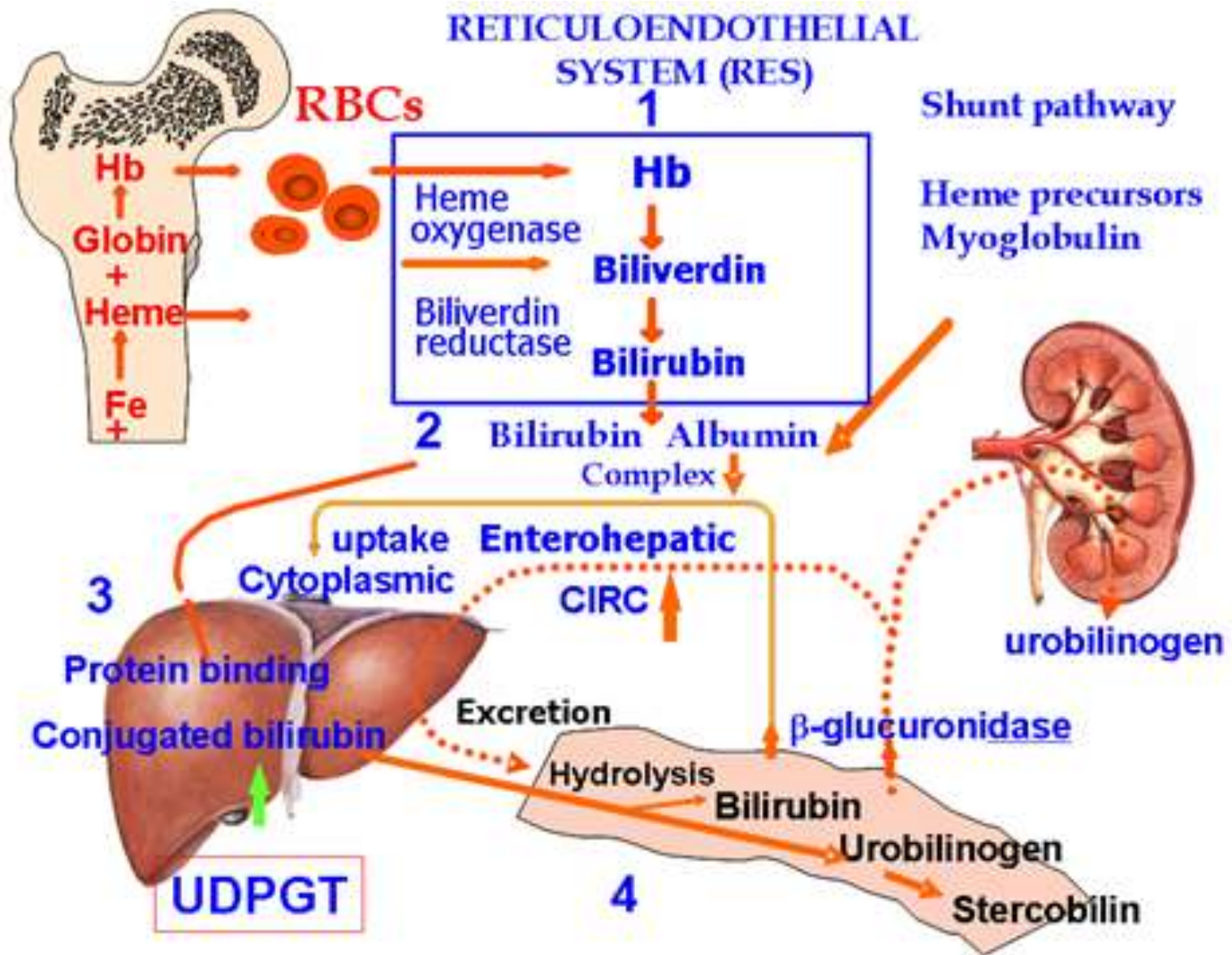


*IS BILIRUBIN a **CURSE** OR a **BOON**?*

- For many years, unconjugated bilirubin (UCB) was thought to be a useless waste product of heme catabolism, with no physiological function, but with potential toxicity.
- Contrary to what you often will hear about how bilirubin levels increasing in a newborn is not a good thing, there is new research which is showing the importance of the presence of bilirubin.

