Complete Summary

GUIDELINE TITLE

Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation.

BIBLIOGRAPHIC SOURCE(S)

Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004 Jul;114(1):297-316. [28 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

American Academy of Pediatrics (AAP) Policies are reviewed every 3 years by the authoring body, at which time a recommendation is made that the policy be retired, revised, or reaffirmed without change. Until the Board of Directors approves a revision or reaffirmation, or retires a statement, the current policy remains in effect.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hyperbilirubinemia; jaundice; kernicterus (bilirubin encephalopathy)

GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Pediatrics

INTENDED USERS

Advanced Practice Nurses
Hospitals
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To promote an approach that will reduce the frequency of severe neonatal hyperbilirubinemia and bilirubin encephalopathy and minimize the risk of unintended harm such as increased anxiety, decreased breastfeeding, or unnecessary treatment for the general population and excessive cost and waste

TARGET POPULATION

Newborn infants of 35 or more weeks of gestation

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention (Primary and Secondary)

1. Maternal prenatal testing for Rh factor and ABO blood type; screening for unusual isoimmune antibodies
2. Testing of umbilical cord blood (Coombs' test; Rh[D] test; blood type)
3. Providing support and advice to mothers on breastfeeding
4. Routine supplementation with water and/or dextrose (not recommended)

Diagnostic Evaluation/Risk Assessment

1. Laboratory assessment for glucose-6-phosphate dehydrogenase deficiency
2. Laboratory measurement of total, direct (or conjugated) serum bilirubin and transcutaneous bilirubin
3. Urinalysis or urine culture
4. Complete blood count and smear; reticulocyte count
5. Measurement of end-tidal carbon monoxide corrected for ambient carbon monoxide
6. Evaluation for signs of hypothyroidism
7. Evaluation for galactosemia
8. Evaluation for signs of sepsis
9. Additional evaluation for signs of cholestasis
10. Risk assessment for hyperbilirubinemia before discharge from nursery

11. Provision of written and verbal information to parents concerning jaundice prior to discharge
12. Follow-up of discharged infants based on risk assessment

Treatment/Management

1. Phototherapy
2. Exchange transfusion
3. Administration of intravenous gamma-globulin
4. Monitoring of serum albumin levels and the bilirubin/albumin ratio
5. Continuation of breastfeeding or substitution of formula for breast milk

MAJOR OUTCOMES CONSIDERED

- Accuracy and predictive value of diagnostic tests for hyperbilirubinemia
- Risk for hyperbilirubinemia and kernicterus
- Total serum bilirubin level
- Behavioral/neurodevelopmental outcome
- Risks and complications of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A comprehensive literature review was performed by the New England Medical Center Evidence-Based Practice Center to answer the following key questions:

- Question 1: What is the relationship between peak bilirubin levels and/or duration of hyperbilirubinemia and neurodevelopmental outcome?
- Question 2: What is the evidence for effect modification of the results in question 1 by gestational age (GA), hemolysis, serum albumin, and other factors?
- Question 3: What are the quantitative estimates of efficacy treatment for 1) reducing peak bilirubin levels (e.g., number needed to treat [NNT] at 20 mg/dL to keep total serum bilirubin [TSB] from rising); 2) reducing the duration of hyperbilirubinemia (e.g., average number of hours by which time TSB is higher than 20 mg/dL may be shortened by treatment); and 3) improving neurodevelopmental outcomes?
- Question 4: What is the efficacy of various strategies for predicting hyperbilirubinemia, including hour-specific bilirubin percentiles?
- Question 5: What is the accuracy of transcutaneous bilirubin [TcB] measurements?

