Assessment and Treatment of Jaundiced Newborn Infants 35 0/7 or more Weeks of Gestation

Revised Recommendations from the Swiss Society of Neonatology

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1. Introduction

Within the first few days of life jaundice occurs in about 60% of all newborn infants. Among the large number of newborn infants who develop harmless jaundice, the medical and nursing challenge consists of identifying those few who develop serious hyperbilirubinaemia with the risk of ensuing encephalopathy. In the last few years, reports on children with bilirubin encephalopathy have increased.[1-3] Depending on the country and its health system, reasons for this increase might be due to insufficient surveillance on the maternity ward or to early postnatal discharge, and to underestimating or trivialising the toxic effects of bilirubin on the nervous system. The aforementioned reports[1-3] underscore the importance of guidelines as proposed in this publication.

In 1984 and 1993, the Swiss Society of Neonatology published recommendations for the treatment of jaundiced newborn infants.[4,5] In light of the current data, the Society deems it necessary to update the recommendations of 1993.

The present revised recommendation take into account new insights from the current literature and cross reference to updated recommendations of other societies.[6-8] Our practical recommendations are valid for healthy newborn infants of 35 0/7 and more weeks of gestation on maternity wards and/or of a birth weight of more than 2000 grams. The intention is to avoid over treatment and parental insecurity. Newborn infants of less than 35 weeks gestational age or less than 2000 grams who are jaundiced are part of a high risk group, and as such should be assessed and treated on a neonatal ward.

2. Clinical Assessment

The occurrence and progression of jaundice should be assessed with every diaper change or any other routine care of the newborn, but no less than every 8 to 12 hours. Clinical evaluation consists of blanching the skin with digital pressure under good lighting conditions, preferably in daylight, and the results noted in the infant's records. Dark skinned infants need to be evaluated extra carefully, since clinical assessment is more challenging.

The necessary distinction between physiological and pathological jaundice is based primarily on clinical criteria. Pathological jaundice is most likely present if there are, for example: clinical signs (pallor, apathy, lethargy, poor suck, vomiting, fever, dark urine or acholuric stools); early onset jaundice (=visible jaundice within 24 hours of life); rise in serum bilirubin > 10 µmol/l/h; or prolonged jaundice (beyond 14 days of life).

Thus, in the following instances, either the attending physician must be informed, or depending on the hours of life, further exams undertaken according to point 3.2.:

- Clinically relevant jaundice (=jaundice encompassing upper extremities also).
- Early onset jaundice.
- Rise in bilirubin > 10 µmol/l/hour.
- Clinical symptoms compatible with pathological jaundice.
- Jaundice in premature infants.

Before initiating phototherapy each child should be examined by a physician and the parents informed about the ensuing treatment.

3. Additional Analyses

3.1. Transcutaneous Bilirubinmeasurement

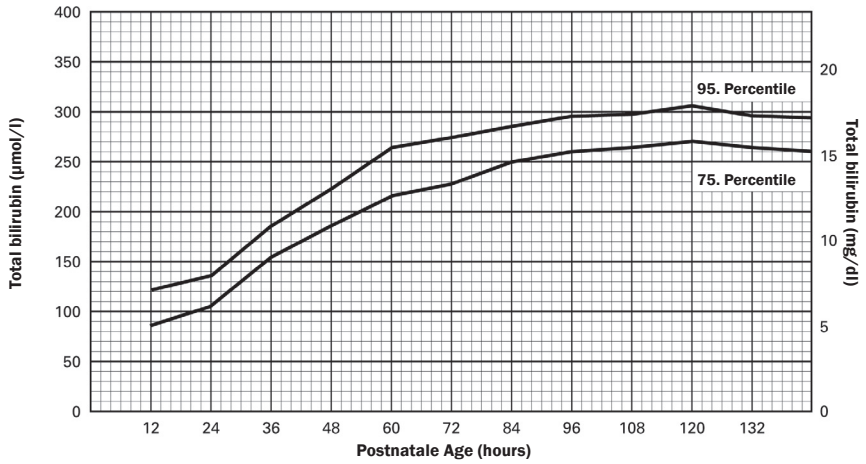
After the clinical assessment, transcutaneous bilirubin measurement is usually the first diagnostic step. This method is simple and non-invasive. However, when using this method the following restrictions must be taken into account:

- With early jaundice, serum bilirubin must be determined in order to follow the trend and decide upon further diagnostic tests.
- A therapeutic decision should never be based on a transcutaneous bilirubin-measurement alone.
- A transcutaneous bilirubin measurement during or after phototherapy, or following an exchange transfusion, is not reliable and should not be used.

