Breastfeeding, Jaundice and Hyperbilirubinemia in the Newborn

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Center for Health Sciences
Table of Contents

• Learning Objectives
• Practice Gap
• The Newborn Baby and Breast Milk
• A Few Benefits of Breast Feeding
• Clinical Reports
• A Few Contraindications to Breast Feeding

• Jaundice Associated with Breast Feeding
• Differential Diagnosis
• Prevention
• Treatment of Hyperbilirubinemia
• Questions...
• ...And Then Answers...
• Resources
Learning Objectives – Breastfeeding

1. Understand the qualitative and quantitative differences between human milk and various infant formulas
2. Recognize the presence and importance of various antibodies (including secretory IgA) in human milk and colostrum
3. Delineate the advantages to the baby of breastfeeding
4. Recognize when breast-feeding should be interrupted because of maternal infection
Learning Objectives – Hyperbilirubinemia

1. Plan the appropriate diagnostic evaluation of jaundice in a full-term infant
2. Understand the differences between physiologic jaundice in pre-term and full-term infants
3. Recognize the association between breast-feeding and physiologic jaundice in the neonatal period
4. Recognize the clinical features and sequelae of acute bilirubin encephalopathy in newborn infants, and manage appropriately
5. Understand strategies to prevent the development of severe hyperbilirubinemia in newborn infants
Practice Gaps

• Human milk provides substantial nutritional, cognitive, emotional, and immunologic benefits for the infant.

• Scientific study and research have accumulated and now constitute a large body of evidence documenting the actual benefits of breastfeeding for the infant and the mother.

• Jaundice occurs in most newborn infants.

• Most jaundice is benign, but because of the potential toxicity of bilirubin, newborn infants must be monitored to identify those who might develop severe hyperbilirubinemia and, in rare cases, acute bilirubin encephalopathy or kernicterus.
Disclosures

I have nothing to disclose.
The Newborn Baby and Breast Milk

aka “Your Baby Isn’t Perfect!”
Developmental Defects in Newborns

• Phagocytes:
  • Poor production, adhesion, migration for first 6 months of life

• Cell-mediated immunity:
  • Limited numbers of memory T-cells
  • Decreased cytokine production: IFN-alpha, IL-2, IL-4, IL-10
  • Poor stimulation of B-cells

• B-Lymphocytes and Immunoglobulins:
  • Limited quantity, quality antibody production
  • Poor Isotype switching
  • IgG production is limited, delayed (matures at 1–7 years of age)

• B-lymphocytes and Immunoglobulins:
  • Serum IgA levels are low (less than adult levels through 6–8 years of age)
  • Poor response to T-cell independent antigens (matures at 2–3 years of age)

• Complement cascade:
  • Decreased function in both the classical and the alternative pathways

## Selected Beneficial Properties of Human Milk

<table>
<thead>
<tr>
<th>Component</th>
<th>Property</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretory IgA</td>
<td>Specific antigen-targeted anti-infective action</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>Immunomodulation, iron chelation, antimicrobial action, anti-adhesive, trophic for intestinal growth</td>
</tr>
<tr>
<td>κ-Casein</td>
<td>Antiadhesive, bacterial flora</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Prevention of bacterial attachment</td>
</tr>
<tr>
<td>Cytokines</td>
<td>Anti-inflammatory, epithelial barrier function</td>
</tr>
</tbody>
</table>

## Selected Beneficial Properties of Human Milk

### Growth Factors

<table>
<thead>
<tr>
<th>Component</th>
<th>Property</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermal growth factor</td>
<td>Luminal surveillance, repair of intestine</td>
</tr>
<tr>
<td>Transforming growth factor (TGF)</td>
<td>• Promotes epithelial cell growth &lt;br&gt; • Suppresses lymphocyte function</td>
</tr>
<tr>
<td>Nerve growth factor</td>
<td>Promotes neural growth</td>
</tr>
</tbody>
</table>

