than in term neonates.

**Wight, N. (2003). *Breastfeeding the Borderline (Near-Term) Preterm Infant. Pediatric Annals, 32 (5): 329-336.***

Breastfeeding the near-term infant can be successful. It is important that health care providers understand and recognize the special physical and developmental needs of near-term infants and their mothers in establishing and maintaining breastfeeding. Most common problems encountered when breastfeeding the near-term infant can be prevented and responded to appropriately.