Indication	Laboratory exam
At delivery Rhesus negative mother or unknown bloodgroup	Bloodgroup, dir. Coombs test[1] (preferably from cord blood)
Mother with antibodies	Bloodgroup, dir. Coombs test, haematocrit or haemoglobin, serum bilirubin
Within 24 hours of birth (early onset jaundice)	Bloodgroup, dir. Coombs test, haematocrit or haemoglobin, serum bilirubin
Beyond 24 hours Significant jaundice[2] or transcutaneous bilirubin measurement beyond predetermined limit	Bloodgroup, dir. Coombs test, haematocrit or haemoglobin, serum bilirubin
Jaundice beyond 2nd week of life (= prolonged jaundice)	Bloodgroup, dir. Coombs test, haematocrit or haemoglobin, total and direct serum bilirubin

Table 1: Laboratory evaluation of the infant

[1] Blood group and Coombs test are once-only laboratory tests
[2] Jaundice is first perceived in the face and then spreads caudally over the body and extremities. Rule of thumb: if jaundice is perceived after blanching the skin with digital pressure on the lower extremities, serum bilirubin will be about 200-250 µmol/l.[9]



Adapted from Bhutani et al., Pediatrics 1999;103: 6–14

Fig. 1: Modified Bhutani Chart

- Depending on the device used, transcutaneous bilirubin measurement is variably reliable in both dark skinned and premature infants. This is why each clinic has to determine its cut off value according to the device used. In principle, when there is a doubt, serum bilirubin values should always be given preference over transcutaneous measurements.

3.2. Laboratory Exams in the Infant

The following laboratory exams are considered a minimal standard: *(see page 1, Table 1)*:

3.3. Clinical Pathway for a Short Hospital Stay (< 48 hours)

In case of a hospital stay of less than 48 hours, clinical assessment at home while performing the Guthrie-test on the 4th day of life becomes particularly important. Should the infant have a significant jaundice or present clinical symptoms of a potentially pathological jaundice, then the serum bilirubin determination should be done. The midwife doing the postnatal care and the child's attending paediatrician are responsible for clinically evaluating the infant and performing the laboratory exams as stated in points 2 and 3.1. to 3.3.

Aside from evaluating clinical risk factors, early transcutaneous or serum bilirubin measurement can help assess the risk of the infant developing a severe hyperbilirubinaemia. *(Fig. 1)*.

a) In case of *discharge soon after delivery (Hospital stay < 24 hours)*, an outpatient determination of serum bilirubin should be drawn between 18–48 hours of age.
b) If jaundice becomes evident during a *short hospital stay of 24–48 hours*, bilirubin should be determined and the infant examined by a paediatrician before discharge.

The bilirubin value should be plotted on the Bhutani chart *(Fig. 1)* to assess the risk of developing significant hyperbilirubinaemia.[10]

Interpreting the Bhutani chart:

- If the bilirubin value lies above the 95th percentile, further laboratory exams as well as a follow up bilirubin measurement within the next 24 hours should be performed, and if needed a treatment initiated *(see page 1, Table 1)*.
- Should the bilirubin value lie between the 75th and the 95th percentile, a follow up bilirubin value should be obtained within 24 to 48 hours.
- If the bilirubin value lies below the 75th percentile, the risk of severe hyperbiliruinaemia is minimal and a follow up bilirubin determination is warranted only if the infant becomes evidently jaundiced. This can be done whilst drawing for the newborn screening test (Guthrie test) on the 4th day of life.

4. Treatment

4.1. Indications for Treatment

Indications for phototherapy and exchange transfusion are shown in *Table 2* and depicted as a nomogram. Following are some remarks with respect to *Table 2*:

- Numbers are total serum bilirubin values. Direct bilirubin values should not be subtracted from total bilirubin values.
- When risk factors are present (e.g. perinatal and neonatal elements, neurological symptoms, rise in bilirubin value beyond 10 µmol/l/h), limits at which therapy is commenced should lie in the lower zones (i.e. gray area under the curve for phototherapy and exchange transfusion respectively).
- The maximum level for an exchange transfusion is predetermined. This fixed upper level is necessary to be able to filter out and follow up those newborn infants whose maximum bilirubin levels were beyond the upper limit for exchange transfusion, as they are at risk of developing bilirubin encephalopathy (see point 7).
- Haemolysis is difficult to diagnose. Direct Coombs testing alone[11,12] is not sufficiently reliable and reliculocyte count has too low a sensitivity and specificity. Main criteria for haemolysis in the clinical setting are:

– Haematocrit < 45% or haemoglobin< 145g/l.
– Early onset jaundice (=within first 24 hours of life).

