

Universal Predischarge Screening for Neonatal Hyperbilirubinemia

Report from Evidence Review
*Secretary's Advisory Committee on Heritable
Disorders in Newborns and Children*
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Recent Progress and Activities

- Neonatal Hyperbilirubinemia
 - Preliminary evidence review presented in January 2011
 - Interim evidence review presented today
- Critical Congenital Cyanotic Heart Disease
 - Paper in progress
- Evidence Evaluation Method Workgroup
 - Webinar conference call March 15, 2011
 - In-person meeting April 13, 2011

Hyperbilirubinemia Team Members

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Neonatal Hyperbilirubinemia Overview

- Bilirubin elevations common in newborns
 - Multiple etiologies
- Detectable risk factor for acute bilirubin encephalopathy (ABE) and chronic bilirubin encephalopathy (kernicterus)
- Primary concern: preventing neurotoxic effects of hyperbilirubinemia

American Academy of Pediatrics Clinical Practice Guidelines

- Prevention and management of hyperbilirubinemia in newborns ≥ 35 weeks' gestational age
- Published 2004 (2009 update with clarifications)
- Main recommendations
 - Promote and support successful breastfeeding
 - Perform systematic assessment before discharge; measurement of pre-discharge bilirubin level (with TSB or TcB) individually or in combination with clinical risk-factor assessment to help assess risk of subsequent hyperbilirubinemia
 - Provide early and focused follow-up based on risk assessment, based on pre-discharge TSB/TcB, gestational age, and other risk factors
 - When indicated, treat newborns with phototherapy or exchange transfusion to decrease serum bilirubin and prevent hyperbilirubinemia and, possibly, bilirubin encephalopathy (kernicterus)

US Preventive Services Task Force (USPSTF) Recommendation

- Evidence review regarding screening infants for hyperbilirubinemia to prevent chronic bilirubin encephalopathy in healthy newborns ≥ 35 weeks' gestational age
- Release: October 2009
- Assessment
 - USPSTF concluded that evidence about the benefits and harms of screening is lacking and could not determine the balance of benefits and harms of screening newborn infants to prevent chronic bilirubin encephalopathy
- Summary of Recommendation
 - Concluded that the evidence is insufficient to recommend screening infants for hyperbilirubinemia to prevent chronic bilirubin encephalopathy

Case Definitions

Neonatal Hyperbilirubinemia

- TSB levels >95th percentile for age in hours in term and near term newborns, which require follow-up and treatment