The Medline database was searched on September 25, 2001, for publications from 1966 to the present using relevant medical subject heading terms

("hyperbilirubinemia"; "hyperbilirubinemia, hereditary"; "bilirubin"; "jaundice, neonatal"; and "kernicterus") and text words ("bilirubin," "hyperbilirubinemia," "jaundice," kernicterus," and "neonatal"). The abstracts were limited to human subjects and English-language studies focusing on newborns between birth and 1 month of age. In addition, the same text words used for the Medline search were used to search the Pre-Medline database. The strategy yielded 4,280 Medline and 45 PreMedline abstracts. Domain experts were consulted and relevant review articles were examined for additional studies. A supplemental search for case reports of kernicterus in reference lists of relevant articles and reviews was performed also.

Screening and Selection Process

In the preliminary screening of abstracts, more than 600 potentially relevant articles were identified in total for questions 1, 2, and 3. To handle this large number of articles, the following scheme was devised to address the key questions and ensure that the report was completed within the time and resource constraints. The Evidence-Based practice Center included only studies that measured neurodevelopmental or behavioral outcomes (except for question 3, part 1, for which they evaluated all studies addressing the efficacy of treatment). For the specific question of quantitative estimates of efficacy of treatment, all studies concerning therapies designed to prevent hyperbilirubinemia (generally bilirubin greater than or equal to 20 mg/dL) were included in the review.

Inclusion Criteria

The target population of this review was healthy, term infants. For the purpose of this review, articles concerning infants who were at least 34 weeks´ estimated gestational age (EGA) at the time of birth were included. From studies that reported birth weight rather than age, infants whose birth weight was greater than or equal to 2,500 g were included. This cutoff was derived from findings of the National Institute of Child Health and Human Development (NICHD) hyperbilirubinemia study, in which none of the 1,339 infants weighing greater than or equal to 2,500 g were less than 34 weeks´ EGA. Articles were selected for inclusion in the systematic review based on the following additional criteria:

Question 1 or 2 (Risk Association)

- Population: infants greater than or equal to 34 weeks´ EGA or birth weight greater than or equal to 2,500 g
- Sample size: more than 5 subjects per arm
- Predictors: jaundice or hyperbilirubinemia
- Outcomes: at least 1 behavioral/neurodevelopmental outcome reported in the article
- Study design: prospective cohorts (more than 2 arms), prospective cross-sectional study, prospective longitudinal study, prospective single-arm study, or retrospective cohorts (more than 2 arms)

Case Reports of Kernicterus

- Population: kernicterus case
- Study design: case reports with kernicterus as a predictor or an outcome

Kernicterus, as defined by authors, included any of the following: acute phase of kernicterus (poor feeding, lethargy, high-pitched cry, increased tone, opisthotonos, or seizures), kernicterus sequelae (motor delay, sensorineural hearing loss, gaze palsy, dental dysplasia, cerebral palsy, or mental retardation), necropsy finding of yellow staining in the brain nuclei.

Question 3 (Efficacy of Treatment at Reducing Serum Bilirubin)

- Population: infants greater than or equal to 34 weeks´ EGA or birth weight greater than or equal to 2,500 g
- Sample size: more than 10 subjects per arm
- Treatments: any treatment for neonatal hyperbilirubinemia
- Outcomes: serum bilirubin level higher than or equal to 20 mg/dL or frequency of blood exchange transfusion specifically for bilirubin level higher than or equal to 20 mg/dL
- Study design: randomized or nonrandomized, controlled trials

For All Other Issues

- Population: infants greater than or equal to 34 weeks´ EGA or birth weight greater than or equal to 2,500 g
- Sample size: more than 10 subjects per arm for phototherapy; any sample size for other treatments
- Treatments: any treatment for neonatal hyperbilirubinemia
- Outcomes: at least 1 neurodevelopmental outcome was reported in the article

Question 4 or 5 (Diagnosis)

- Population: infants greater than or equal to 34 weeks´ EGA or birth weight greater than or equal to 2,500 g
- Sample size: more than 10 subjects
- Reference standard: laboratory-based TSB

Exclusion Criteria

Case reports of kernicterus were excluded if they did not report serum bilirubin level or GA and birth weight.