	Phototherapy	Exchange Transfusion
Term infant > 2500 g, healthy	320 - **350** µmol/l	400 - **430** µmol/l
Term infant > 2500 g, ill or with haemolysis	230 - **300** umol/l	350 - **370** µmol/l
Premature infant of 35 and 36 weeks of gestation or term infant < 2500 g	200 - **260** µmol/l	270 - **320** µmol/l

Table 2: Indications for treatment

Caution: In case of jaundice before 48 hours of life, especially in case of early jaundice, indication to phototherapy should be considered even before bilirubin reaches the lower limits of phototherapy (see figure 2 for indications for treatment).

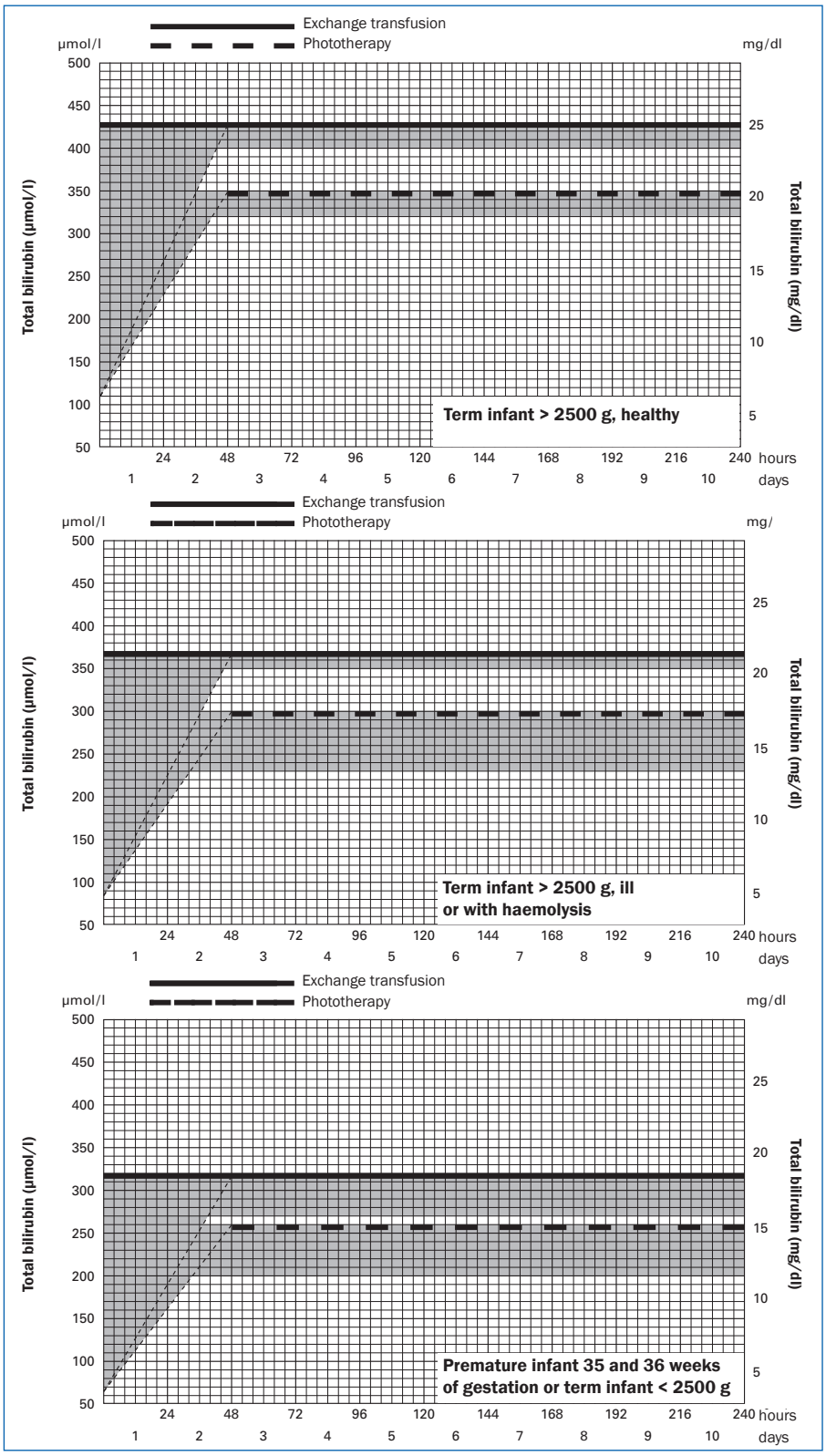


Fig. 2: Indications for Treatment (Nomogram)

- Total serum bilirubin > 240 µmol/l within first 48 hours.
- Positive direct Coombs test.
- Rising bilirubin level despite phototherapy.

The main reasons for haemolysis are Rhesus- and ABO- incompatibility, glucose-6-phosphate dehydrogenase deficiency, pyruvate kinase deficiency, and spherocytosis.