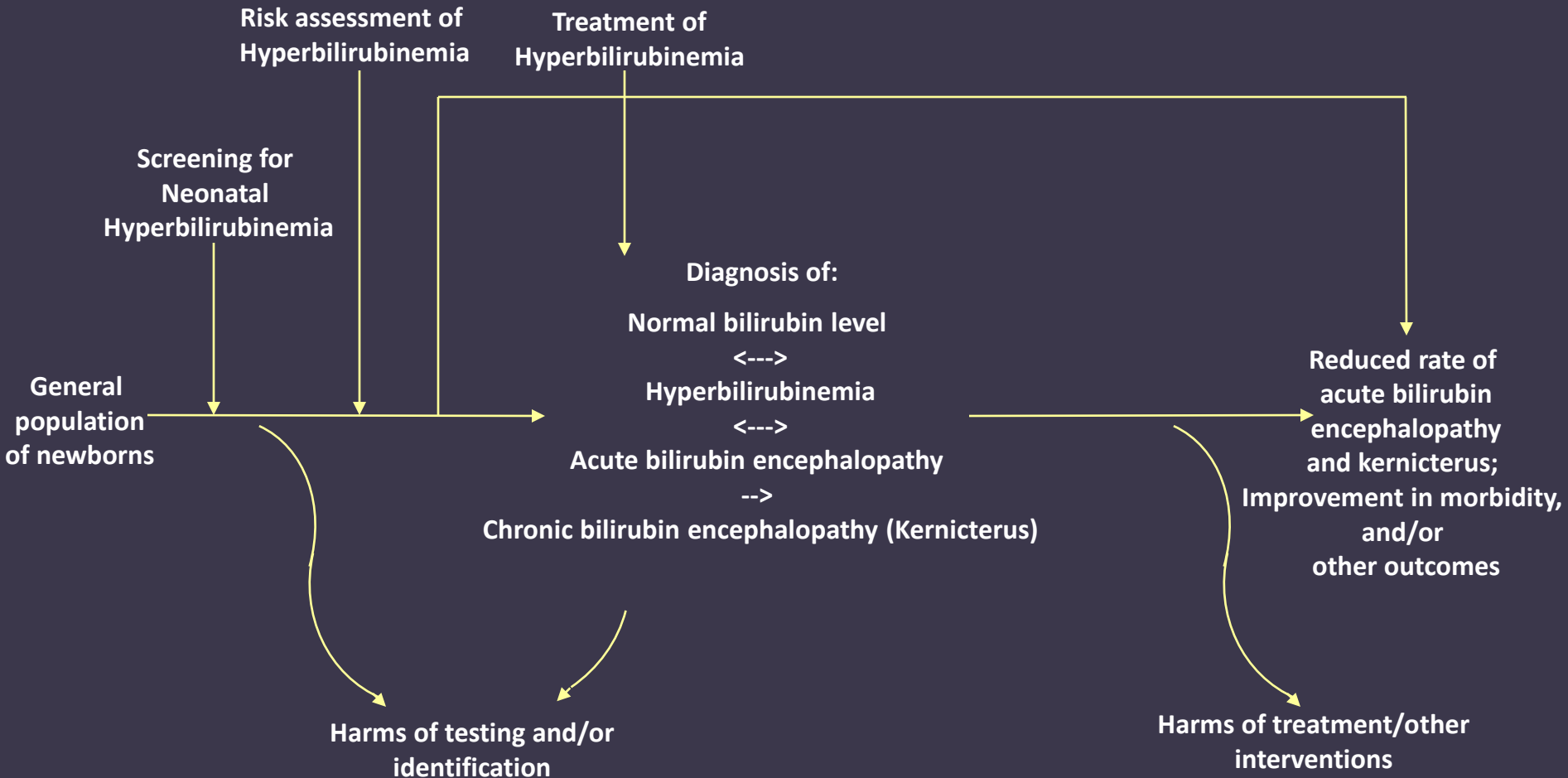
Acute Bilirubin Encephalopathy (ABE)

- Advanced manifestations of bilirubin toxicity in first weeks of life, loss of Moro, extensor hypertonia, high-pitched cry. [Some authors use ABE to describe less severe symptoms, such as somnolence, hypotonia, and fever – not ABE in this report.]

Chronic Bilirubin Encephalopathy (Kernicterus)

- Describes persistent and permanent brain damage from bilirubin toxicity. Characterized by
 - movement disorder (aethetosis, dystonia, spasticity, hypotonia)
 - auditory dysfunction
 - oculomotor impairment
 - dental enamel hypoplasia

Conceptual Framework



Condition Key Questions

- Is neonatal hyperbilirubinemia well-defined? When does it appear clinically? What are known risk factors?
- What characterizes acute and chronic bilirubin encephalopathy?
- What evidence describes the relationships among neonatal hyperbilirubinemia and acute and chronic bilirubin encephalopathy?
- Is neonatal hyperbilirubinemia associated with more subtle adverse outcomes other than acute and chronic bilirubin encephalopathy?

Condition

- Reported incidence of bilirubin levels $>30\text{mg/dL}$ ranges from 3 to 12 per 100,000
- Estimated incidence of ABE is <1 per 200,000 live births
- Estimated incidence of CBE (kernicterus) ranges from 0.49 to 2.7 per 100,000
 - Most evidence indicates rates <1 per 100,000

Hyperbilirubinemia and ABE/CBE

- No specific bilirubin level associated with acute or chronic bilirubin encephalopathy, although in general
 - Higher levels of neonatal bilirubin are associated with higher occurrence of ABE and CBE manifestations
- Most cases of chronic bilirubin encephalopathy have TSB >30mg/dL
 - Rare cases occurring below TSB of 25mg/dL with co-morbidities and/or significant risk factors
- Although some neonates develop less severe signs (than ABE) of hyperbilirubinemia, large majority of studies indicate no long-term effects

Screening Key Questions

- What methods exist to screen newborns for neonatal hyperbilirubinemia? What are their validity, sensitivity, and specificity?
- What tools help to interpret the risk of developing hyperbilirubinemia associated with a newborn's bilirubin value? What is the predictive validity of these tools?
- How do timing of screening after birth, gestational age, threshold levels, and other considerations affect the number of infants identified with or at significant risk for developing neonatal hyperbilirubinemia?