Results of Screening of Titles and Abstracts

There were 158, 174, 99, 153, and 79 abstracts for questions 1, 2, 3, 4, and 5, respectively. Some articles were relevant to more than 1 question.

NUMBER OF SOURCE DOCUMENTS

After full-text screening, 138 retrieved articles were included. There were 35 articles in the correlation section (questions 1 and 2), 28 articles of kernicterus case reports, 21 articles in the treatment section (question 3), and 54 articles in the diagnosis section (questions 4 and 5). There were inevitable overlaps, because treatment effects and assessment of neurodevelopmental outcomes were inherent in many study designs.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The Steering Committee on Quality Improvement and Management categorizes evidence quality in 4 levels:

A. Well-designed, randomized, controlled trials or diagnostic studies on relevant populations
B. Randomized, controlled trials or diagnostic studies with minor limitations; overwhelming, consistent evidence from observational studies
C. Observational studies (case-control and cohort design)
D. Expert opinion, case reports, reasoning from first principles

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Reporting the Results

Articles that passed the full-text screening were grouped according to topic and analyzed in their entirety. Extracted data were synthesized into evidence tables.

Summarizing the Evidence of Individual Studies

Grading of the evidence can be useful for indicating the overall methodologic quality of a study. The evidence-grading scheme assesses 4 dimensions that are important for the proper interpretation of the evidence: study size, applicability, summary of results, and methodologic quality.

Definitions of Terminology

- Confounders (for question 1 only): 1) An ideal study design to answer question 1 would follow 2 groups, jaundiced and normal infants, without treating any infant for a current or consequent jaundice condition and observe their neurodevelopmental outcomes. Therefore, any treatment received by the subjects in the study was defined as a confounder. 2) If subjects had known risk factors for jaundice such as prematurity, breastfeeding, or low birth weight, the risk factors were defined as confounders. 3) Any disease condition other than jaundice was defined as a confounder. 4) Because bilirubin level is the essential predictor, if the study did not report or measure bilirubin levels for the subjects, lack of bilirubin measurements was defined as a confounder.

- Acute phase of kernicterus: poor feeding, lethargy, high-pitched cry, increased tone, opisthotonos, or seizures.
- Chronic kernicterus sequelae: motor delay, sensorineural hearing loss, gaze palsy, dental dysplasia, cerebral palsy, or mental retardation.

Statistical Analyses

Two statistical analyses were performed in which there were sufficient data: the number needed to treat (NNT) and receiver operating characteristics (ROC) curve.

NNT

The NNT can be a clinically meaningful metric to assess the benefits of clinical trials. It is calculated by taking the inverse of the absolute risk difference. The absolute risk difference is the difference between the event rates between the treatment and control groups. For example, if the event rate is 15% in the control group and 10% in the treatment group, the absolute risk difference is 5% (an absolute risk reduction of 5%). The NNT then would be 20 (1 divided by 0.05), meaning that 20 patients will need to be treated to see 1 fewer event. In the setting of neonatal **hyperbilirubinemia**, NNT might be interpreted as the number of newborns needed to be treated (with phototherapy) at 13 to 15 mg/dL to prevent 1 newborn from reaching 20 mg/dL.

ROC Curve

ROC curves were developed for individual studies in question 4 if multiple thresholds of a diagnostic technology were reported. The areas under the curves (AUCs) were calculated to provide an assessment of the overall accuracy of the tests.

Meta-analyses of Diagnostic Test Performance

Meta-analyses were performed to quantify the transcutaneous bilirubin (TcB) measurements for which the data were sufficient. Three complementary methods were used for assessing diagnostic test performance: summary ROC analysis, independently combined sensitivity and specificity values, and meta-analysis of correlation coefficients.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In October 1994, the Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia of the American Academy of Pediatrics (AAP) produced a practice parameter dealing with the management of hyperbilirubinemia in the healthy term newborn. The current guideline represents a consensus of the committee charged by the AAP with reviewing and updating the existing guideline and is based on a careful review of the evidence, including a

comprehensive literature review by the New England Medical Center Evidence-Based Practice Center.

