U.S. Preventive Services Task Force

# Screening of Infants for Hyperbilirubinemia to Prevent Chronic Bilirubin Encephalopathy: Recommendation Statement

▶ See related Putting Prevention into Practice on page 411.

▶ See related editorial on page 336 and Tips from Other Journals starting on page 426.

This summary is one in a series excerpted from the Recommendation Statements released by the U.S. Preventive Services Task Force (USPSTF). These statements address preventive health services for use in primary care clinical settings, including screening tests, counseling, and preventive medications.

EB CME

This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 353.

A collection of USPSTF recommendation statements reprinted in *AFP* is available at http://www.aafp.org/afp/uspstf.

The complete version of this statement, including supporting scientific evidence, evidence tables, grading system, members of the USPSTF at the time this recommendation was finalized, and references, is available on the USPSTF Web site at http://www.ahrq.gov/clinic/uspstf/uspshyperb.htm.

## Summary of Recommendation and Evidence

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend screening infants for hyperbilirubinemia to prevent chronic bilirubin encephalopathy *(Table 1)*. **I statement.**

## Rationale

***Importance.*** *The exact incidence of chronic bilirubin encephalopathy is not known but is believed to be very low; in one study, 90 cases were documented in term and near-term infants in 21 states over 17 years.*[1] *In a recent prospective study in the United Kingdom and Ireland, the incidence of chronic bilirubin encephalopathy was estimated at 0.9 per 100,000 live births.*[2] *Efforts have been made by physicians to eliminate this rare but devastating condition by instituting system-level measures to screen for hyperbilirubinemia and by aggressively managing high bilirubin levels.*

***Detection.*** *There is adequate evidence that screening using risk factors and/or hour-specific bilirubin measurement can identify infants at risk of developing hyperbilirubinemia. However, not all children with chronic bilirubin encephalopathy have a history of hyperbilirubinemia, and there is no known screening test that will reliably identify all infants who are at risk of developing chronic bilirubin encephalopathy.*

***Benefits of detection and early intervention.*** *Early treatment can decrease the number of infants with elevated serum bilirubin levels. However, the USPSTF found inadequate evidence that treating elevated bilirubin levels in term or near-term infants to prevent severe hyperbilirubinemia resulted in the prevention of chronic bilirubin encephalopathy.*

***Harms of detection and early treatment.*** *Hyperbilirubinemia is commonly treated with phototherapy, and severe hyperbilirubinemia may be treated with exchange blood transfusion. The USPSTF found inadequate evidence regarding the harms of phototherapy. Potential harms of phototherapy include weight loss, gastrointestinal problems, interruption of breastfeeding and disruption of the maternal-infant relationship, and possible growth of melanocytic nevi. Significant morbidity (e.g., apnea, bradycardia, cyanosis, vasospasm, thrombosis, necrotizing enterocolitis) occurs in as many as 5 percent of patients who undergo exchange transfusion.*[3]

***USPSTF assessment.*** *The USPSTF concludes that evidence about the benefits and harms of screening is lacking. Therefore, the USPSTF could not determine the balance of benefits and harms of screening newborn infants to prevent chronic bilirubin encephalopathy.*

## Clinical Considerations

• **Considerations for practice when evidence is insufficient.** *Potential preventable burden:* Severe neonatal hyperbilirubinemia is associated with kernicterus, the yellow staining of specific areas of brain tissue in the neonate caused by accumulation of unconjugated bilirubin. Chronic bilirubin encephalopathy describes the clinical neurologic sequelae associated with severe hyperbilirubinemia, including choreoathetoid cerebral palsy, sensorineural hearing loss, gaze paresis, and intellectual deficits. However, hyperbilirubinemia alone is not sufficient to account for these neurologic findings. Infants with extremely high levels of serum bilirubin but no apparent sequelae have been reported, and infants without

**Table 1. Screening of Infants for Hyperbilirubinemia to Prevent Chronic Bilirubin Encephalopathy: Clinical Summary of the USPSTF Recommendation**

| | |
|---|---|
| Population | Healthy term or near-term infants at least 35 weeks' gestation |
| Recommendation | No recommendation because of insufficient evidence<br>I statement: insufficient evidence |
| Risk assessment | Risk factors for hyperbilirubinemia include family history of neonatal jaundice, exclusive breastfeeding, bruising, cephalohematoma, ethnicity (Asian or black), maternal age older than 25 years, male sex, glucose-6-phosphate dehydrogenase deficiency, and gestational age less than 38 weeks. The specific contribution of these risk factors to chronic bilirubin encephalopathy in healthy children is not well understood. |
| Importance | Chronic bilirubin encephalopathy is a rare but devastating condition. Not all children with chronic bilirubin encepahalopathy have a history of hyperbilirubinemia. |
| Rationale for no recommendation | Evidence about the benefits and harms of screening is lacking. Therefore, the USPSTF could not determine the balance of benefits and harms of screening newborns for hyperbilirubinemia to prevent chronic bilirubin encephalopathy. |
| Considerations for practice | In deciding whether to screen, physicians should consider the following:<br>• Potential preventable burden. Bilirubin encephalopathy is a relatively rare disorder. Hyperbilirubinemia alone does not account for the neurologic condition of chronic bilirubin encephalopathy. There is no known screening test that will reliably identify all infants at risk of developing chronic bilirubin encephalopathy.<br>• Potential harms. The potential harms of screening are unmeasured but may be important. Evidence about the potential harms of phototherapy is lacking. Harms of treatment by exchange transfusion may include apnea, bradycardia, cyanosis, vasospasm, thrombosis, necrotizing enterocolitis, and, rarely, death.<br>• Current practice. Universal screening is widespread in the United States. |
| Screening tests | Screening may consist of risk-factor assessment, measurement of bilirubin level in serum or by transcutaneous estimation, or a combination of methods. |
| Interventions | Phototherapy is commonly used to treat hyperbilirubinemia. Exchange transfusion is used to treat extreme hyperbilirubinemia. |
| Relevant USPSTF recommendations | USPSTF recommendations on screening newborns for hearing loss, congenital hypothyroidism, hemoglobinopathies, and phenylketonuria can be found at http://www.preventiveservices.ahrq.gov. |

