Neonatal Jaundice

Joanna Seliga-Siwecka

Fellows rounds

Wednesday, October 6th

Learning objectives

- Explain bilirubin physiology
- Define neonatal jaundice
- List main causes of hiperbilirubinaemia in neonates
- Give examples of treatment for neonatal jaundice

Neonatal Jaundice

- Pathophysiology
- Clinical presentation
- Work up
- Diagnosis
- Management
- Medication
- Follow up

Where it all began…

Fundamentals of Phototherapy for Neonatal Jaundice

Stokowski, Laura A.

Advances in Neonatal Care. 11():S10-S21, October 2011.

doi: 10.1097/ANC.0b013e31822ee62c

FIGURE 1. Miss Jean Ward, in 1956, with one of the earliest infants given phototherapy at Rochford General Hospital. Courtesy of BMJ Publishing Group.

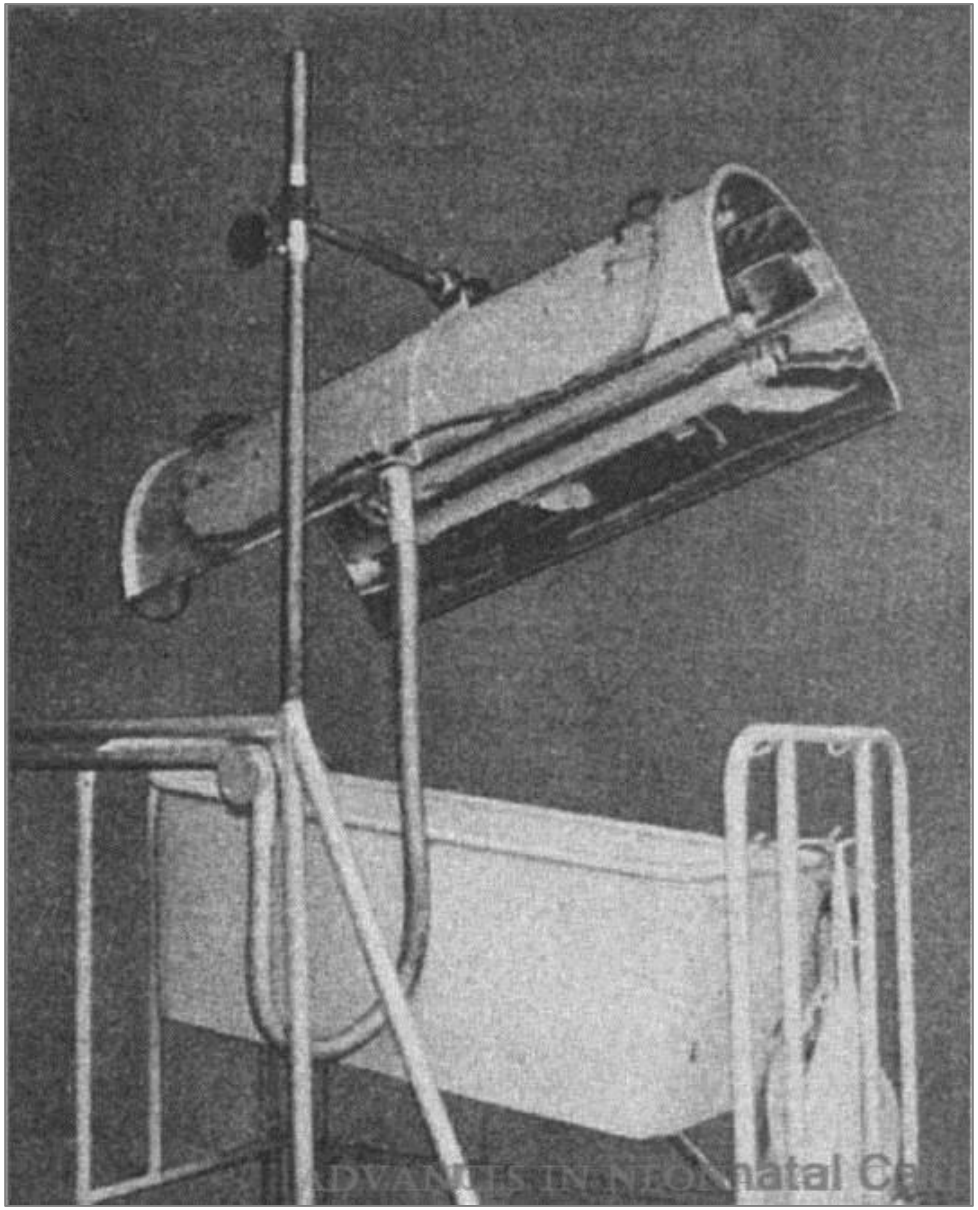

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FIGURE 2. The first artificial light apparatus devised for cradle illumination of infants at Rochford General Hospital. The hemicylindrical stainless steel reflector, suspended on a height-adjustable moveable gantry, contains eight 24-in light blue 40-W fluorescent tubes spaced 2 in apart. A cot can be wheeled underneath the reflector, and the lights can be switched on separately to vary the amount of power delivered.3 Reprinted with permission.

Neonatal Jaundice

- **Pathophysiology**
- Clinical presentation
- Diagnosis
- Follow up
- Medication
- Management
- Work up

Pathophysiology

- Accumulation of unconjugated bilirubin
- Normal transitional phenomenon
- Unconjugated bilirubin is neurotoxic

BILIRUBIN PHYSIOLOGY

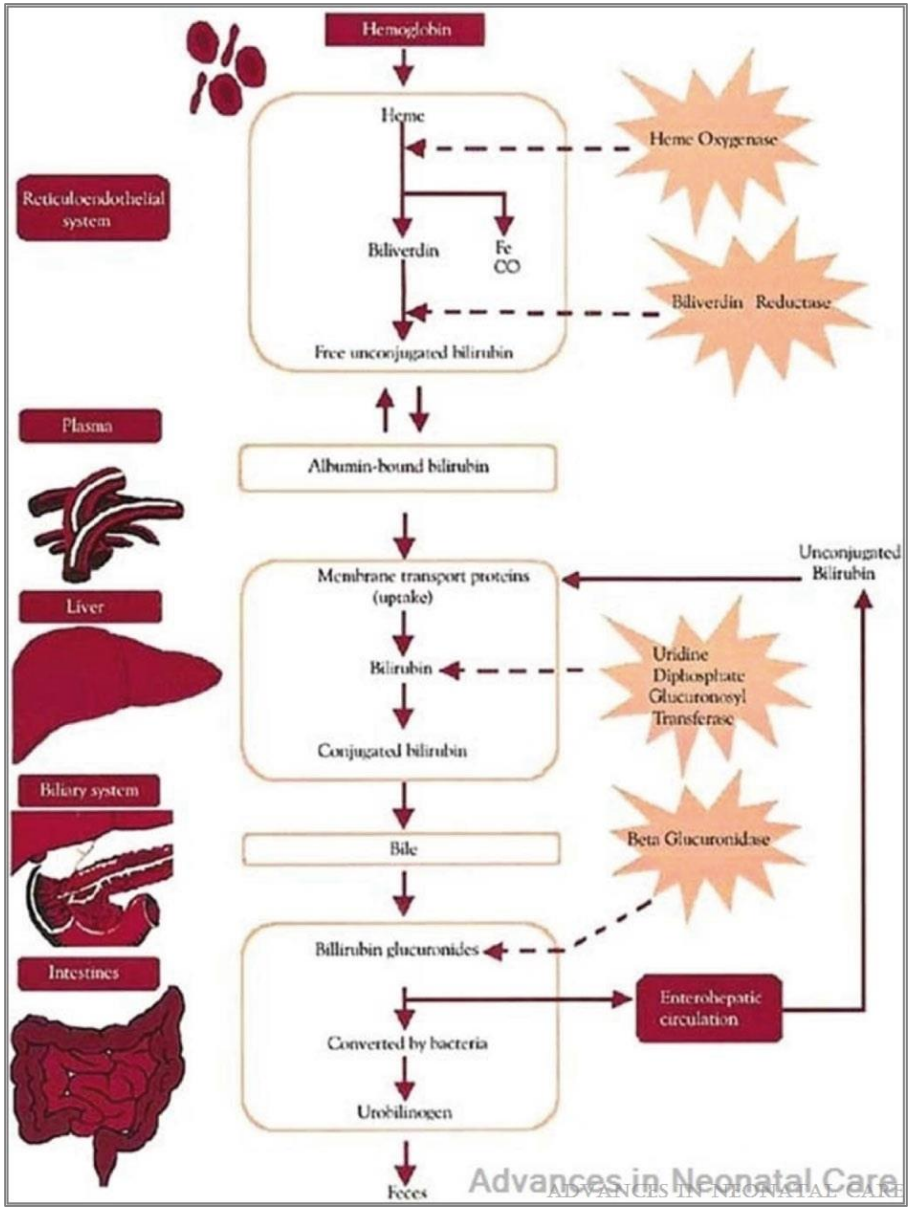

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FIGURE 3. Neonatal bilirubin metabolism. From Stokowski.7 Reprinted with permission.