### Enzymes

<table>
<thead>
<tr>
<th>Component</th>
<th>Property</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet-activating factor-acetylhydrolase</td>
<td>Blocks action of platelet-activating factor</td>
</tr>
<tr>
<td>Glutathione peroxidase</td>
<td>Prevents lipid oxidation</td>
</tr>
<tr>
<td>Nucleotides</td>
<td>Enhance antibody responses, bacterial flora</td>
</tr>
</tbody>
</table>

A Few Benefits of Breastfeeding

“Breast Milk is the Evidence”
Infant Outcomes with Human Milk

Comparison of Human Milk, Cow Milk, and Infant Formula

<table>
<thead>
<tr>
<th>Component</th>
<th>Human Milk</th>
<th>Similac®/Enfamil® Formulas</th>
<th>Cow Milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (kcal/L)</td>
<td>747</td>
<td>700</td>
<td>701</td>
</tr>
<tr>
<td>Protein (g/100 mL)</td>
<td>1.1</td>
<td>1.5</td>
<td>2.8</td>
</tr>
<tr>
<td>Casein</td>
<td>3.7</td>
<td></td>
<td>25.0</td>
</tr>
<tr>
<td>Taurine (mM/100 mL)</td>
<td>25 to 30</td>
<td>Added artificially</td>
<td>&lt; 1.0</td>
</tr>
<tr>
<td>Phenylalanine (mg/100 mL)</td>
<td>48</td>
<td>390 mM/100 mL</td>
<td>172</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>61</td>
<td></td>
<td>179</td>
</tr>
<tr>
<td>Fat (g/1,000 mL)</td>
<td>4.5</td>
<td>2.6</td>
<td>4.4</td>
</tr>
<tr>
<td>Cholesterol (mg/L)</td>
<td>139</td>
<td>0</td>
<td>120</td>
</tr>
<tr>
<td>Carbohydrate (g/1,000 mL)</td>
<td>6.8</td>
<td>7.2</td>
<td>4.7</td>
</tr>
<tr>
<td>Minerals ash (weight %)</td>
<td>0.2</td>
<td>0.33</td>
<td>0.7</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>34</td>
<td>55</td>
<td>118</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>14</td>
<td>44</td>
<td>93</td>
</tr>
<tr>
<td>Calcium/phosphorus ratio</td>
<td>2.4:1</td>
<td>1.2:1</td>
<td>1.3:1</td>
</tr>
<tr>
<td>Sodium (g/L)</td>
<td>0.512 (7 mL Eq/L)</td>
<td>1.1 (6 mL Eq/L)</td>
<td>0.768 g/L</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>4 to 40 IU/L</td>
<td>400 IU</td>
<td>47 to 100 IU</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>0.9 to 6.9 mg/L</td>
<td>4 mg/100 kcal</td>
<td>19 mg/L</td>
</tr>
</tbody>
</table>

Similac® is a product of Abbott Laboratories, North Chicago, IL. Enfamil® is a product of Mead Johnson & Co, Evansville, IN.
Clinical Reports
Relevant Steps in the US Surgeon General’s Call to Action to Support Breastfeeding

1. Give mothers the support they need to breastfeed their infants.
8. Develop systems to guarantee continuity of skilled support for lactation between hospitals and health care settings in the community.
9. Provide education and training in breastfeeding for all health professionals who care for women and children.
10. Include basic support for breastfeeding as a standard of care for midwives, obstetricians, family physicians, nurse practitioners, and pediatricians.

Summary of Breastfeeding Supportive Office Practices

2. Train staff in breastfeeding support skills
3. Discuss breastfeeding during prenatal visits and at well-child visits
4. Encourage exclusive breastfeeding for \( \sim 6 \text{ months} \)
7. Educate mothers on breast-milk expression and return to work
8. Provide noncommercial breastfeeding educational resources for parents
13. Link with breastfeeding community resources
14. Monitor breastfeeding rates in your practice

Jaundice Associated with Breastfeeding
## Patterns of Milk Supply

<table>
<thead>
<tr>
<th>Day of Life</th>
<th>Milk Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Some milk (~5 mL) may be expressed</td>
</tr>
<tr>
<td>Days 2-4</td>
<td>Lactogenesis, milk production increases</td>
</tr>
<tr>
<td>Day 5</td>
<td>Milk present, fullness, leaking felt</td>
</tr>
<tr>
<td>Day 6 onward</td>
<td>Breasts should feel “empty” after feeding</td>
</tr>
</tbody>
</table>