Screening

- Three current forms of screening for hyperbilirubinemia:
 - Visual assessment
 - TcB
 - TSB
- TcB appears as valid screening tool for detecting significant hyperbilirubinemia requiring confirmatory follow-up with TSB
- An hour-specific bilirubin nomogram based on TSB values allows prediction of subsequent hyperbilirubinemia; can apply risk nomogram also to TcB values

Treatment Key Questions

- What methods exist to treat neonatal hyperbilirubinemia and what is their effectiveness? What is the relationship between outcomes and the timing of treatment intervention?
- What proportion of cases of chronic bilirubin encephalopathy would earlier detection and treatment of hyperbilirubinemia prevent? What proportion of cases of other neonatal hyperbilirubinemia manifestations would be preventable?
- What are the potential harms or risks associated with treatment?

Treatment

- RCT evidence that phototherapy effectively decreases levels of bilirubin in the neonatal period
- Indirect evidence that screening and phototherapy decrease rates of chronic bilirubin encephalopathy (kernicterus)
- Case series provide evidence that symptoms of ABE may resolve with treatment
- Indirect evidence that earlier treatment with phototherapy effectively lowers serum bilirubin levels and diminishes the need for treatment with EcT
- Adverse events remain common after EcT, with mortality approximately 0.53 per 100 patients and 0.3 per 100 procedures

Economics Key Questions

- What are the costs associated with
 - the screening test?
 - the failure to find at risk newborns in the pre-symptomatic period?
 - treatment of hyperbilirubinemia? treatment of acute and chronic bilirubin encephalopathy?
- What is the cost-effectiveness of newborn screening for neonatal hyperbilirubinemia?

Economics

- Limited quantity and quality of economic evidence
- Estimated costs of TcB testing
 - Range: <\$1 to \$7.80
- Limited evidence for costs of
 - jaundice readmission
 - phototherapy treatment
 - long-term outcomes

Economics, cont.

- Limited evidence for cost-effectiveness of strategies to prevent kernicterus (1 study)
- Cost per case of kernicterus prevented:
 - TSB: \$5,743,905 (sensitivity analyses: ranges from \$4 million to \$128 million)
 - TcB: \$9,191,352 (range of \$6 million to \$195 million per case prevented)

Harms and Benefits of Predischarge Screening Program

Harms

- Risks of phototherapy include fluid loss, temperature instability, corneal damage, skin rash, diarrhea, delayed parenting/bonding (all minor risks)
- Mortality of EcT (not screening) ~0.53 per 100 patients and ~0.3 per 100 procedures, and morbidity ranging from 12-15.3%