HYPERBILIRUBINEMIA PATHOPHYSIOLOGY

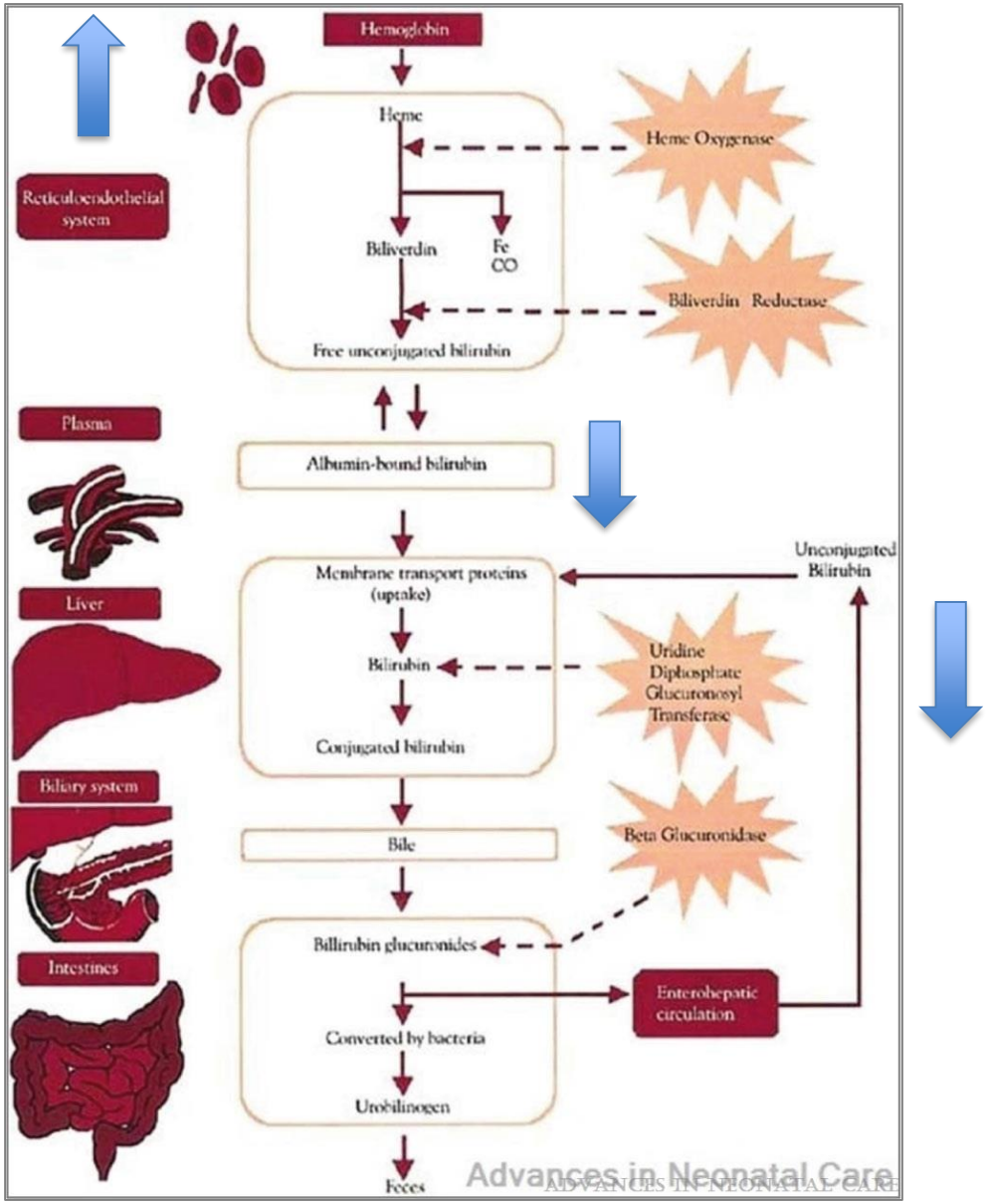

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FIGURE 3. Neonatal bilirubin metabolism. From Stokowski.7 Reprinted with permission.

Breastfeeding jaundice

- Within the first 7 days of life
- Result of increased enterohepatic circulation

Breast milk jaundice

- β-glucuronidase
- genetic polymorphisms in the coding sequences of the *UDPGT1A1* or *OATP2* genes

Epidemiology

- 6.1% infants have bilirubin >220 µmol/L
- 4.3% of 47,801 infants total serum bilirubin levels in a range in which phototherapy
- In some developing countries, the incidence of severe neonatal jaundice may be as much as 100 times higher

Epidemiology

- East Asian, American Indian, and Greek descent
- Male infants
- Inversely proportional to gestational age
- The incidence of kernicterus in North America and Europe ranges from 0.4-2.7 cases per 100,000 births.

Neonatal Jaundice

- Pathophysiology
- **Clinical presentation**
- Work up
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Clinical presentation - history

- On the second or third day of life
- Jaundice that is visible during the first 24 hours of life is likely to be nonphysiologic
- If continues beyond the first 1-2 weeks of life check newborn metabolic screen for galactosemia and congenital hypothyroidism

Clinical presentation – family history

- Previous sibling with jaundice in the neonatal period
- Other family members with jaundice or known family history of Gilbert syndrome
- Anemia, splenectomy, or bile stones in family members or known heredity for hemolytic disorders Liver disease

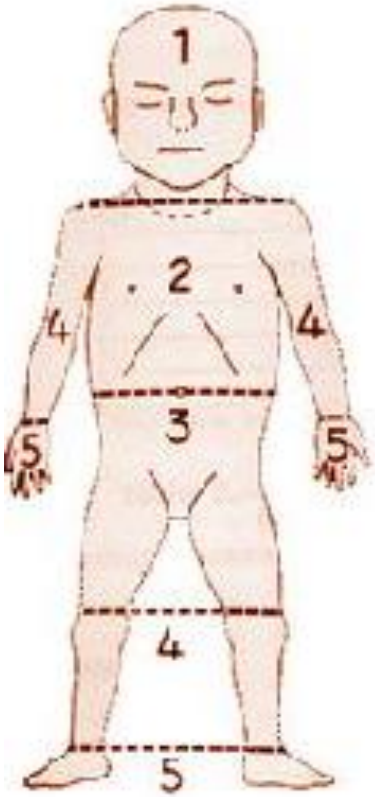
Clinical presentation - MHx

- Maternal illness suggestive of viral or other infection
- Maternal drug intake
- Delayed cord clamping
- Birth trauma with bruising and/or fractures.

Clinical presentation - Postnatal history

- Loss of stool color
- Breastfeeding
- Greater than average weight loss
- Symptoms or signs of hypothyroidism
- Symptoms or signs of metabolic disease (eg, galactosemia)
- Exposure to total parental nutrition

Clinical presentation-physical



The bilirubin range associated with each zone is:

Zone	1	2	3	4	5
SBR (micromol/L)	100	150	200	250	>250

Mechanisms of Hyperbilirubinemia

(1a) Increased Bilirubin Production	(1b) Impaired Conjugation or Excretion
Hemolytic disease of the newborn	**Inadequate or poor feeding intake**
• Rh isoimmunization	• Prematurity (<39 weeks)
• ABO incompatibility	• Delayed or impaired lactogenesis
• Minor blood group incompatibility	• Inadequate milk transfer
	• Other feeding disorders
Polycythemia	**Increased enterohepatic circulation**
	• Intestinal obstruction
	• Meconium ileus
	• Meconium plugging
	• Cystic fibrosis
Red blood cell enzyme disorders	**Hormonal deficiencies**
• G6PD deficiency	• Hypothyroidism
• Pyruvate kinase deficiency	• Hypopituitarism
Red blood cell membrane defects	**Disorders of bilirubin metabolism**
• Hereditary spherocytosis	• Crigler-Najjar syndrome I and II
	• Gilbert disease
	• Lucey-Driscoll syndrome
Birth trauma	
• Vacuum or instrumented delivery	
• Bruising	
• Cephalohematoma or subgaleal bleed	
Neonatal infection	
• Urinary tract infection	
• Sepsis	
Ethnicity	
• Asian ethnic background	