Breastfeeding Jaundice

• Early-onset, indirect hyperbilirubinemia in breastfed infants
  • Hyperbilirubinemia (>12 mg/dL) develops in 13% of breastfed infants
  • Decreased milk intake with dehydration and/or reduced caloric intake.
  • Frequent breastfeeding (>10/24 hr), rooming-in with night feeding, and
    ongoing lactation support may reduce the incidence

• Even when breastfeeding jaundice develops, breastfeeding should be
  continued if possible.
  • It is an option to hold breast-feedings and substitute formula for a day or two.
  • Frequent breastfeeding and supplementation with formula is appropriate if
    intake seems inadequate, weight loss is excessive, or signs of dehydration.
Maximum Bilirubin Levels

• Breast-fed infants typically will have higher maximum bilirubin levels
  • They will typically clear their bilirubin more quickly

• Bottle-fed infants typically will have lower maximum bilirubin levels
  • They will typically clear their bilirubin more slowly

Breast Milk Jaundice

• Significant elevation in unconjugated bilirubin in 2% of breastfed term infants after the 7th day
  • Maximal concentrations: 10-30 mg/dL, reached during the 2nd-3rd wk.
  • If breastfeeding is continued, bilirubin gradually decreases but may persist for 3-10 wk at lower levels.
  • If nursing is discontinued, the serum bilirubin level falls rapidly, reaching normal range within a few days.
  • Resumed breastfeeding seldom returns bilirubin to previously high levels.

• The etiology of breast milk jaundice is not entirely clear
  • Presence of glucuronidase in some breast milk
A Few Contraindications to Breastfeeding

“Breast Feeding Really Isn’t for Everybody!”
Contraindications to Breastfeeding

• Infant Conditions
  • Classic galactosemia (galactose 1-phosphate uridyltransferase deficiency)
  • Maple syrup urine disease
  • Phenylketonuria (partial breastfeeding is possible with careful monitoring)
Contraindications to Breastfeeding

• Maternal Conditions
  • Human immunodeficiency virus 1 infection (if replacement feeding is acceptable, feasible, affordable, sustainable, and safe)
  • Human T-lymphotropic virus 1 and 2 infection (varies by country; in Japan, breastfeeding is initiated)
  • Tuberculosis (active, untreated pulmonary tuberculosis, until effective maternal treatment for the initial 2 weeks or the infant is receiving isoniazid)
  • Herpes simplex virus infection on a breast (until the lesions on the breast are cleared)
  • Medications (those of concern)
Introduction to Hyperbilirubinemia
Introduction

• Jaundice is observed during the 1st wk after birth in approximately 60% of term infants and 80% of preterm infants.
  • Usually from accumulation of unconjugated, nonpolar, lipid-soluble bilirubin pigment in the skin
  • End product of heme-protein catabolism in the reticuloendothelial cells
  • Elevations of indirect, unconjugated bilirubin are potentially neurotoxic.
• The conjugated form is not neurotoxic.
• Direct hyperbilirubinemia indicates a potentially serious hepatic disorder or a systemic illness.
The Reason is Prevention of Kernicterus

- Develops in 30% of infants with untreated hemolytic disease and bilirubin levels >25-30 mg/dL.
- Overt neurologic signs have a grave prognosis
  - More than 75% of infants die
  - 80% of affected survivors have bilateral choreoathetosis with involuntary muscle spasms
  - Mental retardation, deafness, and spastic quadriplegia are common.

