Managing Jaundice in the Breastfed Infant

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Disclosures

• None

Goals

• Review the relationship between breastfeeding and jaundice

• Define pathologic versus physiologic jaundice

• Enable the healthcare provider to assist in initiation of breastfeeding and to support the mother-infant dyad during the evaluation and treatment of jaundice

• Reinforce the universal goal of preventing irreversible consequences of hyperbilirubinemia
Overview

- Historical background
- Pathophysiology of jaundice in the newborn
- Lack-of-breast-milk jaundice vs. breastmilk jaundice
- Breastfeeding and phototherapy
- Consequences of severe hyperbilirubinemia
- American Academy of Pediatrics Guidelines

History of Jaundice

- 1785, Jean Baptist Thimotee Baumes (France)\(^1\)
  - 10 jaundiced newborns, somnolent, poor feeding
  - Believed etiology was delayed passage of meconium; treatment using breastmilk and colostrum
- 1847, Jaques Francois Edouard Hervieux (France)
  - 45 autopsy cases, basis of the epidemiology and clinical course; described bilirubin in CSF
- 1872, Johannes Orth (Germany)
  - Basal ganglia, 3rd and 4th ventricles, hippocampus and cerebellum stained yellow; suggested hematologist cause
- 1904, Christian Georg Schmorl (Germany)
  - Coined the term kernicterus

Neonatal Jaundice

- Defined as “when the concentration of bilirubin in serum increases to the point where the accumulation of bilirubin in skin becomes visible to the unaided eye”\(^4\)
Physiologic Jaundice

- Physiologic jaundice results from normal neonatal bilirubin physiology
  - Commonly encountered in newborns despite feeding method

- Multiple factors
  - High blood volume and hemoglobin
  - Shorter RBC lifespan
  - Decreased hepatic enzyme activity
  - Absent gut flora to convert bilirubin for excretion
  - Increased activity of mucosal enzyme, re-uptake

Figure 1: Bilirubin metabolism in fetal and neonatal life
Hansen T. Bilirubin Metabolism (2010)

Non Physiologic Jaundice

1. Increased heme catabolism
   - Congenital hemolytic anemias: glucose-6-phosphate dehydrogenase deficiency, spherocytosis
   - Immunologically mediated hemolysis: Rh disease, ABO incompatibility
   - Extravasation of blood: bruising, intracranial hemorrhages
Non Physiologic Jaundice

2. Decreased bilirubin conjugation and excretion
   - Mutations in key enzymes, genetic defects in UDGPT: Crigler-Najjar, Gilbert’s
   - Hepatic and biliary disease: neonatal hepatitis, intra- and extrahepatic biliary atresia

Non Physiologic Jaundice

3. Increased enterohepatic circulation of bilirubin (4)
   - Decreased bowel passage: intestinal atresias, necrotizing enterocolitis, fasting, inadequate nutrition
     - Lack-of-breast-milk jaundice
   - Increased de-conjugation of bilirubin in the bowel
     - Breastmilk jaundice

Lack-of-breast-milk Jaundice

- Previously termed breastfeeding jaundice
  - “not enough breastfeeding jaundice”, “breast-nonfeeding jaundice”, “starvation jaundice”
- Occurs within first several days of life
- Small volume feeds → poor caloric intake, dehydration
- Increased enterohepatic circulation
  - Inadequate intake → decreased stool, increased reabsorption of bilirubin from the gut, increased unconjugated hyperbilirubinemia
Preventing Lack-of-breast-milk Jaundice

- Support the mother-infant dyad
- Early initiation of breastfeeding
- Frequent exclusive breastfeeding
- Optimizing skin-to-skin contact, rooming in, preventing separation
- Educate about feeding cues
- Assess infant’s intake

Assessment of Adequate Intake

- Poor feeding
- Excessive weight loss
  - Maximum weight loss 6.1% +/- 2.5% (SD) of birth weight by DOL 3
- Decreased urine and stool output
  - 4 to 6 wet diapers in 24 hours
  - 3 to 4 stools in 24 hours by DOL 4
- Failure to clear meconium
  - Stools change to mustard yellow, mushy stool by DOL 3 to 4

