BREAST FEEDING AND NEONATAL HYPERBILIRUBINEMIA

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No Conflicts to declare
Disclosure

• Neither I nor any member of my immediate family has a financial relationship or interest (currently or within the past 12 months) with any proprietary entity producing health care goods or services consumed by, or used on, patients related to the content of this CME activity.

• I do not intend to discuss an unapproved/investigative use of a commercial product/device.
LEARNING OBJECTIVES

At the conclusion of this presentation, you should be able to:

1. Know the actual relationship between breast feeding and neonatal hyperbilirubinemia.
2. Use the hour-specific bilirubin nomogram
3. Restore Systems Integrity
4. Resolve immediate hurdles to effective phototherapy
5. Foster benign outcomes for neonatal hyperbilirubinemia.
BILIRUBIN METABOLISM

TB (at any given time) \textbf{EQUALS} BILIRUBIN PRODUCTION (hemolysis) \textbf{PLUS} REABSORBED BILIRUBIN (GA, weeks) \textbf{MINUS} BILIRUBIN ELIMINATION
1. Jaundice is a clinical sign
2. This condition is related to bilirubin level
3. Newborn jaundice is not a clinical diagnosis
4. We need to rely on bilirubin level and,
5. We modulate its magnitude for age (hours), prematurity (days) and assess bilirubin production.

Old: physiologic or pathological jaundice
New: Benign or Adverse Hyperbilirubinemia
How common is the problem: Benign vs Adverse

• Jaundice: 80-84% of all term and late preterm newborns

BENIGN:
• Hyperbilirubinemia: TB <40th percentile for age in hours
• ADVERSE: Mild: Use of phototherapy, Severe: Use of Exchange transfusion

ADVERSE:
• USA risk of Kernicterus ~1.4 per 100,000 live-births
• Risk of Kernicterus in USA/CANADA/UK/EUROPE:
  - TB <25 mg/dL: when confounded by sepsis and high NMR
  - TB 25-30 mg/dL: 1 in 17
  - TB 31-35 mg/dL: 1 in 12
  - TB >35 mg/dL: Nearly all
Changes you may wish to make in practice

1. Know your screening set-up and systems.
2. Promote breast feeding
3. Drill the team’s responsiveness to urgency
4. Develop institutional guidelines for management.
Case 1: healthy baby with adverse outcomes

Term baby is being discharged from Well Baby Nursery

- Breast feeding
- Alert and normal; may have icterus, noted night before
- TcB was done at discharge
- Assess bilirubin risk
- Follow-up is arranged.
PRE-DISCHARGE SCREENING
Assess Risk of Neonatal Hyperbilirubinemia.

• How do you assess risk? for bilirubin >10, 15, 20 or 25 mg/dL?
• Clinical factors: prematurity, gender, race, ethnicity, age (hours)
• Bilirubin: adjust TB to age in hours & percentile risk zones
• Process. TcB, TB. Plot value on a bilirubin nomogram
• Project (measure) TB rate of rise (ROR)
• Know signs for ABE (acute bilirubin encephalopathy)
How to use the Nomogram?

Fig 2. Risk designation of term and near-term well newborns based on their hour-specific serum bilirubin values. The high-risk zone is designated by the 95th percentile track. The intermediate-risk zone is subdivided to upper- and lower-risk zones by the 75th percentile track. The low-risk zone has been electively and statistically defined by the 40th percentile track. (Dotted extensions are based on <300 TSB values/epoch).
Pre-discharge identification of severe hyperbilirubinemia at age ≤7 days

TSB = 8.1 mg/dL at age 30 hours
WHY DO YOU SCREEN?
Your baby has hyperbilirubinemia, because

- First, TB >75th %ile, (high risk zone) as plotted
- Next, assess room you have before harm ensues.
- Next, project the rate of rise to reach neurotoxicity (time when it reaches to PhotoRx threshold or harm.
- The margin could be narrow and dangerous unless you measure the rate of bilirubin rise.
Myth: There is a specific bilirubin level at which injury occurs

1. Not true
2. Depends on bilirubin rate of rise
3. Depends on biology: prematurity/illness
4. Relies on albumin-binding of bilirubin.
Increased rate of TSB rise (>0.2 mg/dL/h)

TSB Rate of Rise: >0.2 mg/dL/hour
Increased rate of TSB rise (>0.2 mg/dL/h)

TSB Rate of Rise: >0.2mg/dL/hour
Fig 4. Outcome of newborns as defined by the percentage that remains or moves up to the high-risk zone after their risk assessment with the predischARGE bilirubin value (represented by the shaded area). A, Outcome for newborns designated in the high-risk zone (n = 172); B, outcome of newborns in upper intermediate-risk zone (n = 356); C, outcome of newborns in the lower intermediate-risk zone (n = 556); D, outcome of newborns in the low-risk zone (n = 1756).
Figure 3. The ROC curve for the predictive abilities of the 40th, 75th, and the 95th percentile-based risk zones and their false-positive and false-negative rates (%). (Its location in the upper left corner is indicative of the usefulness of the risk zones.)