<table>
<thead>
<tr>
<th>Table 102-5 Clinical Features of Kernicterus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACUTE FORM</strong></td>
</tr>
<tr>
<td>Phase 1 (1st 1-2 days): poor suck, stupor, hypotonia, seizures</td>
</tr>
<tr>
<td>Phase 2 (mid 1st wk): hypertonia of extensor muscles, opisthotonos, retrocollis, fever</td>
</tr>
<tr>
<td>Phase 3 (after 1st wk): hypertonia</td>
</tr>
<tr>
<td><strong>CHRONIC FORM</strong></td>
</tr>
<tr>
<td>1st year: hypertonia, active deep tendon reflexes, obligatory tonic neck reflexes, delayed motor skills</td>
</tr>
<tr>
<td>After 1st yr: movement disorders (choreoathetosis, ballismus, tremor), upward gaze, sensorineural hearing loss</td>
</tr>
</tbody>
</table>

Kernicterus

• Neurologic syndrome resulting from the deposition of unconjugated (indirect) bilirubin in the basal ganglia and brainstem nuclei.

• The pathogenesis of kernicterus is multifactorial
  • Unconjugated bilirubin levels
  • Albumin binding and unbound bilirubin levels
  • Passage across the blood-brain barrier
  • Neuronal susceptibility to injury.

• Disruption of the blood–brain barrier and maturational changes in blood–brain barrier permeability affect risk.
Etiology
Etiology

• Metabolism of bilirubin
  • Fetal stage, the placenta
  • Adult stage, conjugated form excreted from hepatic cells into the biliary system and gastrointestinal tract

• Unconjugated hyperbilirubinemia may be caused or increased by
  1. Increased load of bilirubin
  2. Damaged or reduced activity of the transferase enzyme
  3. Competing or blocking enzyme
  4. Absence or decreased amount of enzyme
Bilirubin Production in Neonates

- Neonatal production rate of bilirubin
  - 6-8 mg/kg/24 hr
  - 3-4 mg/kg/24 hr in adults
- Intestinal or milk-containing glucuronidases
  - Enterohepatic recirculation of bilirubin
  - Can lead to hyperbilirubinemia
# Major Risk Factors for Severe Hyperbilirubinemia

<table>
<thead>
<tr>
<th>In Approximate Order of Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predischarge TSB level in the high-risk zone</td>
</tr>
<tr>
<td>Jaundice observed in the 1st 24 hr</td>
</tr>
<tr>
<td>Blood group incompatibility with positive direct antiglobulin test</td>
</tr>
<tr>
<td>Gestational age 35-36 wk</td>
</tr>
<tr>
<td>Previous sibling received phototherapy</td>
</tr>
<tr>
<td>Cephalohematoma or significant bruising</td>
</tr>
<tr>
<td>Exclusive breastfeeding, i.e., poor nursing, excessive weight loss</td>
</tr>
<tr>
<td>East Asian race</td>
</tr>
</tbody>
</table>
## Minor Risk Factors for Severe Hyperbilirubinemia

<table>
<thead>
<tr>
<th>In Approximate Order of Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predischarge TSB level in the high intermediate-risk zone</td>
</tr>
<tr>
<td>Gestational age 37-38 wk</td>
</tr>
<tr>
<td>Jaundice observed before discharge</td>
</tr>
<tr>
<td>Previous sibling with jaundice</td>
</tr>
<tr>
<td>Macrosomic infant of a diabetic mother</td>
</tr>
<tr>
<td>Maternal age ≥25 yr</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
</tbody>
</table>
Additional Risk Factors

• Neurotoxic effect risk factors
  • Permeability of the blood–brain barrier
  • Asphyxia
  • Prematurity
  • Hyperosmolality
  • Infection

• Breastfeeding and dehydration increase serum levels of bilirubin

• Meconium contains 1 mg bilirubin/dL
  • Delayed passage is a risk via enterohepatic recirculation

• Risk factors for unconjugated hyperbilirubinemia
  • Polycythemia
  • Infection
  • Prematurity
  • Infant of a diabetic mother
Differential Diagnosis
Reasoning Behind Lack of Workup...

- ALL of these common reasons for jaundice:
  - Have a negative Coombs test
  - Have a normal hemoglobin
  - Have a normal reticulocyte count
  - Have normal red cell morphology
  - Do NOT cause jaundice in 1st 24 hours
  - Do NOT cause prolonged hyperbilirubinemia
Diagnosis of Neonatal Jaundice:
Increased Indirect Bilirubin

- Positive Coombs test
  - Rh incomp.
  - ABO incomp.
  - Other blood group incomp.