ADVANCES IN NEONATAL CARE

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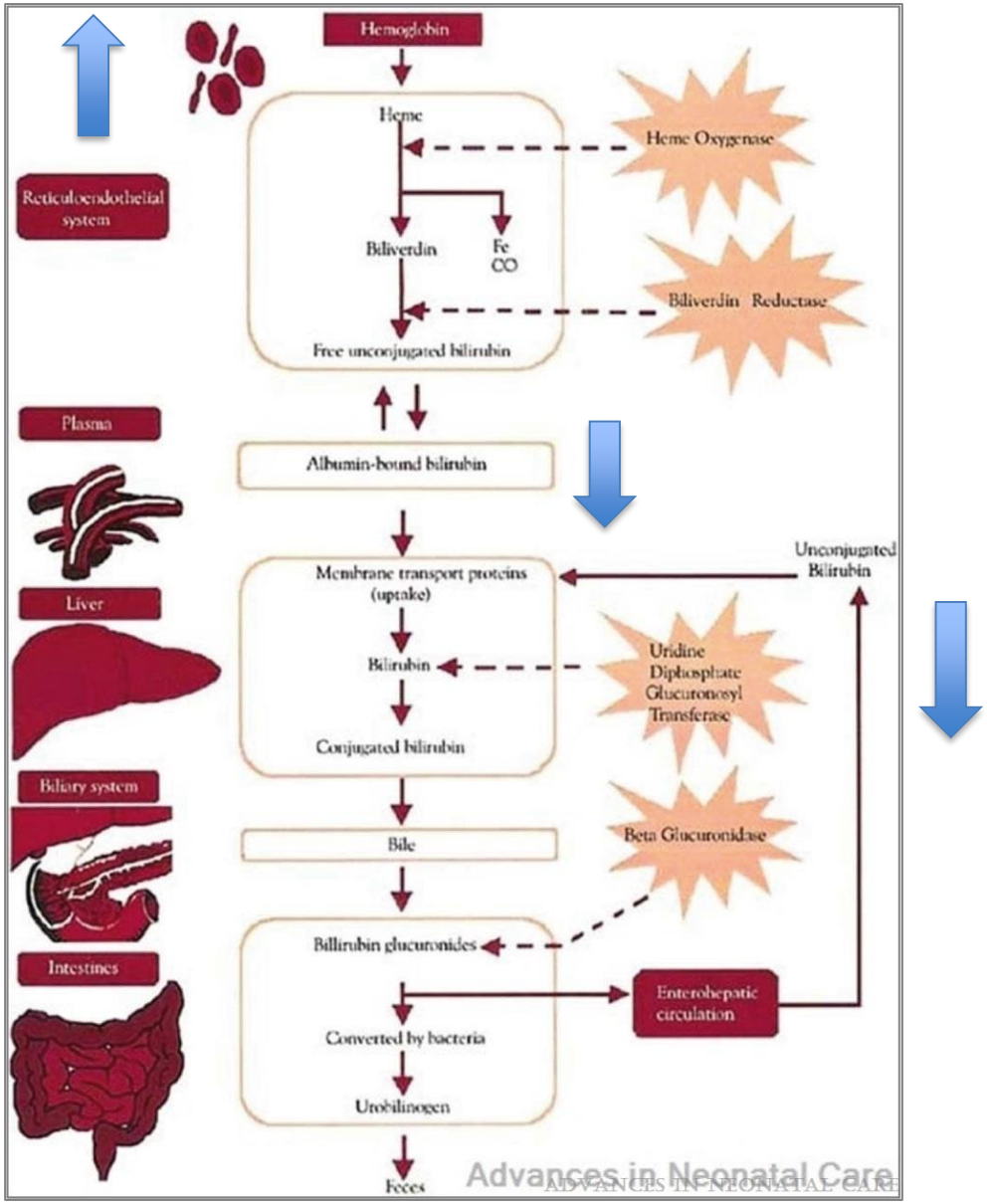

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Neonatal Jaundice

- Pathophysiology
- Clinical presentation
- **Work up**
- Diagnosis
- Management
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Work up – laboratory studies

- Transcutaneous bilirubin
- Total serum bilirubin
- Conjugated bilirubin
- Unconjugated bilirubin

Neonatal Jaundice

- Pathophysiology
- Clinical presentation
- Work up
- **Diagnosis**
- Management
- Medication
- Follow up

Differential diagnosis

- Biliary Atresia
- Breast Milk Jaundice
- Cholestasis
- Cytomegalovirus Infection
- Dubin-Johnson Syndrome
- Duodenal Atresia
- Galactose-1-Phosphate Uridyltransferase Deficiency (Galactosemia)
- Hemolytic Disease of Newborn
- Hepatitis B
- Hypothyroidism

Neonatal Jaundice

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- **Management**
- Medication
- Follow up

Management

- Phototherapy
- IVIG
- Exchange transfusion

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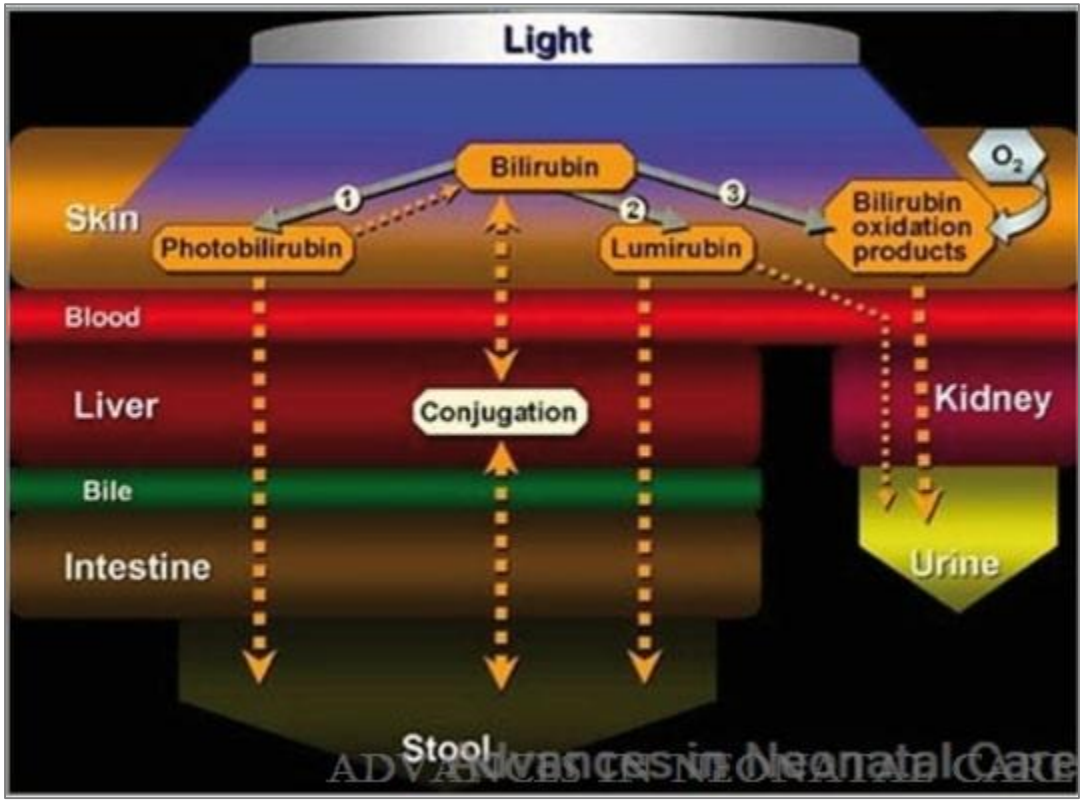

FIGURE 4. Diagram courtesy of Mary Puchalski.

