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Neonatal bilirubin: guidelines and analytical performance

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Neonatal hyperbilirubinaemia

Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month. For most babies, jaundice is not an indication of an underlying disease, and this 'physiological jaundice is usually harmless.

In neonates the immature liver and an increase in haem turnover can cause a transient increase in unconjugated bilirubin, where the total bilirubin level can exceed 100 $\mu\text{mol/L}$, with concentrations in excess of 300 $\mu\text{mol/L}$ carrying a risk of brain damage. Entry of unconjugated bilirubin into the brain can cause both short-term and long-term neurological dysfunction (bilirubin encephalopathy). The term kernicterus is used to denote the clinical features of acute or chronic bilirubin encephalopathy, as well as the yellow staining in the brain associated with the former. Kernicterus is also known to occur at lower levels of bilirubin in term babies who have risk factors, and in preterm babies.

1.2 Care for all babies

1.2.1 Identify babies more likely to develop significant hyperbilirubinaemia: gestational age < 38 weeks, a previous sibling with neonatal jaundice, breastfeed exclusively, visible jaundice in the first 24 hours of life.

1.2.3 In all babies

- check risk factors associated with ↑likelihood of developing significant hyperbilirubinaemia soon after birth
- examine the baby for jaundice at every opportunity especially in the first 72 hours.

1.2.4 Look for jaundice (visual inspection):

- check the naked baby in bright and preferably natural light
- examine the sclerae and gums, and press lightly on the skin to check for signs of jaundice in 'blanched' skin
- be aware that changes to skin pigmentation because of hyperbilirubinaemia may be harder to see in darker skin. [amended 2023]

1.2.6 Do not rely on visual inspection alone to estimate the bilirubin level in a baby with suspected jaundice.

1.2.7 Do not measure bilirubin levels routinely in babies who are not visibly jaundiced. [2010]

Urgent additional care for babies with visible jaundice in the first 24 hours

1.2.10 **In all babies with suspected or obvious jaundice in the first 24 hours of life, measure and record the serum bilirubin level urgently (within 2 hours).**

1.2.11 In all babies with suspected or obvious jaundice in the first 24 hours of life, continue to measure the **serum bilirubin level every 6 hours** until the level is both:

- below the treatment threshold
- stable and/or falling.

1.2.12 Arrange a referral to ensure that an urgent medical review is conducted (as soon as possible and within 6 hours) for babies with suspected or obvious jaundice in the first 24 hours of life to exclude pathological causes of jaundice.

1.2.13 Interpret bilirubin levels according to the baby's postnatal age in hours and manage hyperbilirubinaemia according to the threshold table and the treatment threshold graphs.

1.2.14 Measure and record the bilirubin level **urgently (within 6 hours) in all babies more than 24 hours** old with suspected or obvious jaundice.

1.2.15 Use serum bilirubin measurement for babies:

- in the first 24 hours of life or
- who have a gestational age of less than 35 weeks.

1.2.16 In babies who have a gestational age of 35 weeks or more and who are over 24 hours old:

- use a transcutaneous bilirubinometer to measure the bilirubin level
- if a transcutaneous bilirubinometer is not available, measure the serum bilirubin
- if a transcutaneous bilirubinometer measurement indicates a bilirubin level **>250 $\mu\text{mol/L}$** , measure the serum bilirubin to check the result
- use serum bilirubin measurement if bilirubin levels are at or above the relevant treatment thresholds for their age, and for all subsequent measurements.

1.2.17 Do not use an icterometer to measure bilirubin levels in babies.

1.3 How to manage hyperbilirubinaemia

Note that there is variability between assays from different manufacturers in reported bilirubin measurement. Healthcare professionals should consult their local pathology laboratory when interpreting threshold tables.

1.3.4 Use the bilirubin level to determine the management of hyperbilirubinaemia in all babies (see the threshold table and the treatment threshold graphs).

1.3.5 Do not use the albumin/bilirubin ratio when making decisions about the management of hyperbilirubinaemia.

1.3.6 Do not subtract conjugated bilirubin from total serum bilirubin when making decisions about the management of hyperbilirubinaemia (see management thresholds in the threshold table and the treatment threshold graphs).