4.2. Phototherapy

- Methods of phototherapy:
  - Phototherapy can be done in an incubator, an open unit, in a bili-bed and under certain circumstances on a fibre-opticmat. Please refer to the Cochrane database for the efficiency of each method[13].
- Factors influencing efficiency of phototherapy:
  - Light intensitiy (especially effective in the blue-green spectrum).
  - Distance from light source to skin.
  - Irradiated skin surface.
- Important considerations when using phototherapy:
  - Cover infant with small diaper only, paying special attention to body temperature.
  - One lamp is standard. In exceptional cases 2 lamps may be used.
  - Eye shields (not necessary for bili-bed or fibreoptic mat)
  - Maintain adequate fluid intake. (Increasing fluid intake is not necessary) (see point 5).
  - Phototherapy breaks for feeds and care of the infant for up to 1 hour are permitted (remove eye shields for breaks). Mother-infant contact should be hindered as little as possible.
  - Bilirubin levels should be drawn 8- to 12-hourly during phototherapy. Once bilirubin values start decreasing, values can be determined 12-hourly and up to 24-hourly.
  - Transcutaneous bilirubin measurements during and after phototherapy are not permitted.
  - Stop phototherapy once bilirubin level has dropped below phototherapy level. If phototherapy occurs between 3 to 4 days of life and/or haemolysis is present, a further bilirubin level should be drawn 12–24 hours after phototherapy ends.
- Clinical assessment (of which all values should be charted):
  1. 6-hourly: temperature, heart rate, and breathing frequency.
  2. daily : weight.
- Phototherapy lamps should be maintained regularly, including regulation of light bulbs.

5. Nutrition

Optimal energy and fluid intake during the first days of life are important factors in diminishing the development and the consequences of hyperbilirubinaemia.[14] The nutri-

tional recommendations of the Swiss Society of Paediatrics for healthy newborn infants on the maternity ward can also be used for newborn infants with hyperbilirubinaemia.[15] Mothers should be able to freely breastfeed their children 5–8 times daily until postpartum breast engorgement occurs, and then later on breastfeed 8–12 times daily thereafter.

Although breastfed infants usually have higher bilirubin levels than formula fed infants,[16] breastfeeding should not be hindered during phototherapy nor mothers discouraged from breastfeeding. The advantages of breastfeeding outweigh the disadvantages: 1–2 % of breastfed infants develop prolonged hyperbilirubinaemia with a peak around 10 to 15 days of life, which resolves after 3 to 12 weeks.

As breastmilk jaundice is harmless, interrupting lactation is not necessary. Offering additional fluids and/or breast milk replacement (10% dextrin maltose) can be of significance in positively influencing the risk of hyperbilirubinaemia in the following situations:[15]

- Premature infants on maternity wards.
- Newborn infants of < 2500 g or > 4500 g.
- Small for dates (< 10th percentile).
- Crying and restlessness despite recent and repeated feeds (signs of thirst).
- Dehydration (weight loss >10%) or continues weight loss beyond the 4th to 5th day of life.

6. Recommendations for Transfer of an Infant to a Newborn Unit

In the following situations newborn infants need to be transferred to a neonatal unit for further diagnostic work-up and treatment (intensified phototherapy, exchange transfusion and/or intravenous immunoglobulin treatment): [17]

- Clinical signs compatible with pathological jaundice.
  - Early onset jaundice.
  - Bilirubin levels close to exchange transfusion level.
  - Increase of serum bilirubin of more than 10 µmol/l /h.
  - Anaemia (haematocrit < 45% or haemoglobin < 145 g/l).
  - Increase of bilirubin level during phototherapy (treatment failure).
  - Antenatally diagnosed blood group in compatibility with significant amounts of antibodies and/or intrauterine treatment warrant a delivery in a perinatal centre. In these cases early treatment with IVIG should be considered.[17]

Transfer of jaundiced newborn infants to a neonatal unit should be organized by the involved paediatrician in accordance with the receiving neonatal ward.

7. Registering Bilirubin Encephalopathy in Switzerland

In the past few years reports on bilirubin encephalopathy have increased.[1-3] For this reason children at risk of developing bilirubin encephalopathy in Switzerland should henceforth be registered, as is the practice in other countries (such as Denmark or the USA. The Swiss Paediatric Surveillance Unit should be notified of any child whose bilirubin level was documented to be above the maximum exchange transfusion level (total bilirubin > 430 µmol/l in healthy term newborn infants, > 370 µmol/l for term newborn infants who are ill or with haemolysis, and > 320 µmol/l for premature infants of 35 and 36 weeks of gestation and infants < 2500 g). For these children special developmental follow-up is indicated.

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