Phototherapy

- Wavelenght 450-460nm
- Irradiation level of 30-40 μW/cm2/nm
- Distance to infants skin 10-50cm

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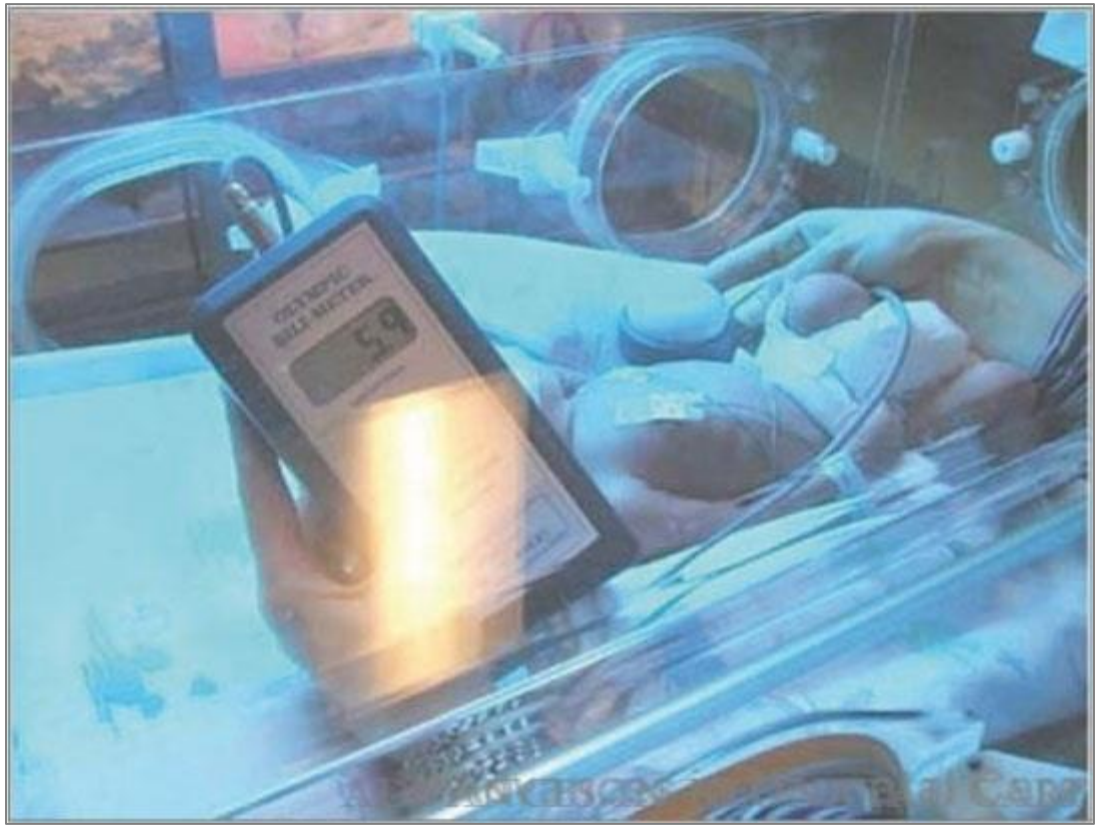

FIGURE 11. Using a radiometer to measure irradiance level during phototherapy.

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FIGURE 5. Two halogen spotlight are used to provide more complete coverage. Note that the lights are not superimposed over the same area of skin but are used to provide coverage over different body surface areas on this large infant.

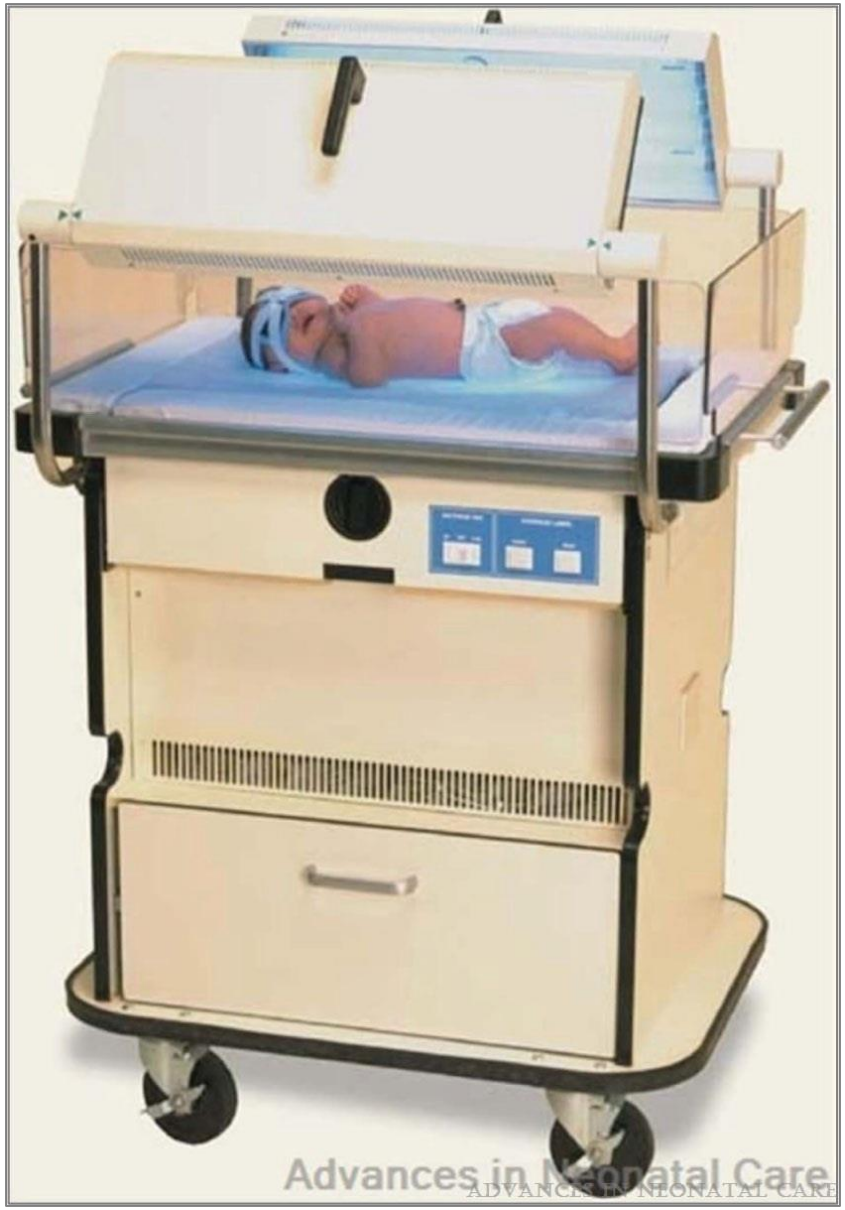

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FIGURE 6. The Bili-Bassinet (Natus Medical Incorporated) is a phototherapy delivery system that provides combination phototherapy. Courtesy of Olympic Medical.