1.5 Factors that influence the risk of kernicterus

Identify babies with hyperbilirubinaemia as being at increased risk of developing kernicterus if they have any of the following:

- a serum bilirubin level **> 340 $\mu\text{mol/L}$** in babies with a gestational age of ≥ 37 weeks
- a rapidly rising bilirubin level of greater than **8.5 $\mu\text{mol/L}$** per hour
- clinical features of acute bilirubin encephalopathy. [2010]

1.4 Phototherapy treatment threshold varies depending on weeks gestation, time from birth and Tbil conc.
> 100 $\mu\text{mol/L}$ for age 0 to >350 $\mu\text{mol/L}$ at 96+hrs for ≥ 38 wks

1.4.4 During phototherapy repeat Tbil every 4-6 hrs or 6-12hrs if stable or falling.

1.4.5 Stop once TBil \downarrow 50 $\mu\text{mol/L}$ below the threshold

1.4.6 Repeat TBil 12–18 hours to check for rebound hyperbilirubinaemia.

1.4.9 Intensified phototherapy:

- recommended when TBil level is rising rapidly ($> 8.5 \mu\text{mol/L}$ per hour)
- TBil at a level within 50 $\mu\text{mol/L}$ below the threshold for which exchange transfusion is indicated after 72 hours or more since birth.
- Tbil level fails to respond to initial phototherapy (i.e, Tbil continues to rise, or does not fall, within 6 hours of starting phototherapy).

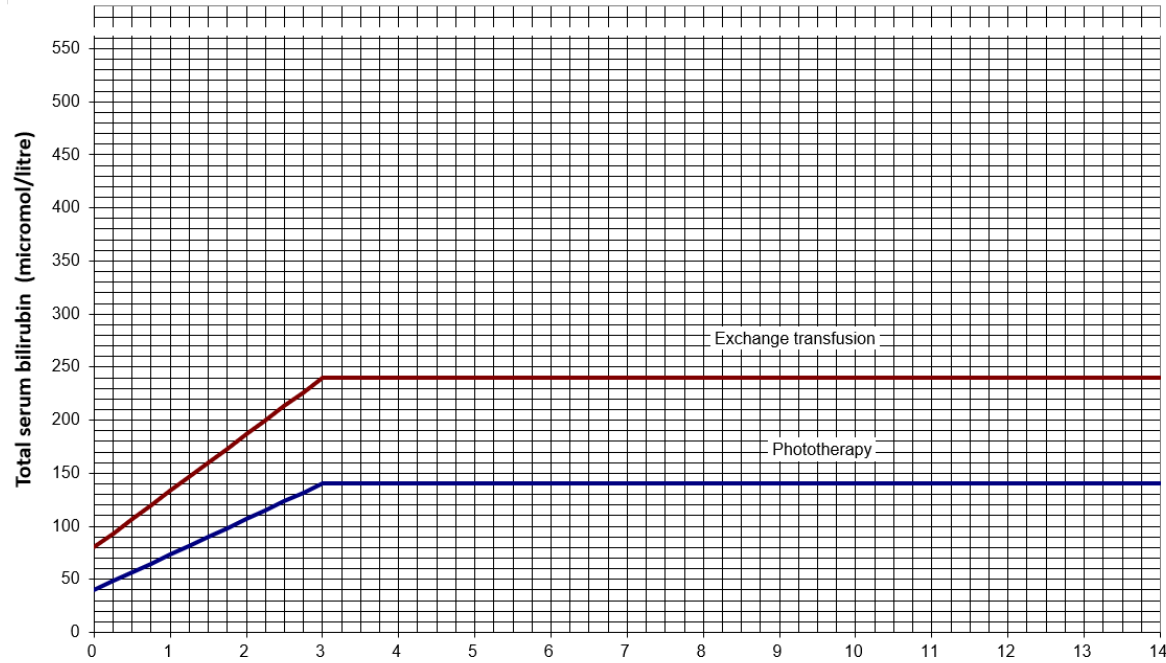
1.9 Exchange transfusion therapy threshold:
> 100 $\mu\text{mol/L}$ for age 0 to >450 $\mu\text{mol/L}$ at 42+hrs for ≥ 38 wks.