- Polycythemia
  - Twin transfusion
  - Delayed cord clamping
  - SGA infant

- Increased reticulocyte count
  - G6PD
  - Spherocytosis
  - DIC
Timeline Considerations for Jaundice

- **Physiologic**
  - Erythroblastosis fetalis
  - Concealed hemorrhage
  - Sepsis
  - TORCH infections
  - At birth or within 1st 24 hours

- **Crigler-Najjar syndrome**
  - Early-onset breastfeeding
  - Polycythemia
  - Within first 2 to 3 days

- **Bacterial sepsis**
  - Urinary tract infection
  - TORCH infections
  - CMV, enterovirus
  - Within day 3 to day 6
Laboratory Evaluation Recommendation

• **RECOMMENDATION 3.0:** A TSB measurement should be performed on every infant who is jaundiced in the first 24 hours after birth. The need for and timing of a repeat TSB measurement will depend on the zone in which the TSB falls, the age of the infant, and the evolution of the hyperbilirubinemia.

Laboratory Evaluation of the Jaundiced Infant ≥35 Wk of Gestation

<table>
<thead>
<tr>
<th>Indications</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaundice in 1st 24 hours</td>
<td>Measure TSB</td>
</tr>
<tr>
<td>Jaundice appears excessive for patient’s age</td>
<td>Measure TSB</td>
</tr>
</tbody>
</table>
Laboratory Evaluation of the Jaundiced Infant ≥35 Wk of Gestation

<table>
<thead>
<tr>
<th>Indications</th>
<th>Assessment</th>
</tr>
</thead>
</table>
| Infant receiving phototherapy or TSB rising rapidly and unexplained by history and physical examination | • Blood type and Coombs test, if not obtained with cord blood  
• Complete blood count and smear  
• Measure direct or conjugated bilirubin  
• It is an option to perform reticulocyte count, G6PD, and ETCO, if available  
• Repeat TSB in 4-24 hr depending on infant’s age and TSB level |
Jaundice that Appears from Day 2 to Day 6

• Jaundice that first appears on the 2nd or 3rd day is usually physiologic.
• Jaundice secondary to extensive ecchymosis or blood extravasation (i.e., cephalohematoma) may occur during the 1st day or later, especially in premature infants.
Cause of Jaundice Recommendation

• **RECOMMENDATION 4.1:** The possible cause of jaundice should be sought in an infant receiving phototherapy or whose TSB level is rising rapidly (i.e., crossing percentiles) and is not explained by the history and physical examination.

*American Academy of Pediatrics Subcommittee on Hyperbilirubinemia: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation, Pediatrics 114:297–316, 2004*
A Small Graphic on the Schematic Approach to the Diagnosis of Neonatal Jaundice

- Blood type and Coombs test, if not obtained with cord blood
- Complete blood count and smear
- Measure direct bilirubin
- Optional: reticulocyte count, G6PD, and ETCO, if available
- Repeat TSB in 4-24 hr depending on infant’s age and TSB level
Diagnosis of Neonatal Jaundice: 
Increased Direct Bilirubin

- **Infectious**
  - Sepsis
  - TORCH

- **Anatomic**
  - Biliary atresia
  - Choledochal cyst

- **Hereditary**
  - Alagille syndrome

- **Metabolic**
  - Galactosemia
  - Cystic fibrosis
  - α-1-AD
  - Tyrosinemia
## Percentage of Cases of Cholestasis