The evidence-based approach to guideline development requires that the evidence in support of a policy be identified, appraised, and summarized and that an explicit link between evidence and recommendations be defined. Evidence-based recommendations are based on the quality of evidence and the balance of benefits and harms that is anticipated when the recommendation is followed. This guideline uses the definitions for quality of evidence and balance of benefits and harms established by the AAP Steering Committee on Quality Improvement Management.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

- **Strong recommendation**: the committee believes that the benefits of the recommended approach clearly exceed the harms of that approach and that the quality of the supporting evidence is either excellent or impossible to obtain. Clinicians should follow these recommendations unless a clear and compelling rationale for an alternative approach is present.
- **Recommendation**: the committee believes that the benefits exceed the harms, but the quality of evidence on which this recommendation is based is not as strong. Clinicians should also generally follow these recommendations but should be alert to new information and sensitive to patient preferences. In this guideline, the term "should" implies a recommendation by the committee.
- **Option**: either the quality of the evidence that exists is suspect or well-performed studies have shown little clear advantage to one approach over another. Patient preference should have a substantial role in influencing clinical decision-making when a policy is described as an option.
- **No recommendation**: there is a lack of pertinent evidence and the anticipated balance of benefits and harms is unclear.

Anticipated Balance Between Benefits and Harms

The presence of clear benefits or harms supports stronger statements for or against a course of action. In some cases, however, recommendations are made when analysis of the balance of benefits and harms provides an exceptional disequilibrium and it would be unethical or impossible to perform clinical trials to "prove" the point. In these cases the balance of benefit and harm is termed "exceptional."

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft practice guideline underwent extensive peer review by committees and sections within the American Academy of Pediatrics (AAP), outside organizations, and other individuals identified by the subcommittee as experts in the field. Liaison representatives to the subcommittee were invited to distribute the draft to other representatives and committees within their specialty organizations. The resulting comments were reviewed by the subcommittee and, when appropriate, incorporated into the guideline.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Rating schemes for strength of evidence and recommendation follow the Major Recommendations.

Primary Prevention

1. Clinicians should advise mothers to nurse their infants at least 8 to 12 times per day for the first several days (American Academy of Pediatrics [AAP], 2002) (***evidence quality C: benefits exceed harms***).
2. The AAP recommends against routine supplementation of nondehydrated breastfed infants with water or dextrose water (***evidence quality B and C: harms exceed benefits***).

Secondary Prevention

1. Clinicians should perform ongoing systematic assessments during the neonatal period for the risk of an infant developing severe hyperbilirubinemia.

Blood Typing

1. All pregnant women should be tested for ABO and Rh (D) blood types and have a serum screen for unusual isoimmune antibodies (***evidence quality B: benefits exceed harms***).
2. If a mother has not had prenatal blood grouping or is Rh-negative, a direct antibody test (or Coombs´ test), blood type, and an Rh (D) type on the infant´s (cord) blood are strongly recommended (***evidence quality B: benefits exceed harms***).
3. 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 (Madlon-Kay, 1992) (***evidence quality C: benefits exceed harms***).

Clinical Assessment

1. 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 (***evidence quality D: benefits versus harms exceptional***).

2. Protocols for the assessment of jaundice should include the circumstances in which nursing staff can obtain a transcutaneous bilirubin (TcB) level or order a total serum bilirubin (TSB) measurement (***evidence quality D: benefits versus harms exceptional***).

