Neonatal Jaundice

Introduction

All babies develop elevated serum bilirubin (SBR) levels, to a greater or lesser degree, in the first week of life. This is due to increased production (accelerated red blood cell breakdown), decreased removal (transient liver enzyme insufficiency), and increased reabsorption (enterohepatic circulation). For example, using Gartner's data\(^1\), the mean SBR for normal babies during the first week is represented by the blue line in the graph below.

However, when a baby does become jaundiced, a common dilemma is deciding at what SBR level to intervene. The decision is influenced by whether the baby is term or preterm, well or sick, and the presence or absence of blood factors predisposing to hyperbilirubinaemia. For good background material, refer to these articles\(^2,3,4,5\).

Incidence and risk factors:

Virtually all babies have a transient rise in SBR, but only about 50% are visibly jaundiced. This varies with race, those of Asian background having a higher incidence.

It is clinically useful to classify jaundice according to the age of the baby when he/she becomes visibly jaundiced.

1. Early (days 1-2) - uncommon
   - Haemolytic jaundice (Rhesus, ABO, others)
2. Normal (days 3-10) - very common
   - Uncomplicated
   - Complicated - see below
3. Late (days 14+)
   - Breast milk - common
   - Conjugated jaundice - uncommon
   - Inherited deficiency of glucuronyl transferase enzymes - very rare

Factors likely to make physiological jaundice worse in a given baby include:

- prematurity
- bruising
- cephalohematoma
- polycythaemia
- delayed passage of meconium
• breast feeding
• certain ethnic groups, esp Chinese

Consequences:

Severe jaundice

• Definition of severe jaundice depends on the clinical setting:
  1. Uncomplicated term babies >450
  2. Babies with haemolytic jaundice - see jaundice - haemolytic
  3. Preterm babies - depends on gestational age - see below
• Kernicterus (bilirubin encephalopathy). This clinical syndrome includes hypertonia progressing to ophthisotonia, seizures, and may lead to death. At autopsy, such babies display evidence of bilirubin staining of the basal gangia.
• Late sequelae to kernicterus. These include sensorineural hearing impairment and cerebral palsy, often with ataxia and chorioathetosis.

Once a baby develops severe jaundice, the risk of progressing to kernicterus is increased by the following:

• acidosis
• drugs which displace bilirubin from albumin (esp. sulphonamides and related compounds)
• hypoalbuminaemia

The late effects of moderate levels of jaundice on extremely preterm infants is unknown, although it is generally accepted they are more at risk than term infants for the same SBR level.

Investigations:

1. Clinical evaluation
Kramer's Rule

Rather than estimating the level of jaundice by simply observing the baby's skin colour, one can utilise the cephalocaudal progression of jaundice. Kramer drew attention to the observation that jaundice starts on the head, and extends towards the feet as the level rises. This is useful in deciding whether or not a baby needs to have the SBR measured. Kramer divided the infant into 5 zones, the SBR range associated with progression to the zones is as follows:

<table>
<thead>
<tr>
<th>Zone</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBR (umol/L)</td>
<td>100</td>
<td>150</td>
<td>200</td>
<td>250</td>
<td>&gt;250</td>
</tr>
</tbody>
</table>

2. Transcutaneous bilirubinometry

Since January 2006 transcutaneous bilirubinometry has been adopted as the first-line screening tool for jaundice in well, full-term babies. The policy guiding the use of this technology specifies the circumstances under which the meter reading determines whether a blood test for jaundice is indicated. This leads to about 50% of blood test previously required being avoided.

Bilirubinometers have not been validated satisfactorily as yet in premature babies, so currently the investigation of jaundice for them still depends on the blood test. Further studies on the use of these meters for premature babies in our department are in progress.

3. Total SBR

Although an indirect measure of risk, the total SBR continues to be the "gold standard" for deciding if a baby's jaundice requires intervention. "Free" bilirubin can be measured, but this is technically difficult and only usually available in a research setting. Unfortunately, it is not known what SBR level is safe for a given baby. Convincing cases of kernicterus in term babies with uncomplicated physiological jaundice are extremely rare.

In the case of preterm infants, greater caution should be exercised. Again, no safe level has ever been determined, and it is clear from post-mortem evidence that these babies are at risk of
kernicterus at lower SBR levels.

### 3. Other investigations

These are guided by day of onset and clinical features

1. **Early onset (day 1/2)**
   - Group & Direct Coombs test - exclude haemolytic jaundice
   - full blood count & film - may reveal spherocytes c/w haemolysis

2. **Normal onset (day 3-8)**
   - G6PD screen (consider if male and appropriate ethnic group)
   - sepsis screen if indicated
   - galactosaemia - check newborn screening, urinary reducing substance, beware of coexisting gram-negative sepsis
   - full blood count & film - may reveal spherocytes or septic changes

3. **Late onset (2-4 weeks)**
   - conjugated SBR - if elevated suspect liver disease - for further investigations, see conjugated jaundice
   - full blood count & film - may reveal septic changes
   - Thyroid function tests: high TSH & low T4 - suspect hypothyroidism; low TSH & low T4 - suspect hypopituitarism

Most institutions have in-house charts which define levels for initiating phototherapy or exchange transfusion, according to gestation and/or etiology. No single chart is widely accepted as "correct", and wide variations in practice are evident. The American Academy of Paediatrics has recently produced guidelines for the management of jaundice, but only for healthy term newborns. In the absence of an overall consensus, we have developed the following charts following a review of available evidence:

### Interventions:

If an underlying pathological cause was identified in the above investigations, then obviously this should be attended to appropriately. Manage the jaundice component as follows:

1. **Phototherapy**

Phototherapy has been shown in a large multicentre RCT to be a safe and effective method for lowering the SBR level. The following chart gives the SBR level for a given day of life and gestational age at which to commence phototherapy in **well babies** with **uncomplicated** jaundice.