<table>
<thead>
<tr>
<th>Major Diagnostic Categories of Prolonged Neonatal Cholestasis</th>
<th>Disorder</th>
<th>Cases, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Idiopathic neonatal hepatitis</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Extrahepatic biliary atresia (BA)</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>α₁-Antitrypsin deficiency</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Genetic syndromes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Progressive familial intrahepatic cholestasis</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>• Alagille syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bile acid secretory defects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TORCH syndrome</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Metabolic disorders</td>
<td>20</td>
</tr>
</tbody>
</table>
**Laboratory Evaluation of the Jaundiced Infant ≥35 Wk of Gestation**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSB concentration approaching exchange levels or not responding to phototherapy</td>
<td>Perform reticulocyte count, G6PD, albumin, ETCO if available</td>
</tr>
<tr>
<td>Elevated direct (or conjugated) bilirubin level</td>
<td>• Do urinalysis and urine culture</td>
</tr>
<tr>
<td></td>
<td>• Evaluate for sepsis if indicated by history and physical examination</td>
</tr>
</tbody>
</table>
Laboratory Evaluation of the Jaundiced Infant ≥35 Wk of Gestation

<table>
<thead>
<tr>
<th>Indications</th>
<th>Assessment</th>
</tr>
</thead>
</table>
| Jaundice present at or beyond age 3 wk, or sick infant | • Total and direct (or conjugated) bilirubin level  
• If direct bilirubin elevated, evaluate for causes of cholestasis  
• Check results of newborn thyroid and galactosemia screen, and evaluate infant for signs or symptoms of hypothyroidism |
Extensive Evaluation for Cholestasis

<table>
<thead>
<tr>
<th>Initial Laboratory Evaluation of the Neonate with Cholestasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractionated serum bilirubin concentration</td>
</tr>
<tr>
<td>Liver chemical tests: ALT, AST, alk phos, ( \gamma )-glutamyl transferase</td>
</tr>
<tr>
<td>Tests of liver function: glucose, albumin, cholesterol, coagulation studies</td>
</tr>
<tr>
<td>Ammonia (if clinically indicated)</td>
</tr>
<tr>
<td>CBC</td>
</tr>
<tr>
<td>( \alpha_1 )-Antitrypsin level and phenotype</td>
</tr>
</tbody>
</table>
Physiologic Jaundice
Indirect Hyperbilirubinemia Incidence

• Under normal circumstances, the level of indirect bilirubin rises at a rate of <5 mg/dL/24 hr
  • Jaundice becomes visible on the 2nd or 3rd day
  • Bilirubin levels usually peak between the 2nd and 4th day
  • Decrease to <2 mg/dL between the 5th and 7th day
  • Decline to adult levels (1 mg/dL) by 10th to 14th day

• Overall, 6-7% of full-term infants have indirect bilirubin levels >13 mg/dL and less than 3% have levels >15 mg/dL.

• Predicting risk for exaggerated physiologic jaundice is based on hour-specific bilirubin levels in the 1st 24-72 hr of life.
Expected Rate of Increase in Bilirubin and Maximum Bilirubin Levels

- Bilirubin starts low...
- ...increases at a slower rate as it nears max level...
- ...increases at its max rate...
- ...hits its peak...
- ...decreases...
- ...and hits normal levels.

• The maximum expected rate of increase of bilirubin in a term well newborn is:
  - 0.2 mg/dL/h, OR
  - 4.8 mg/dL/day
Clinical Assessment Recommendation

• **RECOMMENDATION 2.2:** Clinicians should ensure that all infants are routinely monitored for the development of jaundice. ... Jaundice should be assessed whenever the infant’s vital signs are measured...
  
  • Jaundice can be detected by blanching the skin with digital pressure to reveal underlying color of skin and subcutaneous tissue.
  
  • You must be in a well-lit room preferably in daylight by a window.
  
  • Jaundice is usually seen first in the face and progresses caudally to trunk and extremities.

Risk Assessment Before Discharge
Recommendations

• RECOMMENDATION 5.1: 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.