1.9.4 Following exchange transfusion:

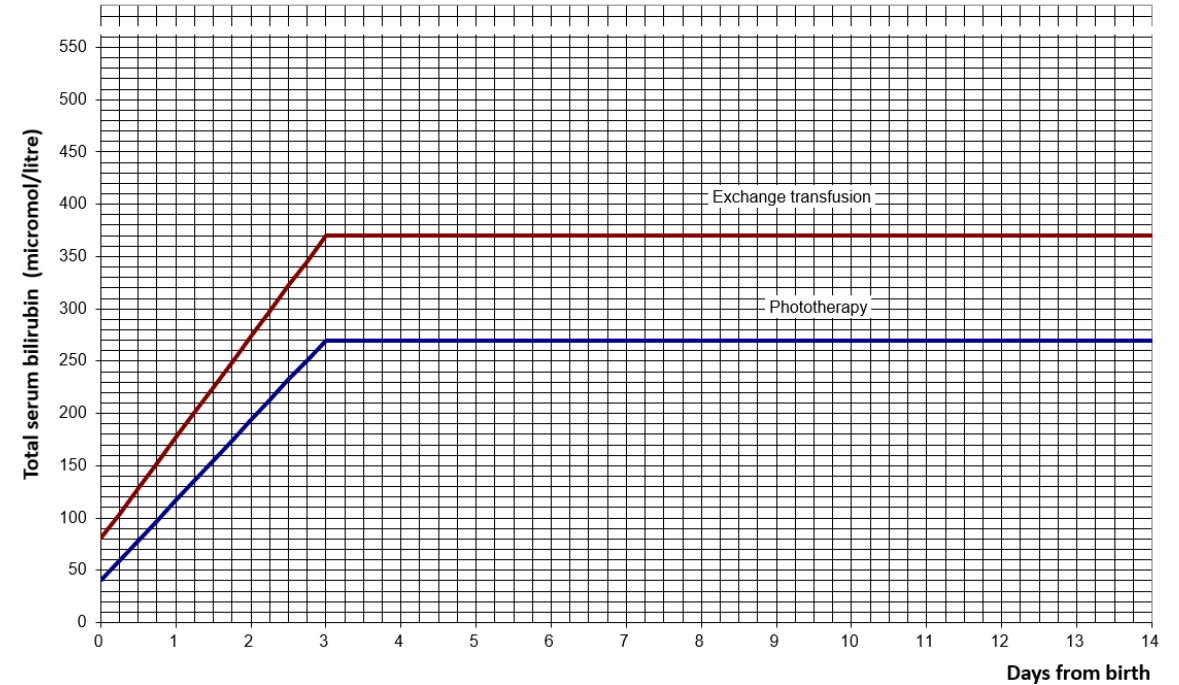
- maintain continuous intensified phototherapy
- measure Tbil level within 2 hours and manage according to the threshold table and the treatment threshold graphs.

Treatment thresholds

made for phototherapy Baby's blood group _____ Mother's blood group _____ **24** weeks gestation



made for phototherapy Baby's blood group _____ Mother's blood group _____ **37** weeks gestation