Laboratory Evaluation

1. A TcB and/or TSB measurement should be performed on every infant who is jaundiced in the first 24 hours after birth (refer to Figure 1 and Table 1 in the original guideline document) (Newman, Liljestrand, & Escobar, 2002) (***evidence quality C: benefits exceed harms***). The need for and timing of a repeat TcB or TSB measurement will depend on the zone in which the TSB falls (refer to Fig 2 in the original guideline document) (Bhutani et al., 2000; Bhutani, Johnson, & Sivieri, 1999), the age of the infant, and the evolution of the hyperbilirubinemia. Recommendations for TSB measurements after the age of 24 hours are provided in Figure 1 and Table 1 in the original guideline document.
2. A TcB and/or TSB measurement should be performed if the jaundice appears excessive for the infant´s age (***evidence quality D: benefits versus harms exceptional***). If there is any doubt about the degree of jaundice, the TSB or TcB should be measured. Visual estimation of bilirubin levels from the degree of jaundice can lead to errors, particularly in darkly pigmented infants (***evidence quality C: benefits exceed harms***).
3. All bilirubin levels should be interpreted according to the infant´s age in hours (Figure 2 in the original guideline document) (***evidence quality C: benefits exceed harms***).

Cause of Jaundice

1. The possible cause of jaundice should be sought in an infant receiving phototherapy or whose TSB level is rising rapidly (i.e., crossing percentiles [Figure 2 in the original guideline document]) and is not explained by the history and physical examination (***evidence quality D: benefits versus harms exceptional***).
2. Infants who have an elevation of direct-reacting or conjugated bilirubin should have a urinalysis and urine culture.(Garcia & Nager, 2002) Additional laboratory evaluation for sepsis should be performed if indicated by history and physical examination (***evidence quality C: benefits exceed harms***).
3. Sick infants and those who are jaundiced at or beyond 3 weeks should have a measurement of total and direct or conjugated bilirubin to identify cholestasis (Table 1 in the original guideline document) (***evidence quality D: benefit versus harms exceptional***). The results of the newborn thyroid and galactosemia screen should also be checked in these infants (***evidence quality D: benefits versus harms exceptional***).
4. If the direct-reacting or conjugated bilirubin level is elevated, additional evaluation for the causes of cholestasis is recommended (***evidence quality C: benefits exceed harms***).
5. Measurement of the glucose-6-phosphate dehydrogenase (G6PD) level is recommended for a jaundiced infant who is receiving phototherapy and whose family history or ethnic or geographic origin suggest the likelihood of G6PD deficiency or for an infant in whom the response to phototherapy is poor

(Figure 3 in the original guideline document) (***evidence quality C: benefits exceed harms***).

Risk Assessment Before Discharge

1. 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 (***evidence quality C: benefits exceed harms***).
2. 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 (***evidence quality C: benefits exceed harms***).

Hospital Policies and Procedures

1. All hospitals should provide written and verbal information for parents at the time of discharge, which should include an explanation of jaundice, the need to monitor infants for jaundice, and advice on how monitoring should be done (***evidence quality D: benefits versus harms exceptional***).

Follow-up

1. All infants should be examined by a qualified health care professional in the first few days after discharge to assess infant well-being and the presence or absence of jaundice. The timing and location of this assessment will be determined by the length of stay in the nursery, presence or absence of risk factors for hyperbilirubinemia (Table 2 and Figure 2 in the original guideline document), and risk of other neonatal problems (***evidence quality C: benefits exceed harms***).

Timing of Follow-up

1. Follow-up should be provided as follows:
    a. Infant discharged before age 24 h should be seen by age 72 h
    b. Infant discharged between 24 and 47.9 h should be seen by age 96 h
    c. Infant discharged between 48 and 72 h should be seen by age 120 h

    For some newborns discharged before 48 hours, 2 follow-up visits may be required, the first visit between 24 and 72 hours and the second between 72 and 120 hours. Clinical judgment should be used in determining follow-up. Earlier or more frequent follow-up should be provided for those who have risk factors for hyperbilirubinemia (see Table 2 in the original guideline document), whereas those discharged with few or no risk factors can be seen after longer intervals (***evidence quality C: benefits exceed harms***).

