Hyperbilirubinemia and Kernicterus: Not Gone and Not Forgotten

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Why worry about jaundice?
• Occurs in almost all babies
• Source of anxiety and aggravation to families and doctors
• Can lead to kernicterus

Sentinel Event ALERT

Kernicterus threatens healthy newborns
Kernicterus is a condition of newborns that leads to severe, disabling brain damage or death. It results from hyperbilirubinemia that can be caused by a number of factors. Kernicterus is preventable with techniques currently available. Nevertheless, in recent years cases of kernicterus have continued to be reported. One registry includes 90 cases in the United States from 1988 to the present in which three of the newborns died and all others sustained brain damage. "This is probably happening more than clinicians know about," says Sue Sherbala, spokesperson for the advocacy, educational and support group PICK. Parents of Infants and Children with

Group warns of jaundice-linked brain damage in infants

Hospitals Asked to Be on Alert for Jaundice Problem in Babies

By Jane Allen
Time Health Writer

A prominent health care organization warned U.S. hospitals Wednesday to watch out for the return of a rare but preventable type of brain damage in newborns that has not been at the rise with shorter hospital stays and increased breastfeeding. The Joint Commission on Accreditation of Healthcare Organizations, a health care accrediting group, issued an alert to 3,000 U.S. hospitals about kernicterus, a highly unusual condition that stems from severe jaundice.

Within two days of going home, those first few days after birth are a critical time for a baby. Although mothers and clind may have been home several days, it’s four to five days after birth that bilirubin levels peak. And it’s during those same few days that mothers may be struggling with nursing difficulties and their milk may not yet be in. Undertreatment is a risk factor for kernicterus, so mothers with nursing troubles should make sure they get breastfeeding help or feed the baby supplement. Maisels said.

Other risk factors include:

LA Times May 3, 2001
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

Causes of Hyperbilirubinemia in Kernicterus Registry

- Idiopathic 37%
- Hemolysis 14%
- G6PD deficiency 25%
- Other 23%

Bhutani et al, Pediatr Res 2004;24:650

Kernicterus in Healthy Breastfed Term Infants

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>BW (g)</th>
<th>Gestation (w)</th>
<th>Peak serum bilirubin (mg/dL)</th>
<th>Age at peak bilirubin (days)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>2820</td>
<td>37</td>
<td>49.7</td>
<td>7</td>
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<td>2</td>
<td>M</td>
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<td>M</td>
<td>4280</td>
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<td>4</td>
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</tbody>
</table>


Kernicterus

- Still occurring and can occur in a healthy breastfed infant
- Relatively rare disease (8,000 new cases of CP/yr in the US)
- But, unlike other causes of CP, almost always preventable
Why is this happening?

Natural History of Bilirubinemia

Have a high degree of humility when you do a visual estimate of the bilirubin level

S

Are Drive-through Deliveries So Bad?
Shorter hospital stays may not endanger infants

Newsweek Aug 4, 1997
Practitioners do not assess jaundice risks the way they assess other risks

Other important risk factors
- Jaundice in first 24 hours
- Previous sibling jaundiced/phototherapy
- Cephalhematoma or bruising (vacuum extraction)
- ABO incompatibility with positive DAT
- Predischarge bilirubin >95th percentile

Kernicterus Registry
- 69% male
- Nearly all breastfed
- 97% discharged <72 hr (57.5% <48hr)
- 40% <38 weeks

Maisels MJ, Pediatrics 1998;101:995
Bhutani et al, J Perinatol 2004;24:650

RISK OF BEING READMITTED FOR PHOTOTHERAPY

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>ODDS RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>35 - 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>7.5</td>
</tr>
<tr>
<td>LOS &lt; 72 h</td>
<td>3.2</td>
</tr>
</tbody>
</table>

30,000 discharges from well baby nursery 1988-94
4.2/1,000 readmitted for phototherapy
Effective breastfeeding is one intervention that could significantly reduce the risk of severe hyperbilirubinemia.

Should you supplement breastfed newborns with water?
AAP Jaundice Guideline
The 10 Key Elements

1. Promote and support successful breastfeeding.
2. Establish nursery protocols – include circumstances in which nurses can order a bilirubin.
3. Measure TSB or TcB if jaundiced in the first 24 hours.
4. Visual estimation of jaundice can lead to errors, particularly in darkly pigmented infants.
5. Interpret bilirubin levels according to the infant’s age in hours.

AAP Jaundice Guideline
The 10 Key Elements (cont)

6. Infants <38 weeks, particularly if breastfed, are high risk
7. Perform risk assessment prior to discharge.
8. Give parents written and oral information.
9. Provide appropriate follow-up based on time of discharge and risk assessment.
10. Treat newborns, when indicated, with phototherapy or exchange transfusion.

Risk Assessment
New Recommendation by Advisory Group

- Do this on every baby
  - Clinical risk factors (gestation most important)
  - Measure TcB or TSB

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
**Conclusion**

Risk of developing hyperbilirubinemia can be accurately assessed by measuring predischarge TSB or TcB and gestational age.

**Follow-up**

- Provide appropriate follow-up, according to time of discharge and risk factors.
- If cannot do this, assess risk and do TcB or TSB level, get outpatient TSB prn.

If you discharge an infant before age 72 hours, you or a nurse should see the infant within 2 days of discharge.
If many risk factors, see earlier. If few risk factors, can see later but document your reasons in chart

Implementation

Give Physicians the Tools to Implement the Guidelines
- Risk assessment tool at bedside
- Wallet-sized nomogram and guidelines
- PDA
- Hospital computer access and website
- Lab reports of bilirubin to include age in hours and percentile with recommendations for follow up and phototherapy

Give Physicians the Tools to Implement the Guidelines
- Risk assessment tool at bedside

*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.

Any infant discharged before age 72 hours should be seen within 2 days of discharge.

The risk factors listed above are conditions that might affect the likelihood of brain damage.
Give Physicians the Tools to Implement the Guidelines

Wallet-sized nomogram and guidelines

Quality improvement programs
If have a very jaundiced baby, send baby to pediatric floor or NICU not to emergency department.

Jaundice is now predominantly an outpatient problem.

Drive through deliveries should not be a problem as long as you don’t abandon the baby.

Newborn follow up in one to two weeks is abandonment.

Need a high degree of humility when assessing jaundice clinically.
Follow The AAP Guidelines

No system is perfect, use common sense

“This is an age in which one cannot find common sense without a search warrant”

George Will

References:

References

References

References
• Sgro M, Campbell D, Shah V. Incidence and causes of severe hyperbilirubinemia in Canada. CMAJ 2006; 175: 587-90
• Canadian Pediatric Society. Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (35 or more weeks’ gestation) Pediatr Child Health 2007; 12; 11-B. (suppl).
• Manning D et al Prospective surveillance of severe hyperbilirubinemia in the newborn in the UK and Ireland. Arch Dis Child Fetal Neonatal Ed 2007; 92: 342-346