Neonatal Jaundice





- Bilirubin has the ability to function as an antioxidant in the brain, scavenging free radicals and protecting the brain against oxidative damage.
- Babies with higher bilirubin levels are more disease-resistant,” said Dr. Sylvain Dore of Johns Hopkins School of Medicine, Baltimore, Maryland.
- Dr. Dore has done research on the neuroprotective effect of bilirubin in the hippocampus. His studies have indicated that low concentrations of bilirubin decreased oxygen-radical mediated injury, suggesting that bilirubin could act as an antioxidant.



B-barekatain ,Neonatologist

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- Bilirubin also “protects against retinopathy in premature babies.”

Dore S, Snyder SH. Neuroprotective action of bilirubin against oxidative stress in primary hippocampal cultures. Ann N Y Acad Sci.72-890:167;1999.

- “Bilirubin also has bacteriostatic effect???”

The antibacterial effects of bilirubin on gram-negative bacterial agents of sepsis. Huseyin Agah Terzi, Hakan Kardes. Biomedical Research (2016) Volume 27, Issue 1

- In some experiments researchers prevented bilirubin synthesis by eliminating the gene for hemoxygenase and found, as a result, twice the level of stroke damage in mice.

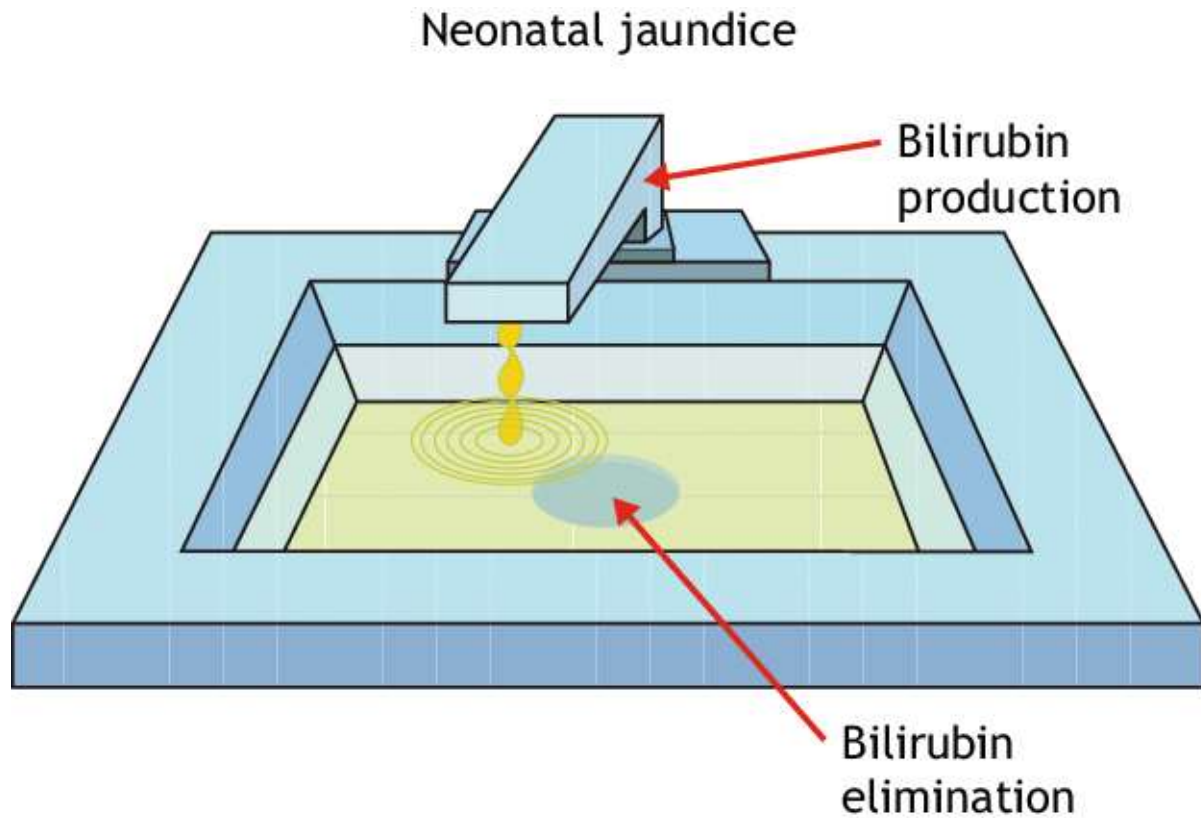
Tomaro ML, Battle AMD. Bilirubin: its role in cytoprotection against oxidative stress.Int J Biochem Cell Biol 2002;34:216–20.