NOTE: *For the full USPSTF recommendation statement and supporting documents, visit http://www.preventiveservices.ahrq.gov.*

*USPSTF = U.S. Preventive Services Task Force.*

documented high serum levels of bilirubin have been found to have kernicterus. As mentioned previously, the incidence of bilirubin encephalopathy in the United Kingdom is estimated at 0.9 in 100,000 live births.[2]

*Potential harms:* Potential harms of screening are unmeasured, but may be important. These include interference with breastfeeding, disruption of maternal-infant bonding, pain caused by heel stick or venipuncture, weight loss, gastrointestinal problems, possible growth of melanocytic nevi, and labeling of infants who have elevated bilirubin levels.

*Costs:* The monetary cost to provide universal screening would be very large, particularly if serum or transcutaneous bilirubin measurement is adopted as a universal screening tool.

*Current practice:* Universal screening with a variety of methods is widespread in the United States.

• **Patient population.** This USPSTF recommendation addresses screening for hyperbilirubinemia to reduce the incidence of chronic bilirubin encephalopathy in healthy term or near-term infants (at least 35 weeks' gestation).

• **Assessment of risk.** Risk factors for hyperbilirubinemia include exclusive breastfeeding, family history of neonatal jaundice, bruising, cephalohematoma, ethnicity (Asian or black), maternal age (older than 25 years), male sex, glucose-6-phosphate dehydrogenase deficiency, and gestational age of less than 38 weeks. The contribution of these risk factors to chronic bilirubin encephalopathy in otherwise healthy children is not well understood.

• **Screening tests.** Screening for hyperbilirubinemia may consist of risk-factor assessment, measurement of bilirubin level (in serum or by transcutaneous estimation), or a combination of methods.

• **Treatment.** Phototherapy is commonly used to treat hyperbilirubinemia. A previous systematic review reported that one needs to treat six to 10 otherwise healthy neonates with jaundice and total serum bilirubin levels of at least 15 mg per dL (256.56 μmol per L) with phototherapy to prevent the total serum bilirubin level in one additional infant from rising above 20 mg per dL (342.08 μmol per L).[4]

Exchange transfusion is used to treat extreme hyperbilirubinemia. Although death as a complication of

exchange transfusion is rare, significant morbidity (e.g., apnea, bradycardia, cyanosis, vasospasm, thrombosis, necrotizing enterocolitis) occurs in as many as 5 percent of exchange transfusions, and the risks associated with the use of blood products must always be considered. Hypoxic-ischemic encephalopathy and AIDS have occurred in otherwise healthy infants receiving exchange transfusions.

## Other Considerations

- **Research needs and gaps.** Further understanding is needed of the natural history of chronic bilirubin encephalopathy. Population-based surveillance for kernicterus and chronic bilirubin encephalopathy is necessary for an understanding of the incidence of the disease and of its risk factors. Such surveillance could also demonstrate whether the current efforts to systematically screen neonates to prevent severe hyperbilirubinemia is temporally associated with a reduction in chronic bilirubin encephalopathy. A better understanding of the harms from phototherapy is also needed. For example, data from prospective and controlled studies would be helpful in clarifying the relationship between exposure to neonatal phototherapy and the development of melanocytic nevi.

This recommendation statement was first published in *Pediatrics*. 2009; 124(4):1172-1177.

The "Discussion" and "Recommendations of Others" sections of this recommendation statement are available at http://www.ahrq.gov/clinic/uspstf/uspshyperb.htm.

The U.S. Preventive Services Task Force Recommendations are independent of the U.S. government. They do not represent the views of the Agency for Healthcare Research and Quality, the U.S. Department of Health and Human Services, or the U.S. Public Health Service.

### REFERENCES

1. Johnson LH, Bhutani VK, Brown AK. System-based approach to management of neonatal jaundice and prevention of kernicterus. *J Pediatr.* 2002;140(4):396-403.
2. Manning D, Todd P, Maxwell M, Platt MJ. Prospective surveillance study of severe hyperbilirubinaemia in the newborn in the UK and Ireland. *Arch Dis Child Fetal Neonatal Ed.* 2007;92(5):F342-F346.
3. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation [published correction appears in *Pediatrics.* 2004;114(4):1138]. *Pediatrics.* 2004;114(1):297-316.
4. Ip S, Glicken S, Kulig J, O'Brien R, Sege R. Management of neonatal hyperbilirubinemia. *Evid Rep Technol Assess (Summ).* 2002;(65):1-5. ■