Safe and Healthy Beginnings

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Risk Factors

• There are 2 kinds
  – Those that increase the risk of subsequently developing a high bilirubin level (↓gestation, breastfeeding, TSB/TcB >75th percentile, bruising etc). **Use these in assessing risk before the baby is discharged and at the first follow up visit**
  – Those that increase the risk of brain damage at a particular bilirubin level. **Use these in deciding when to start phototherapy or do an exchange transfusion**
Risk Factors for Developing Hyperbilirubinemia

• TSB or TCB >75%
• Jaundice <24 hr or before discharge
• ABO with +ve DAT or other hemolytic disease (G6PD)
• Gestation <39 wk
• Previous sibling jaundiced
• Cephalhematoma or bruising (vacuum)
• Exclusive breastfeeding
• East Asian
• Male
• Discharge <72 hr
Risk Factors for Brain Damage in Infant with Hyperbilirubinemia

• Isoimmune hemolytic disease
• G6PD deficiency
• Asphyxia
• Significant lethargy
• Temperature instability
• Sepsis
• Acidosis
RISK OF BEING READMITTED FOR PHOTOTHERAPY

30,000 discharges from well baby nursery 1988-94 4.2/1,000 readmitted for phototherapy

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>ODDS RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 36 wks</td>
<td>13.2</td>
</tr>
<tr>
<td>36 – 38 wks</td>
<td>7.5</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>4.2</td>
</tr>
<tr>
<td>Jaundice in nursery</td>
<td>7.8</td>
</tr>
<tr>
<td>LOS &lt; 72 h</td>
<td>3.2</td>
</tr>
</tbody>
</table>

FIGURE 3
ROC curves for risk-assessment strategies using predischarge bilirubin level, other clinical risk factors, or both. a The clinical risk factors model included GA, method of feeding, black race, extent of jaundice, and gender. b The combination model included predischarge bilirubin risk zone, GA, and percentage of weight loss per day over the first 2 days.
FIGURE 4
Probability of significant hyperbilirubinemia given predischarge bilirubin and GA.
FIGURE 5
Risk of significant hyperbilirubinemia according to predischarge bilirubin percentile and GA.

<table>
<thead>
<tr>
<th>LEGEND</th>
<th>Risk Category</th>
<th>No. (%) in Risk Category</th>
<th>No. Developed Significant Hyperbilirubinemia</th>
<th>Probability of Significant Hyperbilirubinemia, % (95% CI)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL</td>
<td>Very low</td>
<td>523 (70)</td>
<td>1</td>
<td>0.2 (0.005–1.000)</td>
<td>0.028</td>
</tr>
<tr>
<td>L</td>
<td>Low</td>
<td>127 (17)</td>
<td>5</td>
<td>4 (1–9)</td>
<td>0.600</td>
</tr>
<tr>
<td>H</td>
<td>High</td>
<td>100 (13)</td>
<td>42</td>
<td>42 (32–52)</td>
<td>10.600</td>
</tr>
</tbody>
</table>
Predischarge Risk Assessment

- Combining predischarge TSB or TcB with risk factors provides most accurate prediction
- Cannot rely on TSB or TcB alone because false negatives occur
- Still need to look at the baby and consider risk factors
Follow-up

• Discharge <72hr, see within 2 days
• Can adjust this according to time of discharge and risk factors
• If cannot see in 2 days, assess risk, do TcB or TSB and make alternative plan
  - home nurse visit
  - see in after hours clinic
  - outpatient TSB or TcB
Guidelines for Exchange Transfusion in infants ≥35 wk Gestation

- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Perform immediate exchange if infant shows signs of acute bilirubin encephalopathy, (hypertonia, arching, reticollis, opisthotonos, fever, high pitched cry) or if TSB is ≥5 mg/dL above these lines.
- Risk factors*: isoimmune hemolytic disease, G6PD deficiency, asphyxia, respiratory distress, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0 g/dL (if measured).
- For well infants 35-36 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wks.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL below those shown but home phototherapy should not be used in any infant with risk factors.