- UCB is a **curse** at high concentrations, producing apoptosis and cell death, but a **boon** at more physiological levels, protecting cells against oxidant damage.

J D Ostrow. Research Service, VA Puget Sound Health Care System-Seattle Division, and GI/Hepatology Division, Department of Medicine, University of Washington School of Medicine, Seattle, WA, USA.



Treatment is undertaken to prevent neurological damage



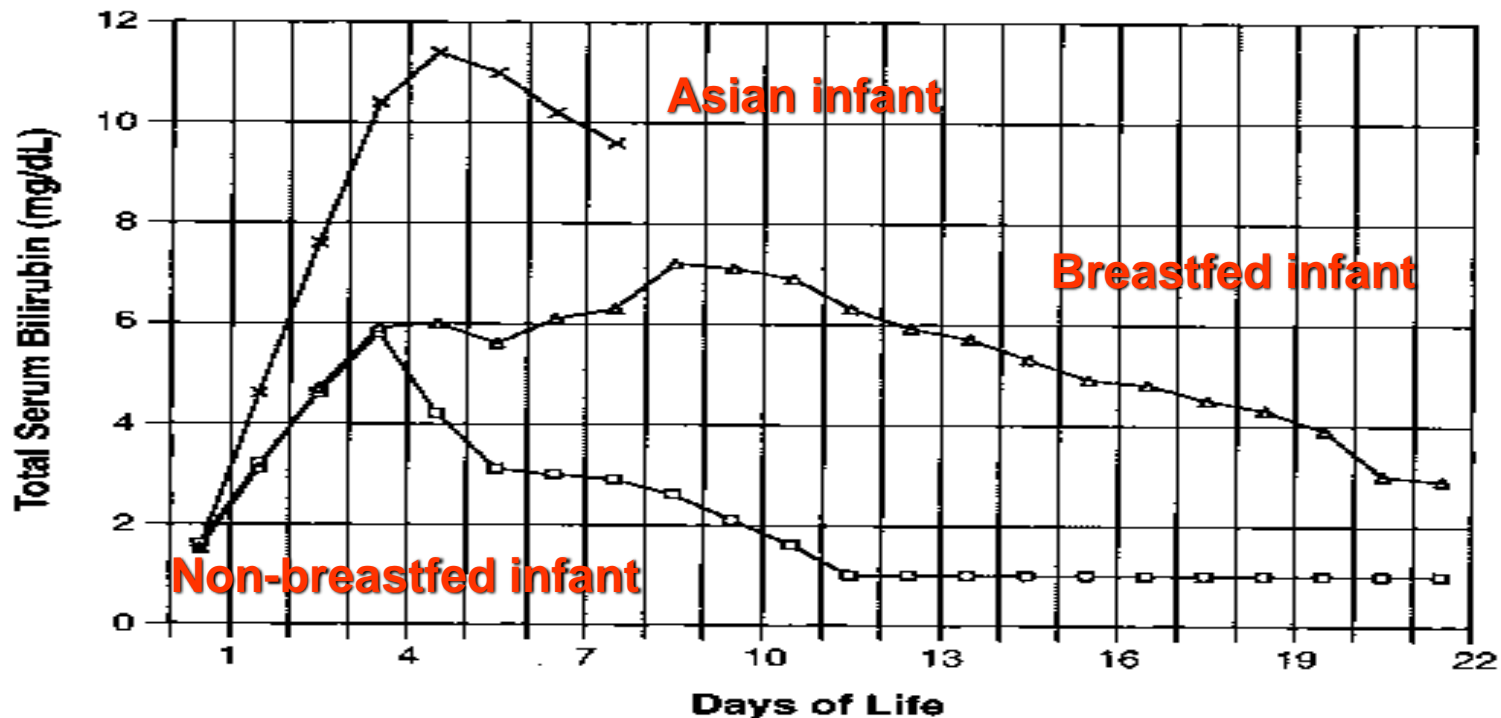
- Hyperbilirubinemia is a common and, in most cases, **benign problem** in neonates.
- untreated, **severe indirect hyperbilirubinemia** is potentially **neurotoxic**
- **conjugated-direct** hyperbilirubinemia often signifies a **serious hepatic or systemic illness**.
- Jaundice is observed during the 1st wk of life in approximately **60%** of term infants and **80%** of preterm infants.