Risk Designation of Term Well Newborns
Risk Zone as a Predictor of Hyperbilirubinemia

<table>
<thead>
<tr>
<th>TSB Before Discharge</th>
<th>Newborns (Total = 2840), n (%)</th>
<th>Newborns Who Subsequently Developed a TSB Level &gt;95th Percentile, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk zone (&gt;95th percentile)</td>
<td>172 (6.0)</td>
<td>68 (39.5)</td>
</tr>
<tr>
<td>High intermediate-risk zone</td>
<td>356 (12.5)</td>
<td>46 (12.9)</td>
</tr>
<tr>
<td>Low intermediate-risk zone</td>
<td>556 (19.6)</td>
<td>12 (2.26)</td>
</tr>
<tr>
<td>Low-risk zone</td>
<td>1756 (61.8)</td>
<td>0</td>
</tr>
</tbody>
</table>

Outcomes of Newborns in the Low-risk Zone

<table>
<thead>
<tr>
<th>Predictive Characteristics</th>
<th>Value</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Predictive Value</td>
<td>11.6%</td>
<td></td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>64.7%</td>
<td></td>
</tr>
</tbody>
</table>

Outcomes of Newborns in the Low-intermediate-risk Zone

<table>
<thead>
<tr>
<th>Predictive Characteristics</th>
<th>Value</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Predictive Value</td>
<td>21.6%</td>
<td></td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>99.5%</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>90.5%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>84.7%</td>
<td></td>
</tr>
</tbody>
</table>

Outcomes of Newborns in the High-intermediate-risk Zone

- **Predictive Characteristics**

<table>
<thead>
<tr>
<th>Value</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Predictive Value</td>
<td>21.6%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>99.5%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>90.5%</td>
</tr>
<tr>
<td>Specificity</td>
<td>84.7%</td>
</tr>
</tbody>
</table>

Outcomes of Newborns in the High-risk Zone

<table>
<thead>
<tr>
<th>Predictive Characteristics</th>
<th>Value</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Predictive Value</td>
<td>39.5%</td>
<td></td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>97.8%</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>54.0%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>96.2%</td>
<td></td>
</tr>
</tbody>
</table>

Primary Prevention Recommendation

• RECOMMENDATION 1.0: Clinicians should advise mothers to nurse their infants at least 8 to 12 times per day for the first several days
  • Poor caloric intake and/or dehydration may contribute to development of hyperbilirubinemia.
  • Baby should have 4-6 wet diapers in 24 hours and pass 3-4 stools a day by the 4th day of life.
  • Stools should be mustard yellow and no longer meconium like.

Correlation of Breast-feeding Frequency and Incidence of Hyperbilirubinemia

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 2 hours</td>
<td>0%</td>
</tr>
<tr>
<td>Every 3 hours</td>
<td>12%</td>
</tr>
<tr>
<td>Every 4 hours</td>
<td>15%</td>
</tr>
<tr>
<td>Every 6 hours</td>
<td>25%</td>
</tr>
<tr>
<td>Every 12 hours</td>
<td>28%</td>
</tr>
</tbody>
</table>

Secondary Prevention Recommendations

• **RECOMMENDATION 2.0:** Clinicians should perform ongoing systematic assessments during the neonatal period for the risk of an infant developing severe hyperbilirubinemia.
  • Blood typing
  • Clinical assessment

*American Academy of Pediatrics Subcommittee on Hyperbilirubinemia: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation, Pediatrics 114:297–316, 2004*
Blood Typing Recommendation

• **RECOMMENDATION 2.1:** *All pregnant women should be tested for ABO and Rh (D) blood types and have a serum screen for unusual isoimmune antibodies.*
  • If no blood typing or mom is Rh -, then a DAT or Coombs’ test on infant’s cord blood is strongly recommended
  • If maternal blood type O+, it is an option to test cord blood for infant’s blood type and DAT but not required provided appropriate surveillance and follow-up

*American Academy of Pediatrics Subcommittee on Hyperbilirubinemia: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation, Pediatrics 114:297–316, 2004*
Hospital Policies and Procedures

Recommendations

• **RECOMMENDATION 6.1:** 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.

Timing of Follow-up

- All infants should be examined by qualified healthcare professional in first few days after discharge to assess infant well-being and presence of jaundice.
- Earlier follow-up visit may be necessary if patient has risk factors for hyperbilirubinemia; may need to see within 24 hours of discharge.