Assessment of Additional Risk Factors

- Identifying infants at risk for hyperbilirubinemia
  - Family history: previous jaundiced infant, G6PD, Gilbert’s
  - ABO incompatibility
  - Mother with minor blood group antibodies (anti-c, anti-E, anti-e)
  - Rh sensitization
  - Significant bruising
Addressing Lack-of-breast-milk Jaundice

- Mothers:
  - Lactation specialist
  - Encourage mothers to pump frequently, goal is to increase supply
- Infant:
  - Serum bilirubin levels
  - Phototherapy, if required
  - Close monitoring for dehydration
  - Supplement with expressed breast milk

Breastmilk Jaundice

- Etiology not completely known
- Theories:
  - Higher levels of epidermal growth factors in serum and milk → enhancing intestinal absorption of unconjugated bilirubin
  - High levels of beta-glucuronidase in human milk
  - Inhibits hepatic glucuronyl transferase, promoter of bilirubin conjugation

Breastmilk Jaundice

- Develops at the end of 1st week of life, 2nd week of life
- Pattern of bilirubin level:
  - Peaks on DOL 4 to 5
  - Possible second rise in level by 2nd week of life
  - Declines over weeks to normal level by 3 months of age
  - Level usually less than 20-25 mg/dl
Diagnosing Breastmilk Jaundice

- Infant must demonstrate
  - Normal weight gain
  - Normal stool and urine output
  - Normal examination
  - Thriving
  - Total bilirubin level < 12 mg/dl
- AND other causes ruled out clinically or by laboratory evaluation

Formula and Breastmilk Jaundice

- Historically, substituting formula demonstrated a decrease in bilirubin level
- Adverse effects:
  - May jeopardize infant’s ability to return to exclusive breastfeeding
  - Trial may falsely reassure diagnosis while preventing evaluation of underlying etiology
  - Interrupt mother-infant dyad

Addressing Breastmilk Jaundice

- No intervention needed if bilirubin level < 12 mg/dl
  - Continue breastfeeding
- If bilirubin level > 12 mg/dl
  - Evaluation to identify factors contributing or exaggerating hyperbilirubinemia
  - May require phototherapy depending on the level and post-natal age
### Characteristic Differences

<table>
<thead>
<tr>
<th></th>
<th>Lack-of-breast-milk Jaundice</th>
<th>Breastmilk Jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presentation</strong></td>
<td>1st week of life</td>
<td>Late in 1st week to 2nd week of life</td>
</tr>
<tr>
<td><strong>Feeding</strong></td>
<td>Poor</td>
<td>Well</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>Excessive weight loss or poor weight gain</td>
<td>Normal weight gain</td>
</tr>
<tr>
<td><strong>Urine</strong></td>
<td>Infrequent urine output</td>
<td>Frequent urine output</td>
</tr>
<tr>
<td><strong>Stool</strong></td>
<td>Infrequent meconium or transitional stools</td>
<td>Frequent yellow stools</td>
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<tr>
<td><strong>Treatment</strong></td>
<td>1. Bilirubin measurement</td>
<td>Further evaluation depending on bilirubin level</td>
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<td></td>
<td>2. Phototherapy, if indicated</td>
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<tr>
<td><strong>Breastfeeding Management</strong></td>
<td>1. Lactation support</td>
<td>Continue breastfeeding</td>
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<tr>
<td></td>
<td>2. Continue breastfeeding</td>
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<tr>
<td>Resolution</td>
<td>Resolves with improved enteral intake and bilirubin excretion in stool</td>
<td>Spontaneous, gradually resolves over the first 2-3 months of life</td>
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</table>

Table 1: Raso, Phillips (2011)

### Indications for Further Evaluation

- Evaluation of pathologic etiologies required for
  - Jaundice presenting within first 24 hours of life
  - Prolonged hyperbilirubinemia
  - Elevated levels of bilirubin
  - Rapidly rising bilirubin > 0.5 mg/dl per hour
  - Ongoing hemolysis

### Laboratory Evaluation

- Jaundice excessive for age or appears in first 24 hours of life
- Measurement of transcutaneous or serum bilirubin
- Infant receiving phototherapy, bilirubin levels rising, unexplained by history of physical examination
  - Blood type, Coombs test, complete blood count, smear, direct bilirubin level, trend bilirubin
  - Rapidly rising, not responding to phototherapy
    - Reticulocyte count, testing for G6PD, sepsis evaluation
Promoting Breastfeeding During Phototherapy