Physiologic Jaundice

■ Features

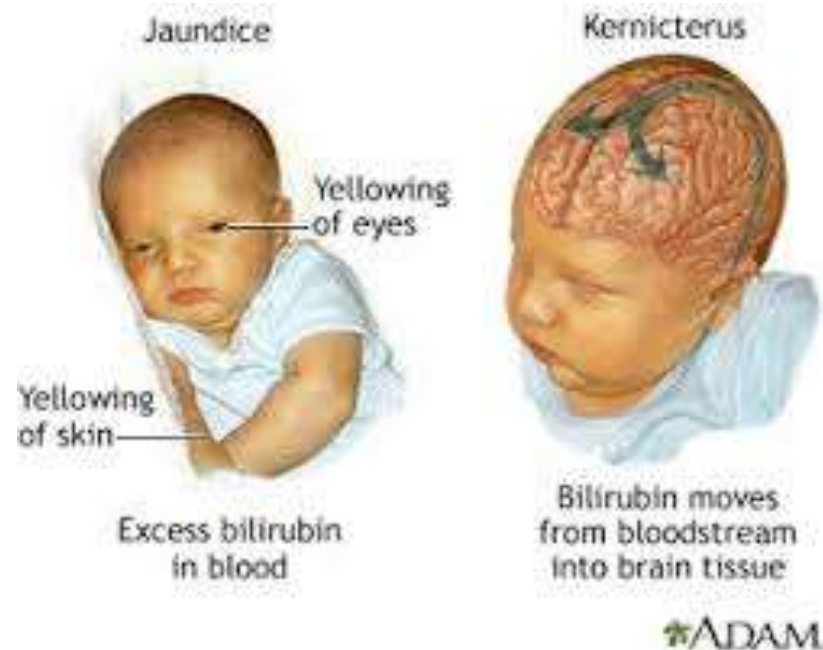
- Elevated unconjugated bilirubin
- TSB generally peaks @ 5-6 mg/dL on day 3-4 and then declines to adult levels by day 10
 - Asian infants peak at higher values (10 mg/dL)
- Exaggerated physiologic (up to 17 mg/dL)



Sequelae of Unconjugated Hyperbilirubinemia

Acute hyperbillirubin encephalopathy

kernicterus



Acute Bilirubin Encephalopathy

□ Phase 1- poor suck, hypotonia, and depressed sensorium

□ Phase 2- fever and hypertonia or opisthotonus

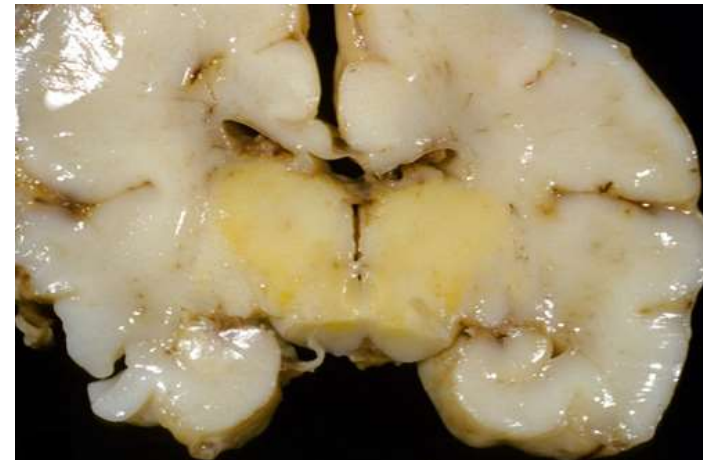
□ Phase 3- less hypertonia, high pitched cry, hearing and visual abnormalities, poor feeding, athetosis