TABLE 2. Predictive Characteristics of Percentile Tracks as Risk Demarcators for Location of Predictive PredischARGE TSB Vector Outcome: Subsequent Significant Hyperbilirubinemia

<table>
<thead>
<tr>
<th>Percentile Track as Risk Demarcator</th>
<th>Number of Newborns (Total = 2840)</th>
<th>Present (Total = 126)</th>
<th>Absent (Total = 2714)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above 95th percentile</td>
<td>172</td>
<td>68</td>
<td>104</td>
</tr>
<tr>
<td>Below 95th percentile</td>
<td>2668</td>
<td>58</td>
<td>2610</td>
</tr>
<tr>
<td>Above 75th percentile</td>
<td>528</td>
<td>114</td>
<td>414</td>
</tr>
<tr>
<td>Below 75th percentile</td>
<td>2312</td>
<td>12</td>
<td>2300</td>
</tr>
<tr>
<td>Above 40th percentile</td>
<td>1084</td>
<td>126</td>
<td>958</td>
</tr>
<tr>
<td>Below 40th percentile</td>
<td>1756</td>
<td>0</td>
<td>1756</td>
</tr>
</tbody>
</table>
Thus, when you plot of TB for risk status

1. You assess TB rate of rise (ROR) >0.2 mg/dL/hour
2. You can assess how soon the TB reaches a level of 20 or, at the time of next visit, what is the likely TB.
3. You can guestimate TB ROR from birth (cord blood).
4. You can decide when to schedule the first follow-up visit.
5. You may reassure the family if TB (<40th percentile).
Major Reasons for Increased TB ROR

Rhesus disease
ABO incompatibility (regardless of DAT)
Bruises and hematomas
G6PD enzyme deficiency
Inherited RBC disorders
Unusual bilirubin elimination disorders.
SCREEN TO GUIDE FOLLOW-UP
Follow-Up (Pediatrics, 2009).

A

Gestational age
35–37⁶/₇ wk + other hyperbilirubinemia risk factors

Predischarge TcB/TSB

Assign bilirubin risk zone

High
Evaluate for phototherapy
TSB in 4–8 h

High-intermediate
Evaluate for phototherapy
TSB/TcB in 4–24 h

Low-intermediate
If discharging <72 h, follow-up within 2 d
Consider TSB/TcB at follow-up

Low
If discharging <72 h, follow-up within 2 d

AAP. 2009
AAP. 2009

Gestation 35–37\textsuperscript{6/7} wk, no hyperbilirubinemia risk factors 
or
Gestation ≥38 wk + other hyperbilirubinemia risk factors\textsuperscript{a}

Predischarge TcB/TSB

Assign bilirubin risk zone\textsuperscript{b}

High
- Evaluate for phototherapy\textsuperscript{c}
  - TSB in 4–24 h\textsuperscript{d}

High-intermediate
- Evaluate for phototherapy
  - TcB/TSB within 24 h\textsuperscript{d}

Low-intermediate
- If discharging <72 h, follow-up within 2 d

Low
- If discharging <72 h, follow-up within 2–3 d
C

Gestation \( \geq 38 \) wk, no hyperbilirubinemia risk factor

Predischarge TcB/TSB

Assign bilirubin risk zone

- High
  - Evaluate for phototherapy
  - TSB in 4–24 h

- High-intermediate
  - Follow-up within 2 d
  - Consider TcB/TSB at follow-up

- Low-intermediate
  - If discharging <72 h, follow-up within 2–3 d

- Low
  - If discharging <72 h, time follow-up according to age at discharge or concerns other than jaundice (e.g., breastfeeding)

AAP. 2009
THE OFFICE CRISIS
Case 2: healthy babies with adverse outcome

Late preterm, @36 weeks, is having a rough morning,
1. You ask: “what happened?”
2. You check for any neurologic signs?
3. Where would you manage this baby?
4. What is the risk of bilirubin neurotoxicity?
Case 2: Assess for risk of bilirubin neurotoxicity