Timing of Follow-up

RECOMMENDATION 6.1.2: Follow-up should be provided as follows:

<table>
<thead>
<tr>
<th>Infant Discharged</th>
<th>Should Be Seen by Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before age 24 h</td>
<td>72 h</td>
</tr>
<tr>
<td>Between 24 and 47.9 h</td>
<td>96 h</td>
</tr>
<tr>
<td>Between 48 and 72 h</td>
<td>120 h</td>
</tr>
</tbody>
</table>

Treatment of Hyperbilirubinemia
Goals of Therapy

• Regardless of the cause, the goal of therapy is to prevent neurotoxicity related to indirect-reacting bilirubin while not causing undue harm.

• Phototherapy and, if it is unsuccessful, exchange transfusion remain the primary treatment modalities used to keep the maximal total serum bilirubin below pathologic levels.
Principles Behind Starting Phototherapy

• There is lack of consensus regarding the exact bilirubin level at which to initiate phototherapy.
• Because phototherapy may require 6-12 hr to have a measurable effect, it must be started at bilirubin levels below those indicated for exchange transfusion.
• Phototherapy is usually started at 50-70% of the maximal indirect level.
• If values greatly exceed this level, if phototherapy is unsuccessful in reducing the maximal bilirubin level, or if signs of kernicterus are evident, exchange transfusion is indicated.
Guidelines for Phototherapy

• Risk factors
  • Isoimmune hemolytic disease
  • G6PD deficiency
  • Asphyxia
  • Significant lethargy
  • Temperature instability
  • Sepsis
  • Acidosis
  • Albumin 3.0 g/dL (if measured)

### Suggested Maximal Indirect Serum Bilirubin Concentrations (mg/dL) in Preterm Infants

<table>
<thead>
<tr>
<th>BIRTHWEIGHT (g)</th>
<th>UNCOMPLICATED*</th>
<th>COMPLICATED*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1,000</td>
<td>12 – 13</td>
<td>10 – 12</td>
</tr>
<tr>
<td>1000 – 1,250</td>
<td>12 – 14</td>
<td>10 – 12</td>
</tr>
<tr>
<td>1,251 – 1,499</td>
<td>14 – 16</td>
<td>12 – 14</td>
</tr>
<tr>
<td>1,500 – 1,999</td>
<td>16 – 20</td>
<td>15 – 17</td>
</tr>
<tr>
<td>2,000 – 2,500</td>
<td>20 – 22</td>
<td>18 – 20</td>
</tr>
</tbody>
</table>

*Complications include perinatal asphyxia, acidosis, hypoxia, hypothermia, hypoalbuminemia, meningitis, intraventricular hemorrhage, hemolysis, hypoglycemia, or signs of kernicterus.
How Phototherapy Works

• Clinical jaundice and indirect hyperbilirubinemia are reduced by exposure to a high intensity of light in the visible spectrum.
  • Bilirubin absorbs light maximally in the blue range (420-470 nm).
  • Broad-spectrum white, blue, and special narrow-spectrum (super) blue lights have been effective in reducing bilirubin levels.

• Bilirubin in the skin absorbs light energy, causing several photochemical reactions.
  • Major products from phototherapy are an isomer which can then be excreted in bile without conjugation and an isomer that can be excreted by the kidneys.
Phototherapy Effectiveness

• Dependent factors
  1. Light energy emitted in the effective range of wavelengths
  2. Distance between the lights and the infant
  3. Surface area of exposed skin
  4. Rate of hemolysis
  5. In vivo metabolism and excretion of bilirubin

• Increasing effectiveness
  1. Using “special blue” fluorescent tubes
  2. Placing the lamps within 15-20 cm of the infant
  3. Putting a fiberoptic phototherapy blanket under the infant’s back to increase the exposed surface area
Phototherapy Considerations

• Skin color cannot be relied on for evaluating the effectiveness of phototherapy
  • Skin exposed to phototherapy may appear to be almost without jaundice

• NOT necessary for all affected infants, but
  • Intravenous fluid supplementation added to oral feedings
  • Dehydrated patients
  • Infants with bilirubin levels nearing those requiring exchange transfusion
Questions
Resources

Pediatric Review Education Program
American Academy of Pediatrics
Nelson Textbook of Pediatrics