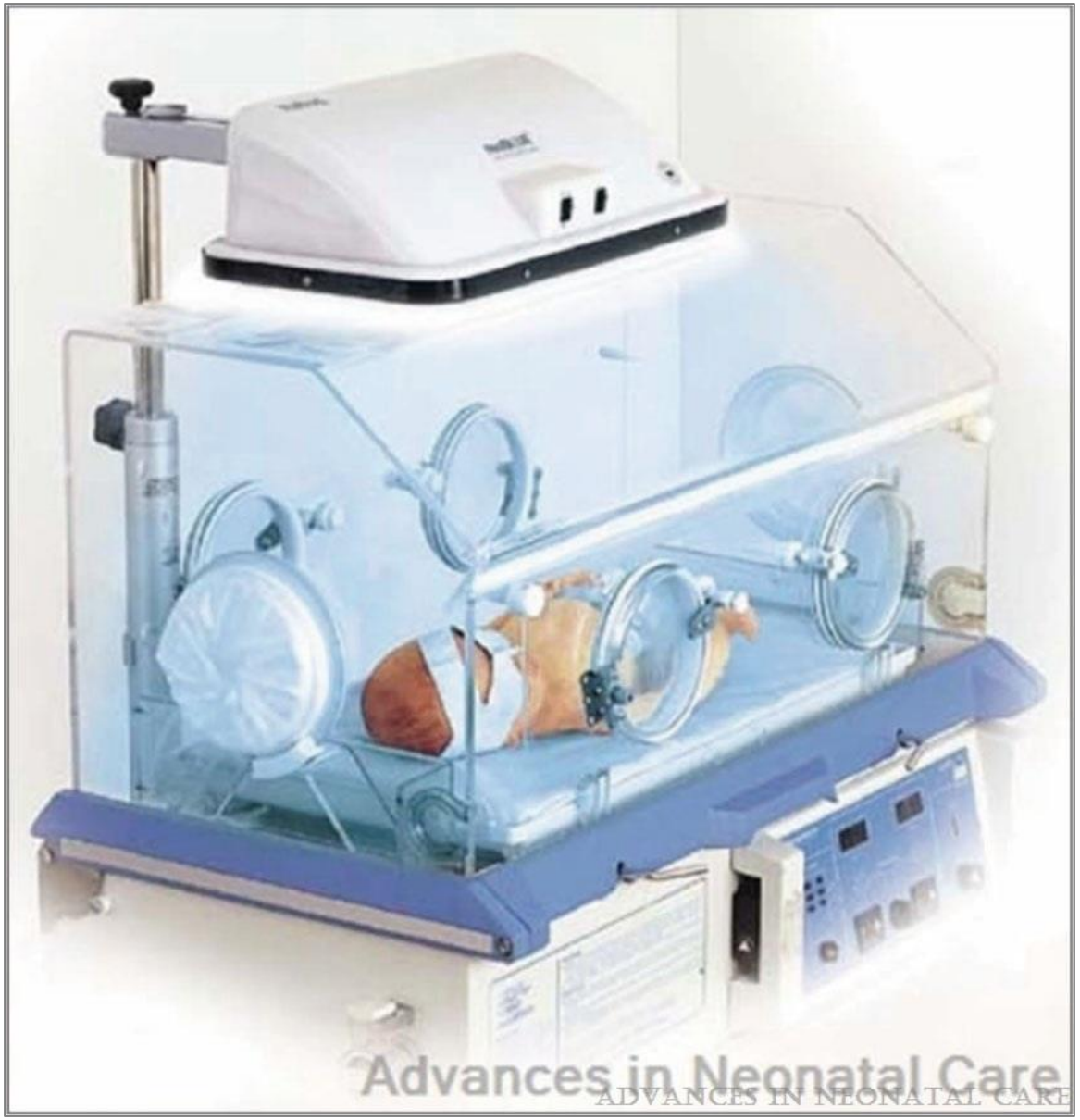

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FIGURE 7. Phototherapy system that comprises a light-emitting diode and the option to switch between single or double phototherapy at the touch of a button (NeoBlue, Natus Medical Inc, San Carlos, California). Courtesy of Natus Medical Inc.

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FIGURE 8. Halogen spot light phototherapy system. Courtesy of GE Healthcare. Reprinted with permission.

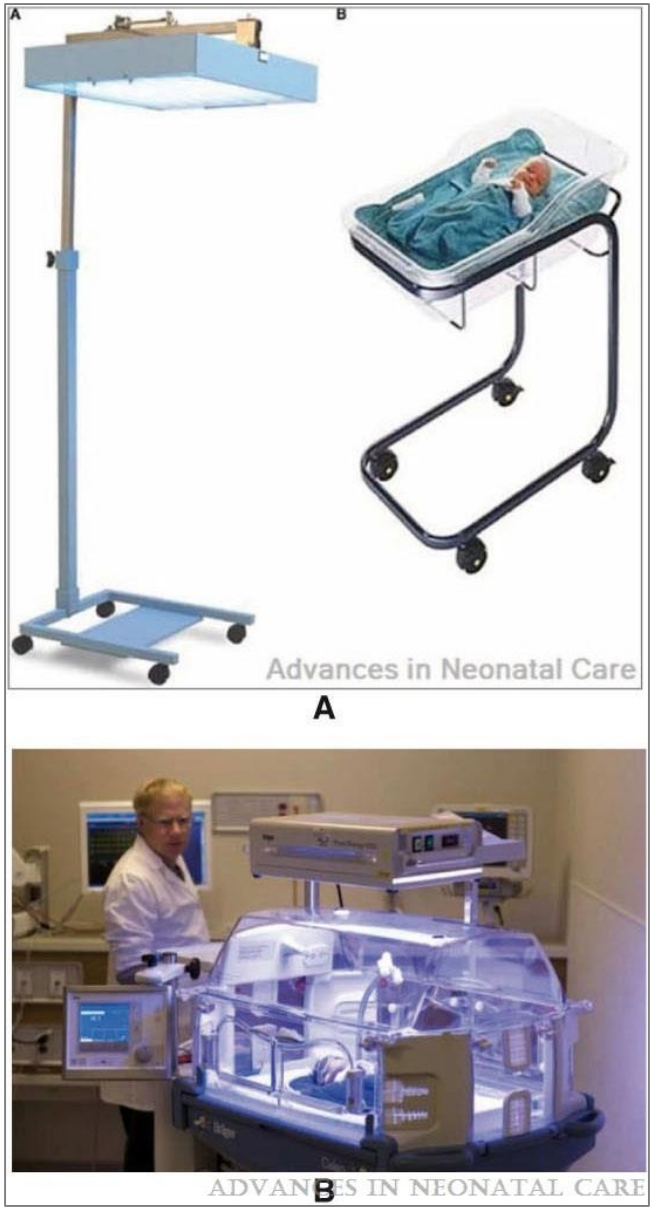

FIGURE 9. Phototherapy systems that incorporate fluorescent tubes. Conventional bank lights (A) can be positioned over an infant in a bassinet or incubator. Courtesy of Olympic Medical. An overhead system that combines blue and white tubes is both effective and caregiver friendly (B). Courtesy of Draeger Medical. With the BiliBed (C), the infant lays on a soft mattress of fluorescent tubes, receiving high-intensity phototherapy from below. Courtesy of Medela, Inc.

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FIGURE 10. Fiberoptic blanket phototherapy system. Courtesy of GE Healthcare.