2. If appropriate follow-up cannot be ensured in the presence of elevated risk for developing severe hyperbilirubinemia, it may be necessary to delay discharge either until appropriate follow-up can be ensured or the period of greatest risk

has passed (72 to 96 hours) (***evidence quality D: benefits versus harms exceptional***).

Follow-up Assessment

1. The follow-up assessment should include the infant´s weight and percent change from birth weight, adequacy of intake, the pattern of voiding and stooling, and the presence or absence of jaundice (***evidence quality C: benefits exceed harms***). Clinical judgment should be used to determine the need for a bilirubin measurement. If there is any doubt about the degree of jaundice, the TSB or TcB level should be measured. Visual estimation of bilirubin levels can lead to errors, particularly in darkly pigmented infants (***evidence quality C: benefits exceed harms***).

Treatment

Phototherapy and Exchange Transfusion

1. Recommendations for treatment are given in Table 3 and Figures 3 and 4 in the original guideline document (***evidence quality C: benefits exceed harms***). If the TSB does not fall or continues to rise despite intensive phototherapy, it is very likely that hemolysis is occurring. The committee´s recommendations for discontinuing phototherapy can be found in Appendix 2 in the original guideline document.
2. In using the guidelines for phototherapy and exchange transfusion (Figures 3 and 4 in the original guideline document), the direct-reacting (or conjugated) bilirubin level should not be subtracted from the total (***evidence quality D: benefits versus harms exceptional***).
3. If the TSB is at a level at which exchange transfusion is recommended (Figure 4 in the original guideline document) or if the TSB level is 25 mg/dL (428 micromoles/L) or higher at any time, it is a medical emergency and the infant should be admitted immediately and directly to a hospital pediatric service for intensive phototherapy. These infants should not be referred to the emergency department, because it delays the initiation of treatment (Garland et al., 1994) (***evidence quality C: benefits exceed harms***).
4. Exchange transfusions should be performed only by trained personnel in a neonatal intensive care unit with full monitoring and resuscitation capabilities (***evidence quality D: benefits versus harms exceptional***).
5. In isoimmune hemolytic disease, administration of intravenous gamma-globulin (0.5–1 g/kg over 2 hours) is recommended if the TSB is rising despite intensive phototherapy or the TSB level is within 2 to 3 mg/dL (34–51micromoles/L) of the exchange level (Figure 4 in the original guideline document) (Gottstein & Cooke, 2003). If necessary, this dose can be repeated in 12 hours (***evidence quality B: benefits exceed harms***).

Serum Albumin Levels and the Bilirubin/Albumin Ratio

1. It is an option to measure the serum albumin level and consider an albumin level of less than 3.0 g/dL as one risk factor for lowering the threshold for phototherapy use (see Figure 3 in the original guideline document) (***evidence quality D: benefits versus risks exceptional***).

2. If an exchange transfusion is being considered, the serum albumin level should be measured and the bilirubin/albumin (B/A) ratio used in conjunction with the TSB level and other factors in determining the need for exchange transfusion (see Figure 4 in the original guideline document) (***evidence quality D: benefits versus harms exceptional***).

Acute Bilirubin Encephalopathy

1. Immediate exchange transfusion is recommended in any infant who is jaundiced and manifests the signs of the intermediate to advanced stages of acute bilirubin encephalopathy (Volpe, 2001; Harris et al., 2001) (hypertonia, arching, retrocollis, opisthotonos, fever, high-pitched cry) even if the TSB is falling (***evidence quality D: benefits versus risks exceptional***).

Phototherapy

1. All nurseries and services treating infants should have the necessary equipment to provide intensive phototherapy (see Appendix 2 in the original guideline document) (***evidence quality D: benefits exceed risks***).