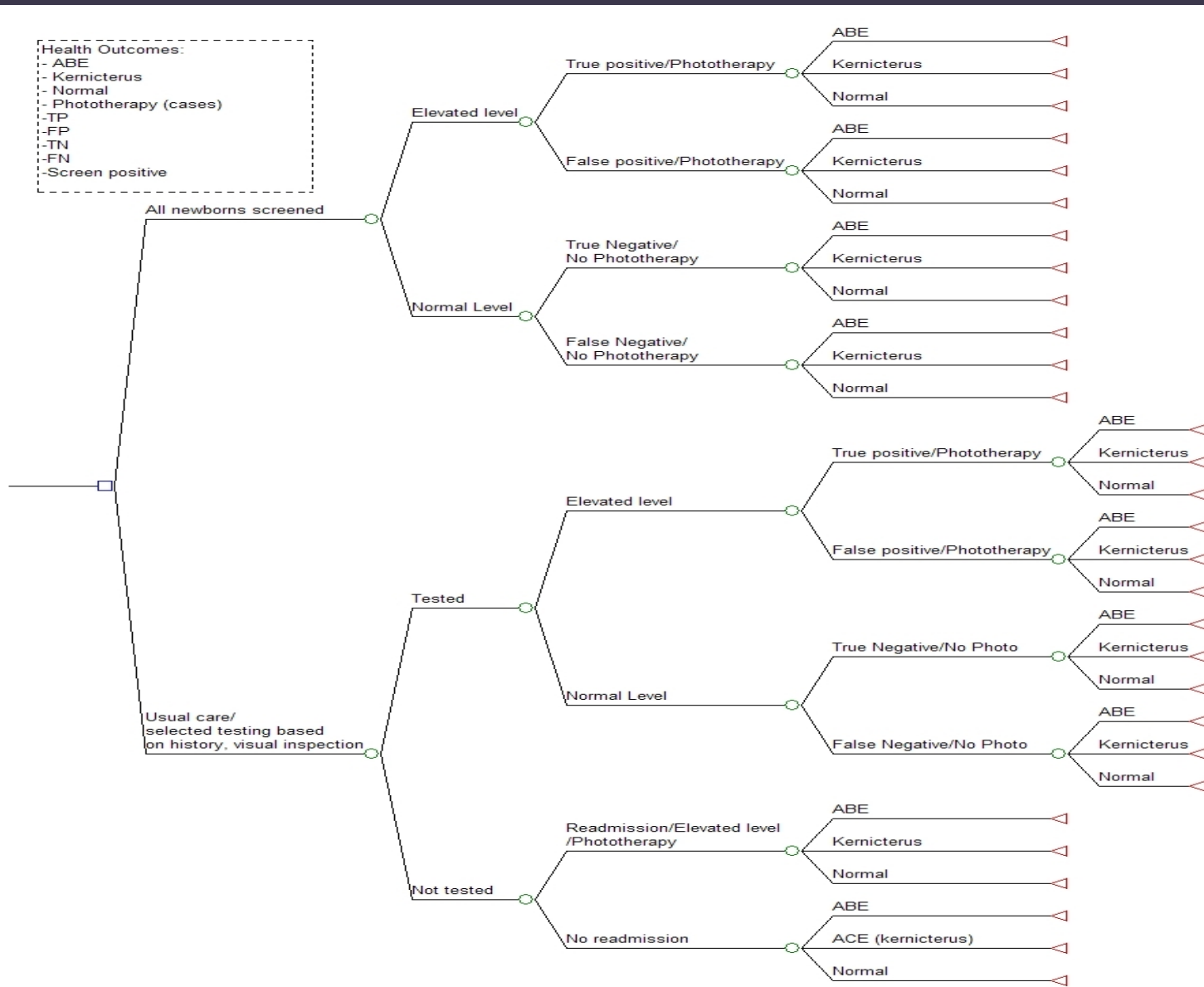
Benefits

- Identifies newborns who will likely develop TSB >30mg/dL
- Lowering bilirubin level reduces the risk of newborn developing ABE and CBE
- Early identification and early treatment with phototherapy may prevent need for EcT or readmission to hospital

Boundaries of Benefit

- With estimated 4 million US births per year and incidence of CBE 0.49-2.7 per 100,000, an upper bound of 20-108 cases per year of CBE could be prevented with earlier detection and treatment
- With reported incidence of TSB levels $>30\text{mg/dL}$ of 3-12 per 100,000, earlier detection and treatment could prevent maximum of 120-480 infants per year from reaching these levels

Proposed Decision Tree



Gaps in Evidence

- Clear connection between specific bilirubin levels and chronic bilirubin encephalopathy (kernicterus)
- If treating clinically significant neonatal hyperbilirubinemia prevents chronic bilirubin encephalopathy
 - How many cases of CBE could universal screening prevent?
- Predischarge bilirubin newborn screening logistics and large-scale screening impact
- Cost-effectiveness of predischarge bilirubin newborn screening

Thank you