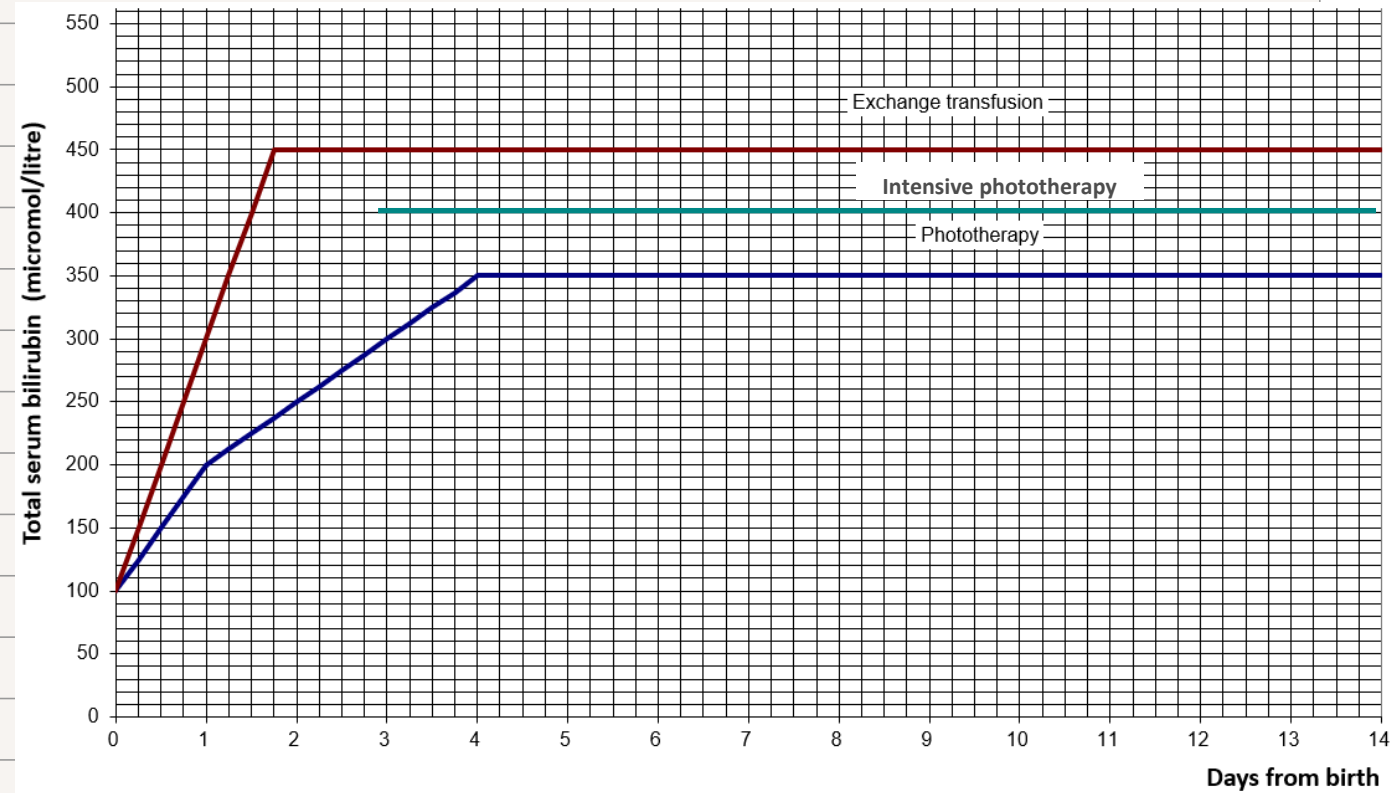


At 6 hrs, phototherapy threshold is $> 56\mu\text{mol/L}$
 Transfusion threshold is $> 106\mu\text{mol/L}$

At 6 hrs, phototherapy threshold is $> 78\mu\text{mol/L}$
 Transfusion threshold is $> 128\mu\text{mol/L}$

Treatment Threshold table ≥ 38 wks gestation

Age (hours)	Bilirubin ($\mu\text{mol/L}$)		Δ Bilirubin ($\mu\text{mol/L}$) for a change in treatment category
0	>100	>100	0
6	126-150	151-200	25
12	151-175	201-250	50
18	176-200	251-300	75
24	201-212	301-350	100
30	213-225	351-400	138
36	226-237	401-450	163
42	238-250	>450	
48	251-262	>450	
54	263-275	>450	
60	276-287	>450	
66	288-300	>450	
72	301-312	>450	
78	313-325	>450	
84	326-337	>450	
90	338-350	>450	
96+	>350	>450	
Action	Start phototherapy	Perform an exchange transfusion unless the bilirubin level falls below threshold while the treatment is being prepared	



What Performance do we need?

TaT – < 2 hours

Trueness (Minimal bias) – global threshold targets used to determine treatment

Reproducibility (Low imprecision)– need to establish significance of Δ change (rise / fall) in Tbil to help manage treatment.

What is the current performance?
Is it good enough?