Outpatient Management of the Jaundiced Breastfed Infant

1. In breastfed infants who require phototherapy (Figure 3 in the original guideline document), the AAP recommends that, if possible, breastfeeding should be continued (***evidence quality C: benefits exceed harms***). It is also an option to interrupt temporarily breastfeeding and substitute formula. This can reduce bilirubin levels and/or enhance the efficacy of phototherapy (Osborn & Bolus, 1985; Martinez et al., 1993; Amato, Howald, & von Muralt, 1985) (***evidence quality B: benefits exceed harms***). In breastfed infants receiving phototherapy, supplementation with expressed breast milk or formula is appropriate if the infant´s intake seems inadequate, weight loss is excessive, or the infant seems dehydrated.

Definitions:

Rating Scheme for Strength of Evidence

A. Well-designed, randomized, controlled trials or diagnostic studies on relevant populations
B. Randomized, controlled trials or diagnostic studies with minor limitations; overwhelming, consistent evidence from observational studies
C. Observational studies (case-control and cohort design)
D. Expert opinion, case reports, reasoning from first principles

Rating Scheme for Strength of Recommendation

- **Strong recommendation**: the committee believes that the benefits of the recommended approach clearly exceed the harms of that approach and that the quality of the supporting evidence is either excellent or impossible to obtain. Clinicians should follow these recommendations unless a clear and compelling rationale for an alternative approach is present.

- **Recommendation**: the committee believes that the benefits exceed the harms, but the quality of evidence on which this recommendation is based is not as strong. Clinicians should also generally follow these recommendations but should be alert to new information and sensitive to patient preferences. In this guideline, the term "should" implies a recommendation by the committee.
- **Option**: either the quality of the evidence that exists is suspect or well-performed studies have shown little clear advantage to one approach over another. Patient preference should have a substantial role in influencing clinical decision-making when a policy is described as an option.
- **No recommendation**: there is a lack of pertinent evidence and the anticipated balance of benefits and harms is unclear.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided for the management of jaundice in the newborn nursery.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Reduced incidence of severe hyperbilirubinemia and bilirubin encephalopathy while minimizing the risks of unintended harm such as maternal anxiety, decreased breastfeeding, and unnecessary costs or treatment

POTENTIAL HARMS

- The risk of burns exists with halogen phototherapy lamps.
- Phototherapy has been used in millions of infants for more than 30 years, and reports of significant toxicity are exceptionally rare. Nevertheless, phototherapy in hospital separates mother and infant, and eye patching is disturbing to parents. The most important, but uncommon, clinical complication occurs in infants with cholestatic jaundice. When these infants are exposed to phototherapy, they may develop a dark, grayish-brown discoloration of the skin, serum, and urine (the bronze infant syndrome). The pathogenesis of this syndrome is unknown, but it may be related to an accumulation of porphyrins and other metabolites in the plasma of infants who develop cholestasis. Although it occurs exclusively in infants with cholestasis, not all infants with cholestatic jaundice develop the syndrome.

This syndrome generally has had few deleterious consequences, and if there is a need for phototherapy, the presence of direct hyperbilirubinemia should not be considered a contraindication to its use. Rarely, purpura and bullous eruptions have been described in infants with severe cholestatic jaundice receiving phototherapy, and severe blistering and photosensitivity during phototherapy have occurred in infants with congenital erythropoietic porphyria.

- Because exchange transfusions are now rarely performed, the risks of morbidity and mortality associated with the procedure are difficult to quantify. In addition, the complication rates listed below may not be generalizable to the current era if, like most procedures, frequency of performance is an important determinant of risk. Death associated with exchange transfusion has been reported in approximately 3 in 1,000 procedures, although in otherwise healthy infants of 35 or more weeks´ gestation, the risk is probably much lower. Significant morbidity (apnea, bradycardia, cyanosis, vasospasm, thrombosis, necrotizing enterocolitis) occurs in as many as 5% of exchange transfusions, and the risks associated with the use of blood products must always be considered. Hypoxic-ischemic encephalopathy and acquired immunodeficiency syndrome have occurred in otherwise healthy infants receiving exchange transfusions.