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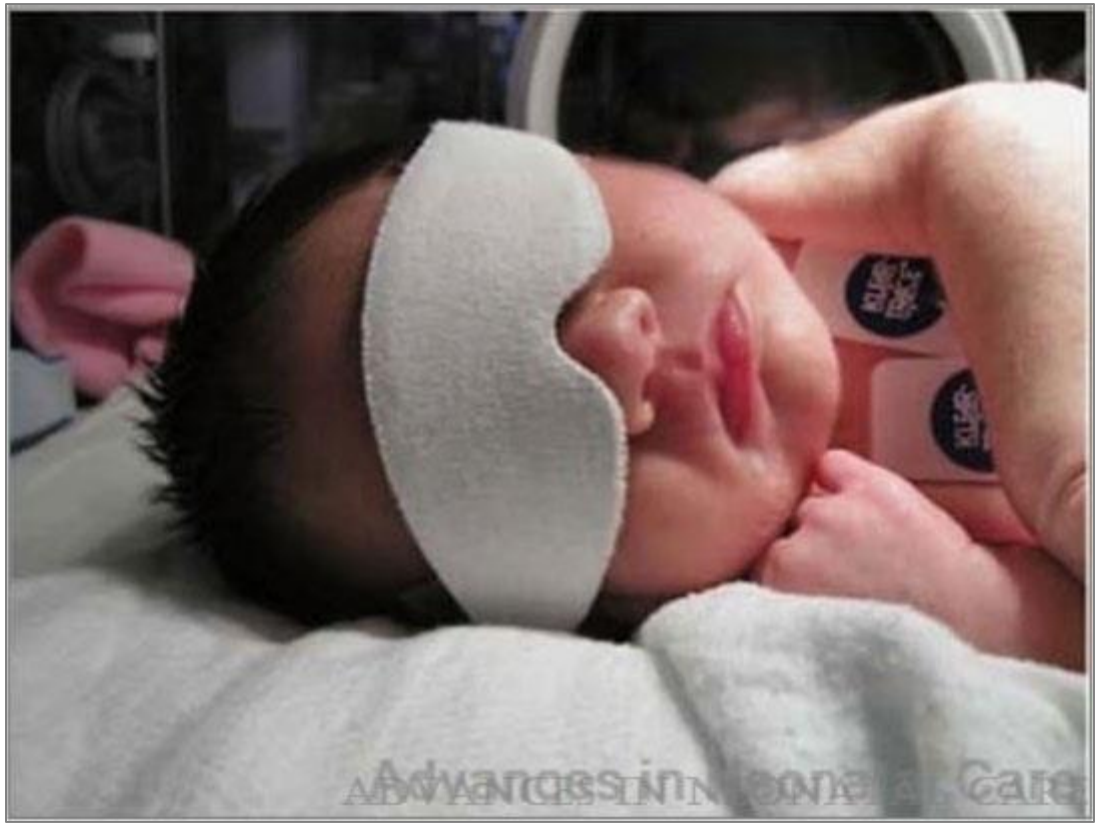
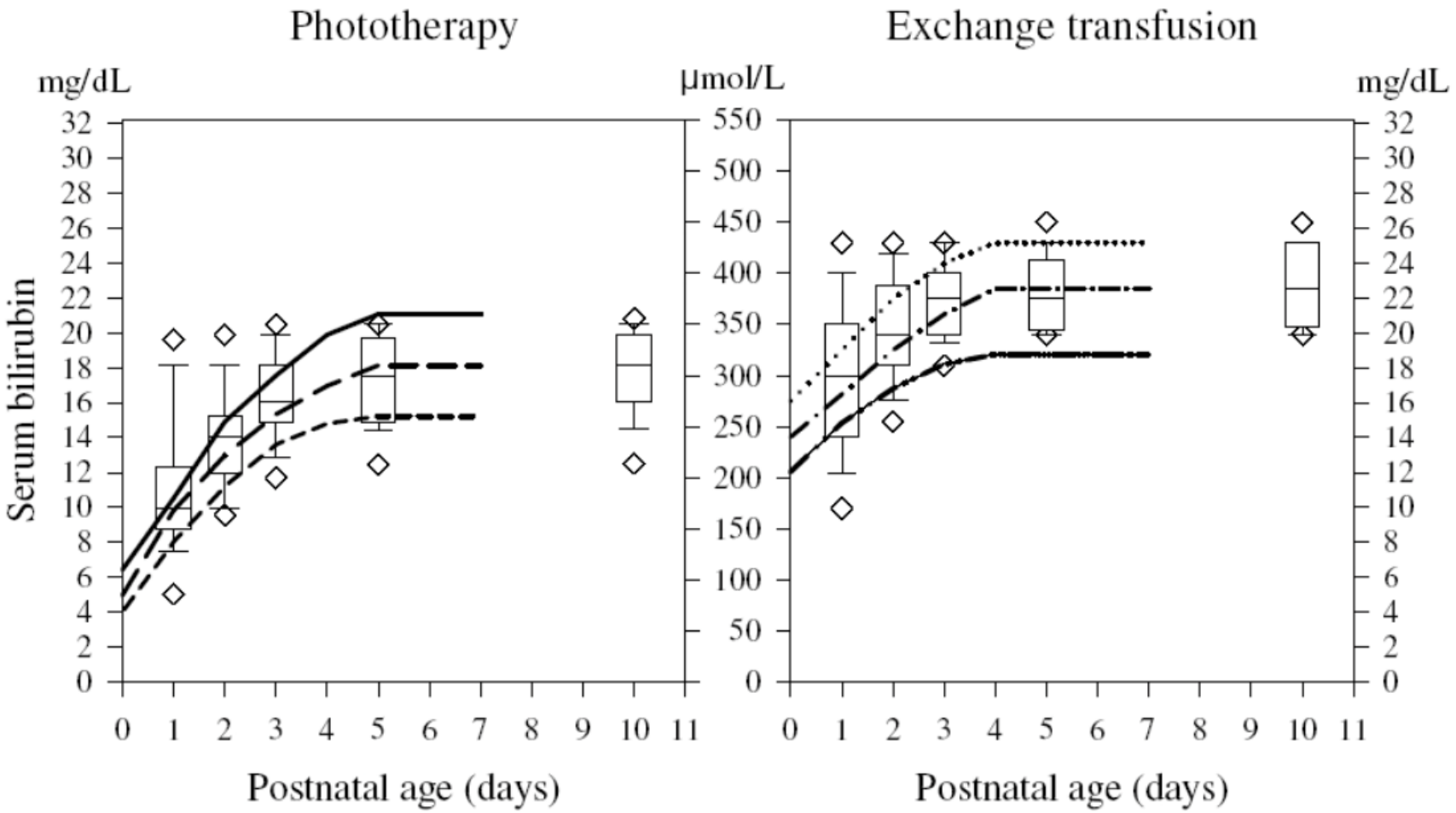


FIGURE 12. Properly positioned phototherapy eye shields.

Phototherapy

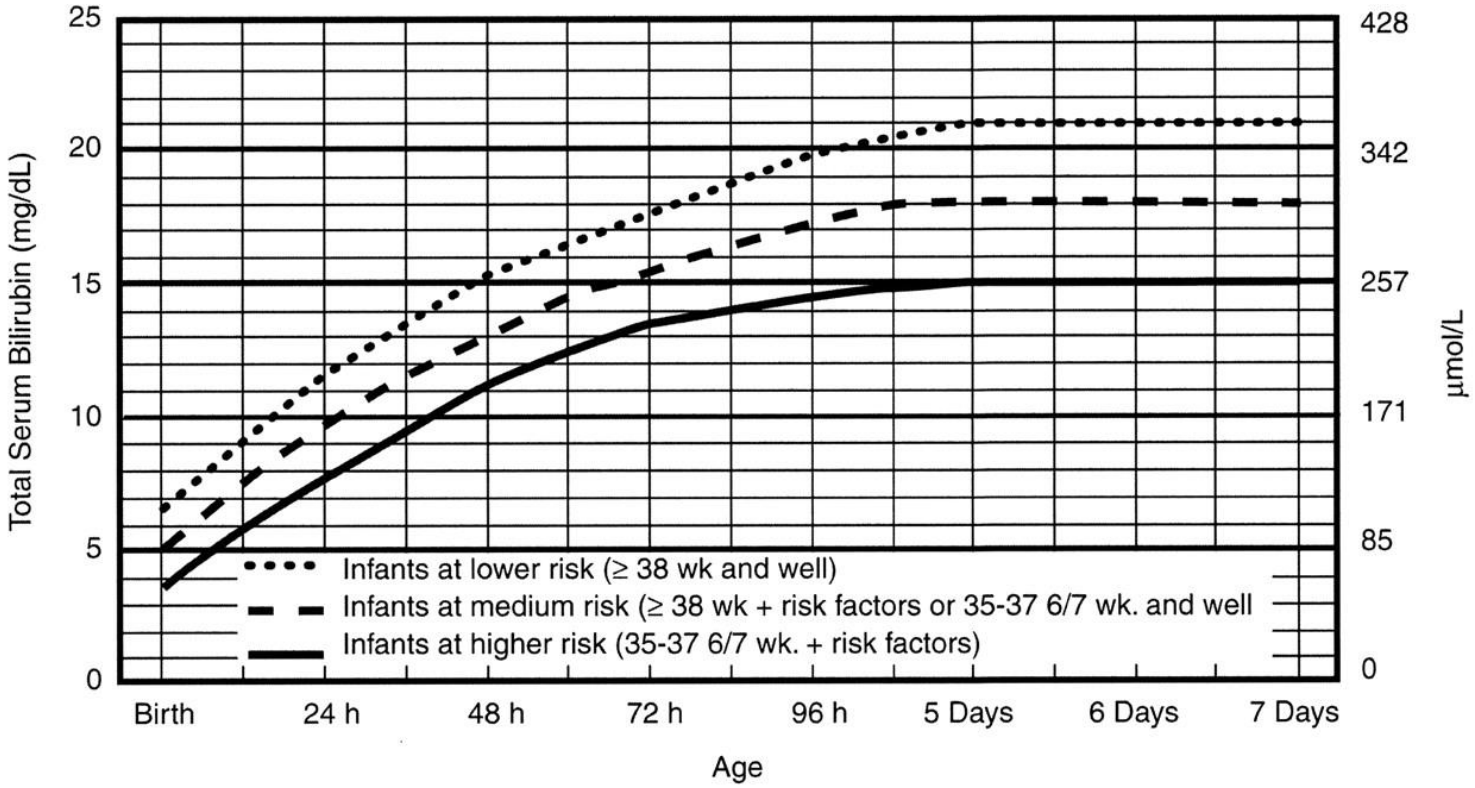


Hansen TW. Therapeutic approaches to neonatal jaundice: an international survey. *Clin Pediatr (Phila)*. Jun 1996;35(6):309-16.

Guidelines

- CPS =AAP
- NICE

Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation. Note: These guidelines are based on limited evidence and the levels shown are approximations.