*The risk factors listed above are conditions that might affect the likelihood of brain damage at different bilirubin levels. These factors increase the risk of brain damage because of their negative effects on albumin binding of bilirubin, the integrity of the blood brain barrier, and the susceptibility of the brain cells to damage by bilirubin.

During birth hospitalization, exchange transfusion is recommended if the TSB rises to these levels despite intensive phototherapy. For readmitted infants, if the TSB level is above the exchange level, repeat TSB measurement every 2 to 3 hours and consider exchange if the TSB remains above the levels indicated after intensive phototherapy for 6 hours. The following B/A ratios can be used together with but not in lieu of the TSB level as an additional factor in determining the need for exchange transfusion.

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>B/A Ratio at Which exchange Transfusion Should be Considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Risk</td>
<td>TSB mg/dL</td>
</tr>
<tr>
<td></td>
<td>8.0</td>
</tr>
<tr>
<td>Medium Risk</td>
<td>7.2</td>
</tr>
<tr>
<td>Higher Risk</td>
<td>6.8</td>
</tr>
</tbody>
</table>

If the TSB is at or approaching the exchange level, send blood for immediate type and cross match. Blood for exchange transfusion is modified whole blood. (red cells and plasma) cross matched against the mother and compatible with the infant.
## Predischarge TcB Percentiles and Subsequent Hyperbilirubinemia

<table>
<thead>
<tr>
<th>TcB Percentiles</th>
<th>Total Population</th>
<th>Post Discharge Total Serum Bilirubin</th>
<th>Relative Risk vs &lt; 50th Percentile (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>≥ 17 mg/dL (75)</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>5727</td>
<td>3</td>
<td>0.05</td>
</tr>
<tr>
<td>50-75</td>
<td>2864</td>
<td>21</td>
<td>0.73</td>
</tr>
<tr>
<td>76-95</td>
<td>2291</td>
<td>24</td>
<td>1.04</td>
</tr>
<tr>
<td>&gt; 95</td>
<td>574</td>
<td>27</td>
<td>4.70</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>11456</td>
<td>75</td>
<td>0.65</td>
</tr>
</tbody>
</table>

* Relative risk calculated assuming a value of 1 for post discharge TSB of ≥ 20 mg/dL with predischarge TcB below 50th percentile
Physiologic Mechanisms of Neonatal Jaundice

• Increased load including enterohepatic circulation
• Decreased hepatic uptake
• Decreased conjugation

But which of these is most important?
• Well baby nursery, infants $\geq 36$ weeks
• Routine TcB (JM-102) by nurses if infant jaundiced
• TSB by protocol according to TcB
• If TSB $> 75^{th}$ percentile (Bhutani) = study group (n=108)
• Controls – no jaundice (no TcB) or TSB $< 75^{th}$ percentile (n=164)
• ETCOc
Predictive Ability of a Predischarge Hour-specific Serum Bilirubin for Subsequent Significant Hyperbilirubinemia in Healthy Term and Near-Term Newborns

Bhutani VK, Johnson L, Sivieri EM. *Pediatrics* 1999;103:6-14
ETCOc in Jaundiced and Control Infants

Maisels. *Pediatrics* 2006;118: 276-279
Conclusion

• Increased heme catabolism (and bilirubin production) are probably the primary events responsible for jaundice in the first 4 days
• Newborns have decreased ability to conjugate but if there was no increase in production would see far less jaundice
• Drugs that interfere with bilirubin production could eliminate most neonatal jaundice
Kernicterus Registry

- 125 cases in USA of infants born between 1979 - 2002 and discharged as “healthy newborns”
- Sources - parents, physicians, nurses, literature, medico-legal
- 69% male
- Nearly all breastfed
- 97% discharged <72 hr (57.5% <48hr)
- 40% <38 weeks

Bhutani et al, J Perinatol 2004;24:650