CONTRAINDICATIONS

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Congenital porphyria or a family history of porphyria is an absolute contraindication to the use of phototherapy, as is the concomitant use of drugs or agents that are photosensitizers.

QUALIFYING STATEMENTS

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- The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances may be appropriate.
- Although originally a pathologic diagnosis characterized by bilirubin staining of the brainstem nuclei and cerebellum, the term "kernicterus" has come to be used interchangeably with both the acute and chronic findings of bilirubin encephalopathy. Bilirubin encephalopathy describes the clinical central nervous system findings caused by bilirubin toxicity to the basal ganglia and various brainstem nuclei. To avoid confusion and encourage greater consistency in the literature, the committee recommends that in infants the term "acute bilirubin encephalopathy" be used to describe the acute manifestations of bilirubin toxicity seen in the first weeks after birth and that the term "kernicterus" be reserved for the chronic and permanent clinical sequelae of bilirubin toxicity.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Institute of Medicine recommends a dramatic change in the way the US health care system ensures the safety of patients. The perspective of safety as a purely individual responsibility must be replaced by the concept of safety as a property of systems. Safe systems are characterized by a shared knowledge of the goal, a culture emphasizing safety, the ability of each person within the system to act in a manner that promotes safety, minimizing the use of memory, and emphasizing the use of standard procedures (such as checklists), and the involvement of patients/families as partners in the process of care. These principles can be applied to the challenge of preventing severe hyperbilirubinemia and kernicterus. A systematic approach to the implementation of these guidelines should result in greater safety. Such approaches might include:

- The establishment of standing protocols for nursing assessment of jaundice, including testing transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) levels, without requiring physician orders
- Checklists or reminders associated with risk factors, age at discharge, and laboratory test results that provide guidance for appropriate follow-up
- Explicit educational materials for parents (a key component of all American Academy of Pediatrics guidelines) concerning the identification of newborns with jaundice

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004 Jul;114(1):297-316. [28 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1994 Oct (revised 2004 Jul)

GUIDELINE DEVELOPER(S)

American Academy of Pediatrics - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Pediatrics

GUIDELINE COMMITTEE

Subcommittee on Hyperbilirubinemia

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Subcommittee on Hyperbilirubinemia: M. Jeffrey Maisels, MB, BCh, *Chairperson*; Richard D. Baltz, MD; Vinod K. Bhutani, MD; Thomas B. Newman, MD, MPH; Heather Palmer, MB, BCh; Warren Rosenfeld, MD; David K. Stevenson, MD; Howard B. Weinblatt, MD

Consultant: Charles J. Homer, MD, MPH, *Chairperson*, American Academy of Pediatrics Steering Committee on Quality Improvement and Management

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

M. Jeffrey Maisels received grant support from Natus Medical, Inc, for multinational study of ambient carbon monoxide; WellSpring Pharmaceutical Corporation for study of Stannsoporfin (tin-mesoporphyrin); and Minolta, Inc, for study of the Minolta/Hill-Rom Air-Shields transcutaneous jaundice meter model JM-103.

Vinod K. Bhutani received grant support from WellSpring Pharmaceutical Corporation for study of Stannsoporfin (tin-mesoporphyrin) and Natus Medical,

Inc, for multinational study of ambient carbon monoxide and is a consultant (volunteer) to SpectrX (BiliChek transcutaneous bilirubinometer).

David K. Stevenson is a consultant to and holds stock options through Natus Medical, Inc.

GUIDELINE STATUS

This is the current release of the guideline.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the American Academy of Pediatrics (AAP) Publications Web site.

Print copies: Available from AAP, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Questions and answers: jaundice and your newborns. Elk Grove Village (IL): American Academy of Pediatrics; 2004 June 25

Electronic copies: Available from the American Academy of Pediatrics (AAP) web site:

- English
- Spanish

Print copies: Available from AAP, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

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NGC STATUS

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