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 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 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

et al. Pediatrics 2004;114:297-316

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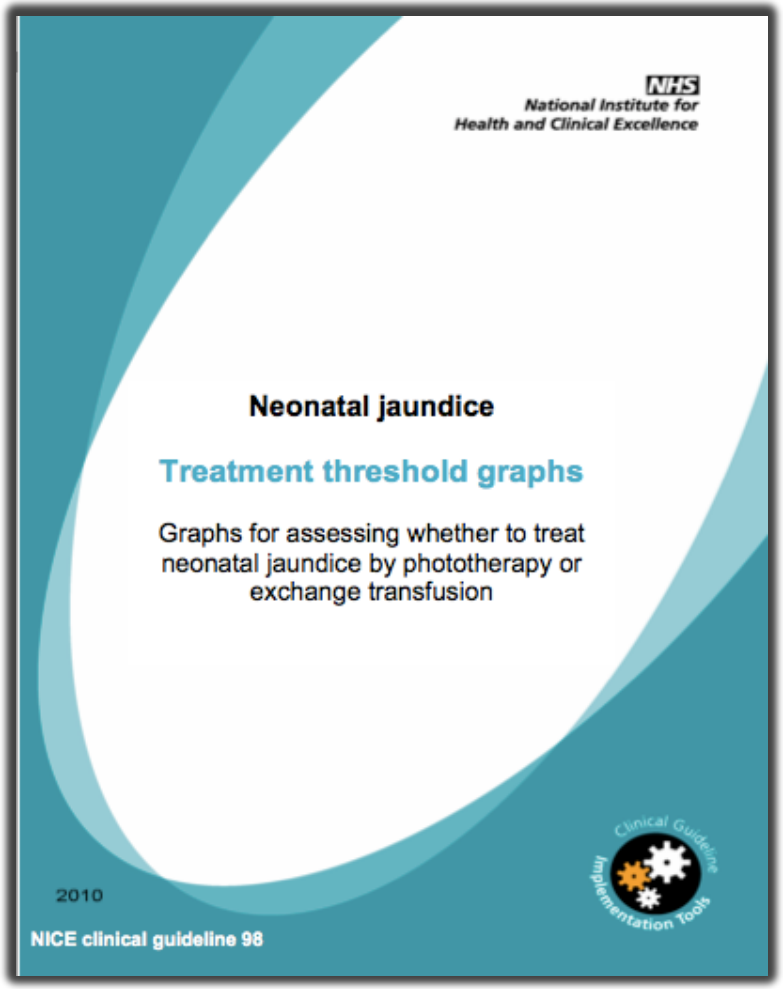
Risk factors

- Isoimmune hemolytic disease
- Sigificant lethargy
- Asphyxia
- Temperature instability
- Acidosis
- Sepsis
- Albumin levels < 3mg/dl

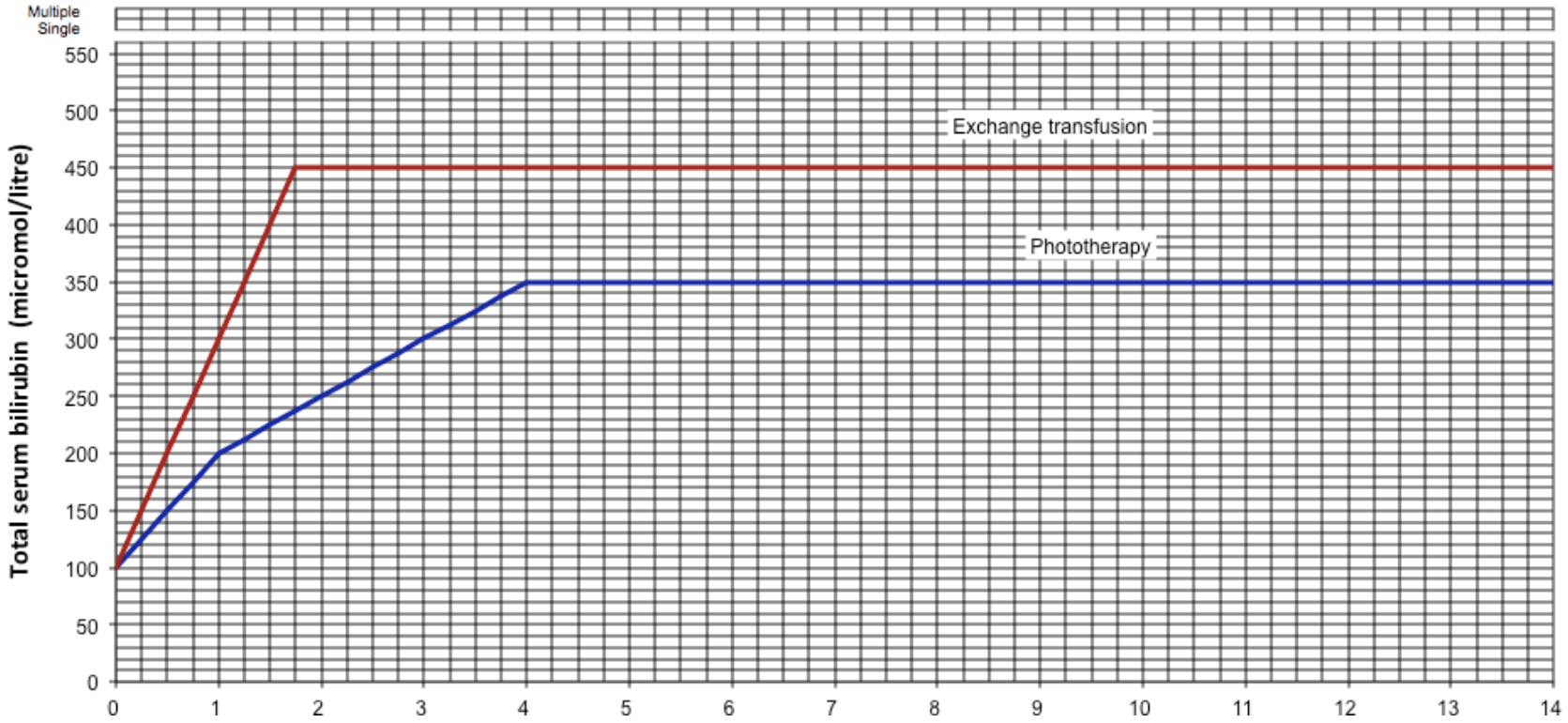

NHS
National Institute for
Health and Clinical Excellence
Neonatal jaundice
Treatment threshold graphs
Graphs for assessing whether to treat neonatal jaundice by phototherapy or exchange transfusion
Clinical Guideline
Implementation Tools
2010
NICE clinical guideline 98

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____

Shade for phototherapy Baby's blood group _____ Mother's blood group _____

Click below and choose gestation

>=38 weeks gestation



Phototherapy – practical aspects

- Naked infants
- Cover inside of bassinet with reflecting material
- No increase of insensible water loss – do not adjust fluids routinely in preterm infants!

Phototherapy - monitoring

- serum bilirubin values (>500 µmol/L or 30 mg/dL), monitor bilirubin q1h
- q 6-12 h
- “The higher the rise the quicker the fall”
- Discontinued bilirubin fall 25-50 µmol/L (1.5-3 mg/dL) below the level that triggered the initiation of phototherapy
- follow-up bilirubin 6-12 h after discontinuation for rebound

IVIG

- 500-1000mg/kg dose over 2-4hours
- Repeat dose if necessary, q 12h if bilirubin continues to rise

Journal of Paediatrics and Child Health

doi:10.1111/jpc.12440

JOURNAL CLUB

Edited by Patrina Caldwell (patrina.caldwell@health.nsw.gov.au)

Should intravenous immunoglobulin be used in infants with isoimmune haemolytic disease due to ABO incompatibility?

Amy K Keir,[1,4] Michael Dunn[1] and Jeannie Callum[2,3]

[1]Division of Neonatology, Department of Paediatrics and [2]Department of Laboratory Medicine and Pathobiology Faculty of Medicine, University of Toronto, [3]Department of Clinical Pathology, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada and [4]School of Paediatrics and Reproductive Health, University of Adelaide, South Australia, Australia

Table 1 Criteria for the disease of isoimmune haemolytic disease of the newborn due to ABO incompatibility (ABO HDN)

Serological evidence consistent with ABO incompatibility:

Mother – group O blood *and*

Infant – blood group A, B or AB *and*

Direct antiglobulin test (DAT) positive (or eluate positive for anti-A/B)

and

Evidence of haemolysis as indicated by:

Elevated reticulocyte count (>137.3 ± 33 × 10(9)/L)[3] *or*

Micro/spherocytes on peripheral blood film *or*

Progressive anaemia on serial complete blood counts *or*

Biochemical markers consistent with haemolysis

(hyperbilirubinaemia and elevated lactate dehydrogenase (LDH))