- Ideally performed in mother’s room, minimize mother-infant separation
- Breastfeeding should be continued
  - If not feeding vigorously, consider syringe or gavage feedings
- Interruption of phototherapy up to 30 minutes will not alter the effectiveness of treatment

Urgent or Emergent Cases

- A period of temporary interruption of breastfeeding may be clinically warranted
  - Intravenous fluid correction for severe hypernatremia, hypoglycemia, systemic illness
- Decision making should involve family, care plan individualized
  - Goal is always to keep mother and infant together
  - Preserve breastfeeding, continue maintaining mothers milk
Kernicterus

- Acute Bilirubin Encephalopathy (7)
  - Describes the acute manifestations of bilirubin toxicity
  - Clinical findings: hypertonia, arching, retrocollis, opisthotonos, high-pitched cry
  - Can progress to kernicterus
- Kernicterus (7)
  - Describes the chronic and permanent clinical sequela of bilirubin toxicity (chronic bilirubin encephalopathy)
  - Clinical findings: athetoid cerebral palsy, auditory dysfunction, paralysis of upward gaze, variable intellectual disabilities

Kernicterus and Breastfeeding?

- Breastfeeding risk factor for severe hyperbilirubinemia
  - Newman et al (2000): family history and breast-feeding were the two strongest predictors of a peak total serum bilirubin > 25 mg/dl (8)
  - United States Kernicterus Registry: 125 infants developed kernicterus; 98% were fully or partially breastfed (6)
- Unique combination with other factors that contributes to kernicterus
- Our role is to support the breastfeeding mother and to continue close monitoring of the breastfed infant

- Aim was to develop an “approach that will reduce frequency of severe hyperbilirubinemia and bilirubin encephalopathy”
- Reduce “unintended harm, such as anxiety, decreased breastfeeding, unnecessary treatment for the general population”

Key Elements

1. Promote and support successful breastfeeding
2. Establish early feeding protocols for the identification and evaluation of hyperbilirubinemia
3. Measure the total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) level on infants jaundiced in the first 24 hours
4. Recognize that visual estimation of the degree of jaundice can lead to errors, particularly in darkly pigmented infants
5. Interpret all bilirubin levels according to the infant’s age in weeks

AAP Guideline: Primary Prevention

- RECOMMENDATION 1.0: Clinicians should advise mothers to nurse their infants at least 8 to 12 times per day for the first several days
  - Provide appropriate support and advice to breastfeeding mothers
  - Increase likelihood of successful breastfeeding

- RECOMMENDATION 1.1: The AAP recommends against routine supplementation of nondehydrated breastfed infants with water or dextrose

AAP Guideline: Secondary Prevention

• **RECOMMENDATION 2.0:** Clinicians should perform ongoing systematic assessments during the neonatal period for the risk of an infant developing severe hyperbilirubinemia
  - ABO and Rh (D) blood type testing

• **RECOMMENDATION 2.2:** 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.
  - Assess skin, evaluating head and then trunk/extremities, nursing with ability to obtain TcB or TSB


AAP Guideline: Laboratory Evaluation

• **RECOMMENDATION 3.0:** A TcB and/or TSB measurement should be performed on every infant who is jaundiced in the first 24 hours after birth.
  - Need to repeat measurement depends on the zone and evolution of hyperbilirubinemia

• **RECOMMENDATION 3.1:** A TcB and/or TSB measurement should be performed if the jaundice appears excessive for the infant’s age. Visual estimation of bilirubin levels from the degree of jaundice can lead to errors.


AAP Guideline: Risk Assessment Before Discharge

• **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.
  - Use of 2 clinical options used individually or in combination for the systematic assessment of risk: TSB or TcB and/or assessment of clinical risk factors

AAP Guideline: Follow up

• RECOMMENDATION 6.1.2: 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.
• Timing of assessment based on length of stay in the nursery and risk factors


References

2. Kernicterus picture. Pickonline.org. 2018
4. Hansen T. Bilirubin Metabolism. Neoreviews. 2010; 11; e316