However, at any gestation consider starting phototherapy at lower levels when babies are at
increased risk due to factors such as ventilation (lower pH), low albumin, multiple medications that might compete for bilirubin binding, bruising and/or cephalohaematomas, and sepsis. The AAP Guidelines provide some advice regarding lower levels according to level of risk in term and near term babies, but no advice for less than 35 weeks. Therefore the decision regarding how much lower to start should be made by the on-call consultant according to the individual baby’s circumstances.

**Summary for healthy, term babies:**

<table>
<thead>
<tr>
<th>Day of life</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBR</td>
<td>200</td>
<td>260</td>
<td>320</td>
<td>350</td>
<td>360</td>
</tr>
</tbody>
</table>

*Note:* For a faster response in babies with SBR levels in the upper range, use “double lights”, i.e. a biliblanket from below, and one or two lights from above. The biliblankets are not very effective on the low power setting, and this should be avoided. They should undergo period testing for their output.

### 2. Intravenous Immunoglobulin (IVIG)

IVIG combined with phototherapy, compared with phototherapy alone, has been shown in randomised, controlled trials to significantly reduce the maximum serum bilirubin and the need for exchange transfusion in babies with isoimmune haemolytic jaundice. See Haemolytic Jaundice
3. Exchange transfusion

For details of the procedure, see medical and nursing guidelines.

This procedure removes bilirubin, removes hemolytic antibody, and corrects anaemia. It is very uncommon to need to exchange without there being rhesus disease or G6PD. Extremely preterm infants occasionally need an urgent exchange when their level becomes dangerously high, bearing in mind that "safe" levels are undefined for such babies. At the same time, extremely premature babies are very responsive to phototherapy.

Indications for exchange:

1. Haemolytic jaundice

For Rhesus disease and other haemolytic conditions, see Haemolytic jaundice.

2. Non-haemolytic jaundice

In the case of term and near-term babies after day 4, the AAP guidelines suggested exchange levels for lower risk (428), middle risk (376), and higher risk (325). This however provides no guidance for babies < 35 weeks, and they should be considered on individual merits by the on-call consultant. The following values are suggested as exchange levels for well babies with non-haemolytic jaundice, but as suggested above for starting phototherapy, exchanging at lower levels must be considered if risk factors are present.

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>SBR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;27</td>
<td>250 umol/L</td>
</tr>
<tr>
<td>28-32</td>
<td>300</td>
</tr>
<tr>
<td>33-37</td>
<td>380</td>
</tr>
<tr>
<td>&gt;37</td>
<td>450</td>
</tr>
</tbody>
</table>

NOTE: Increased acidosis increases risk of bilirubin deposition in the brain. If blood gases indicate increasing acidosis, then ventilation and bicarbonate treatment are advised. If the bilirubin is very high, acute encephalopathy is likely, and hypoventilation is commonly present.

4. Tin mesoporphorin

This substance acts by inhibiting haemoglobin oxidase and thus reducing bilirubin production. Although it appears to be a promising advance, there has been a disappointing lack of quality data to support its use. It has been the subject of a Cochrane Review, which concluded that its
5. Other interventions

While these strategies appear biologically plausible, they are not widely used. Apart from the occasional use of phenobarbitone for severe conjugated jaundice, none are currently employed in this nursery.

- **Improve liver function**: Phenobarbitone (induces enzymes)
- **Reduce enterohepatic circulation**: Agar, activated charcoal, etc. (sequesters bilirubin in gut)
- ** Interruption of breast feeding**: Although there is some observational data associating breast feeding with higher early bilirubin levels there is no evidence that interrupting breast feeding is effective in lowering bilirubin level. Such practice would have important potential harms in terms of interfering with the establishment of lactation or undermining maternal confidence in her ability to successfully breast feed.11

Breast Milk Jaundice

This occurs infrequently, peaks in the 2nd or 3rd week, and may persist at moderately high levels for 3-4 weeks before declining slowly. It is a diagnosis of exclusion. In an otherwise well infant, it is considered a benign condition. If feeding with breast milk is stopped, the serum bilirubin usually falls, however this would very rarely be indicated. The potential harms of stopping breast feeding would outweigh any risks of a mild or moderate hyperbilirubinaemia. The aetiology is unknown, but there is some support for both a hormonal factor in the milk acting on the infant’s hepatic metabolism, and an enzyme (lipase) facilitating intestinal absorption of bilirubin.

Key Points

<table>
<thead>
<tr>
<th>Key Point</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phototherapy is a safe, effective method for lowering serum bilirubin, and reduces the need for exchange transfusion</td>
<td>🌟🌟🌟🌟🌟🌟</td>
</tr>
<tr>
<td>The level for starting phototherapy is based on observational data only</td>
<td>🌟🌟</td>
</tr>
</tbody>
</table>

References

metabolism in the newborn rhesus monkey. *J Pediatr* 1977; **90**: 513-531


Last Updated: May, 2006