(>529 ± 176 IU/L[3,4])

and

Exclusion of other causes of hyperbilirubinaemia

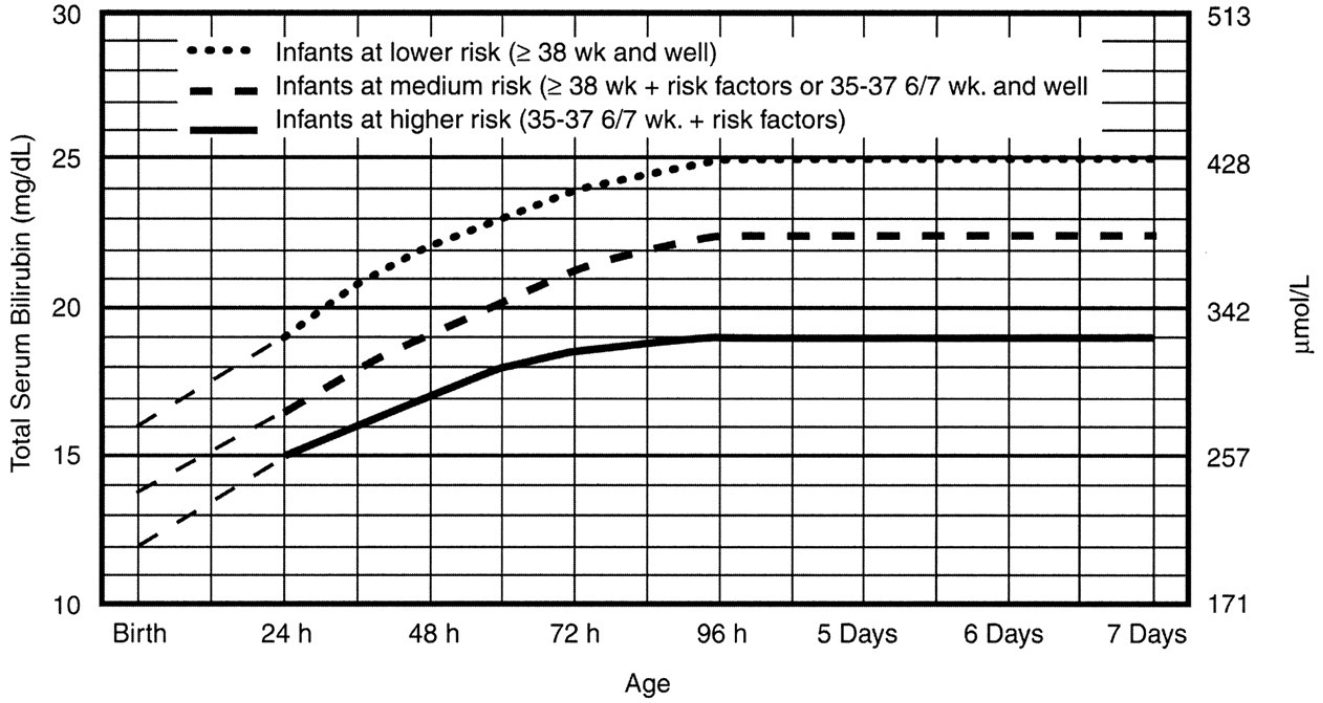
Table 2 Potential complications due to the use of intravenous immunoglobulin in infants

- Infusion adverse reactions: vomiting, allergic reactions, rigors, fever, hypotension, anaphylaxis
- Immune-mediated haemolysis secondary to anti-A and anti-B
- Aseptic meningitis
- Circulatory overload
- Transfusion-associated lung injury
- Thrombosis
- Emerging association with necrotising enterocolitis[5,6]

Indications for exchange transfusion-previous criteria

- anemia (cord hemoglobin < 11 g/dL), elevated cord bilirubin level (>70 µmol/L or 4.5 mg/dL), or both.
- rapid rate of increase in the serum bilirubin level (>15-20 µmol/L /h or 1 mg/dL/h)
- moderate rate of increase (>8- 10 µmol/L/h or 0.5 mg/dL/h) in the presence of moderate anemia (11-13 g/dL)
- vigintiphobia

Guidelines for exchange transfusion in infants 35 or more weeks' gestation.Note that these suggested levels represent a consensus of most of the committee but are based on limited evidence, and the levels shown are approximations.



- 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.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥5 mg/dL (85 µmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend)
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

Subcommittee on Hyperbilirubinemia Pediatrics
2004;114:297-316

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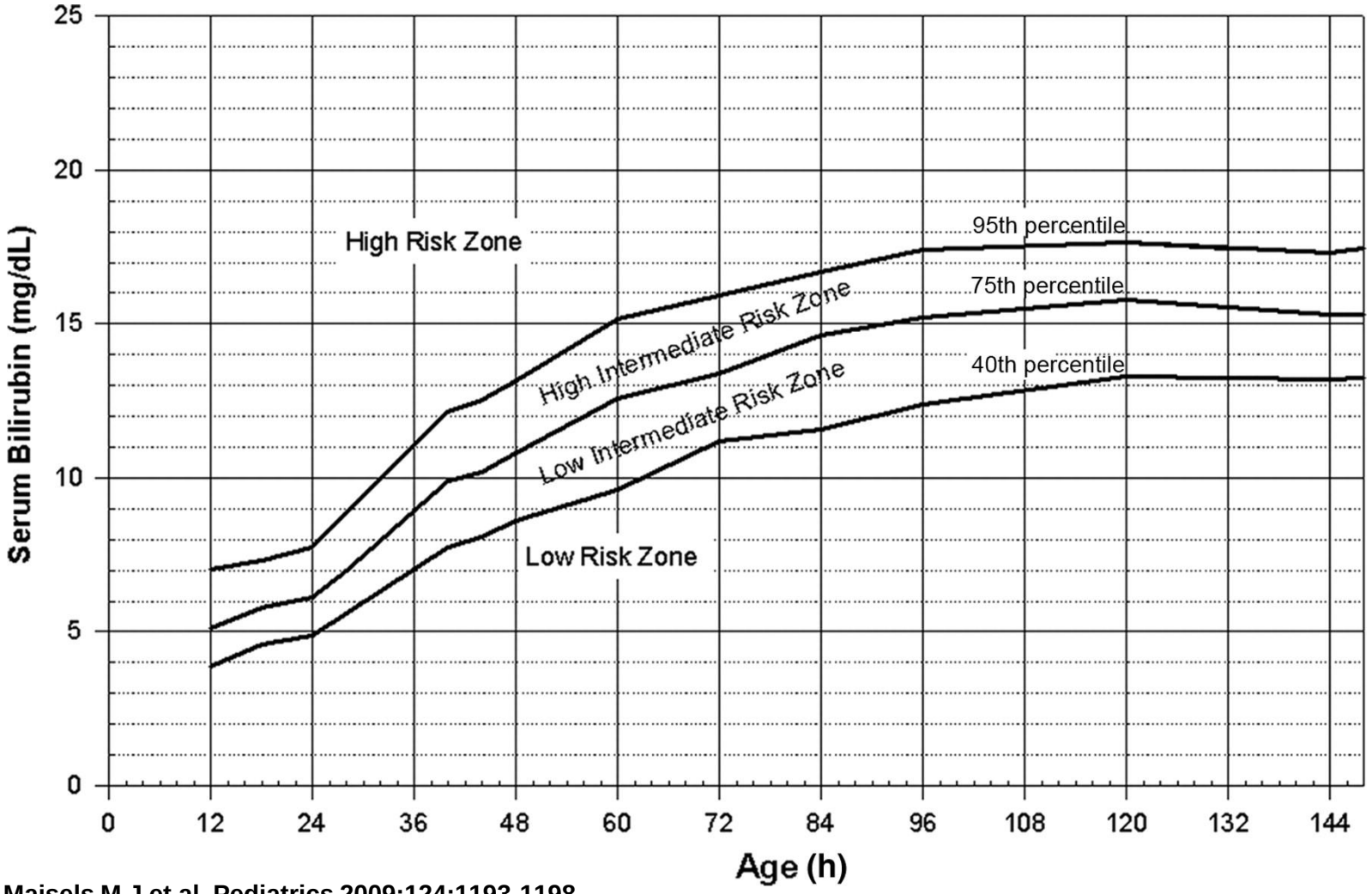
Management of babies readmitted for jaundice

- Start phototherapy ASAP
- Do not start iv fluids unless clinical signs of dehydration are present
- Oral feeding is preferable if tolerated

Follow up

- 2 successive serum bilirubin levels demonstrating a trend towards lower values.
- auditory function prior to discharge in infants who have had severe jaundice.

Nomogram for designation of risk in 2840 well newborns at ≥36 weeks' gestational age with birth weight of ≥2000 g or ≥35 weeks' gestational age and birth weight of ≥2500 g based on the hour-specific serum bilirubin values.



Maisels M J et al. Pediatrics 2009;124:1193-1198

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References

- http://pediatrics.aappublications.org/content/114/1/297.full
- http://emedicine.medscape.com/article/974786-overview
- http://onlinelibrary.wiley.com/doi/10.1111/jpc.12262/abstract