- History and physical exam (neurologic)
- Assess for sub-optimal breastfeeding
- Check Bilirubin level and TB ROR
- Track response to phototherapy
- Quality Measure: timeliness (drill and practice)
Bilirubin Reduction Strategies

1. Assess bilirubin risk status
2. Assess for hemolysis
3. Promote enteral feeds.
4. Consider natural resolution with age.
5. Consider use of phototherapy

Exchange transfusion is the last resort but risky.
The American Heart Association/American Stroke Association (AHA/ASA) practice guidelines recommend Intravenous Streptokinase, is recommended for selected patients within 3 hours of ischemic stroke sign/symptom.

The AAP practice guidelines recommend Effective Phototherapy is recommended for patients with severe neonatal hyperbilirubinemia as soon as possible.
Myth: You can use any light.

1. NO.
2. Specific Blue Light (LED): 476nm.
3. Select dose: 25-35 microwatts/cm²
4. Initial dose for uninterrupted 6 hours
Other treatments: none proven or harmful

- No Laxatives, Suppositories, Cathartics
- No known medication or chemoprevention
- Role of IVIG. Unproven
- IV fluids. None needed, only if baby is dehydrated
- Direct Sunlight. NO. NO. NO. NO
BILIRUBIN MINEFIELD
• Read AAP “fine print” about G6PD def.
• Know: it occurs in 12.2% of AA male
• Know: for East Asians, Hispanics and Native Americans it is ~5%.
• Know: Caucasian female: 0% incidence; unless, Italian or Greek (Med)
• Concurrent B-UGT immaturity/mutation
• Triggers are in the environment, sepsis, certain foods and drugs (in breast milk).
Bilirubin Elimination Disorders

- Starvation: sub-optimal breast feeds
- Prematurity: each week of GA
- Illness: Urosepsis, Sepsis, Hypothyroidism, IEM
- UGT immaturity
- UGT mutation (Gilbert’s disease)
- UGT defect (partial): Crigler Najjar II
- UGT absence: Crigler Najjar I
Case 3: When is bilirubin ROR dangerous?

- Unrecognized hemolysis such as Iso-immunization, G6PD def, inherited RBC defects, etc
- Bilirubin ROR is $>0.25 \text{ mg/dL/hour}$ or 6 mg/in 24 hours
- Associated factors: Albumin level, Altered bilirubin binding to albumin, appearance of “free bilirubin”. Infant vulnerability.
MYTH: Exchange Transfusion Cures Kernicterus

- Exchange dramatically lowers bilirubin
- However, underlying process continues
- Bilirubin blood-brain breach not a threshold
- Breach of blood brain barrier: injury continues
- Babies manifest neurotoxicity post-exchange
- Exchange saves life; it is not brain protective.
SWISS-CHEESE MODEL OF HEALTHCARE
Where the seams of care are breached

1. Not knowing that the baby is hemolyzing
2. Not knowing the TB ROR
3. Not knowing worrying about prematurity
4. Not letting the baby starve
5. Not scheduling a precise follow-up visit
6. Not recognizing a dire situation in your office.
7. Not referring a distressed baby to ED.
8. Not knowing that photons act immediately
9. No one can rescue you by doing a timely ExTx.
10. Not following up an adverse event.
TAKE-HOME MESSAGES FOR YOUR PRACTICE

KNOW YOUR SYSTEM’S INTEGRITY.

1. Mostly hyperbilirubinemia is benign and responsive
2. Systems-approach can monitor for timeliness
3. Use of effective phototherapy (should be <6%).
4. Remain vigilant for early signs of ABE
5. When needed, team acts urgently for timely interventions
SUMMARY

• Pre-discharge screening to ensure benign outcome.
• Hyperbilirubinemia is often predictable and can be managed.
• Diverse manifestations such that it may be unpredictable.
• Favism (G6PD def.) is often under-predicted.
• Direct re-admission to the NICU is the safest option.
• Most readmitted infants need immediate intervention.
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• Hyperbilirubinemia is often predictable and can be managed
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• Most readmitted infants need immediate intervention.

PHOTOTHERAPY DELIVERS PHOTONS THAT HAVE IMMEDIATE EFFECT
Thank You!

You may contact me at bhutani@stanford.edu if you have any answered questions about bilirubin.
References

2. AAP 2009. Clarifications (Follow-up)
3. AAP TECHNICAL REPORT for phototherapy (2011)
4. NEOREVIEW (2012). Neonatal G6PD deficiency