KERNICTERUS

- If early acute bilirubin encephalopathy is unrecognized or untreated, it may progress to permanent neurologic impairment.
- The term kernicterus (German kern, kernel or nucleus, and ikteros, jaundice) has been traditionally used to describe the pathologic findings of bilirubin toxicity within the brain:

staining and necrosis of neurons in the basal ganglia, hippocampal cortex, subthalamic nuclei, and cerebellum, followed by gliosis of these areas in survivors.






The cerebral cortex is generally spared.

About half of all infants with kernicterus observed at autopsy also have extraneural lesions of bilirubin toxicity.

These include necrosis of renal tubular cells, intestinal mucosa, and pancreatic cells in association with intracellular crystals of bilirubin. Gastrointestinal hemorrhage may accompany these lesions.

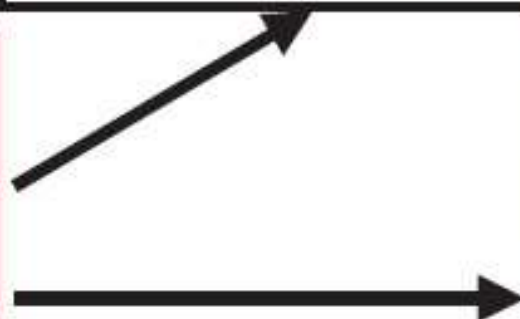
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- survivors often demonstrate the classic signs of kernicterus, including *choreoathetoid cerebral palsy*, *upward gaze palsy*, *sensorineural hearing loss*, and dental dysplasia during later infancy and childhood.
 - The intellect may be spared, and mental retardation is not universally encountered.
 - However, infants with normal intelligence frequently have severe physical handicaps, making rehabilitation, education, and independent living unlikely.
 - These sequelae of bilirubin toxicity may also develop in neonates who never manifested clinical signs of acute bilirubin encephalopathy during the newborn period.

Kernicterus Spectrum Disorders: Adverse Bilirubin Outcomes

Acute Bilirubin
Encephalopathy

Death: Acute
Respiratory Failure

Chronic Post-Icteric
Sequelae (Kernicterus)



Outcome
influenced by
timely intervention



Auditory Neuropathy
(isolated)

Subtle manifestations (extrapyramidal and
central processing disorders)
suspected but not yet proven

Bilirubin-Induced Neurologic Dysfunction (BIND)



MEASUREMENT OF BILIRUBIN FRACTIONS

VISUAL ASESSEMENT- KRAMER's RULE



Table 1. Visual Assessment of Neonatal Jaundice (Kramer's rule)

Area of the Body	Level	Range of Serum Bilirubin	
		$\mu\text{mol/L}$	mg/dL
Head and neck	1	68 - 133	4 - 8
Upper trunk (above umbilicus)	2	85 - 204	5 - 12
Lower trunk and thighs (below umbilicus)	3	136 - 272	8 - 16
Arms and lower legs	4	187 - 306	11 - 18
Palms and soles	5	≥ 306	≥ 18

Kramer's rule describes the relationship between serum bilirubin levels & the progression of skin discolouration

- Total Serum Bilirubin Measurement
- Transcutaneous Bilirubinometry

Today other noninvasive methods, specifically TcB, to assess jaundice have become routine practice in the newborn nursery as a screening method more sensitive than visual assessment for jaundice.

There are two commercially available transcutaneous instruments approved by the Food and Drug Administration (FDA) to measure TcB in neonates:

The Philips Children's Medical Ventures BiliChek (Respironics, Inc, Murrysville, PA)




and the Konica Minolta Air-Shields Transcutaneous Jaundice Meter 103 (JM-103, Draeger Medical Systems, Inc, Telford, PA).





B-barekataan ,Neonatologist



TcB measurements have been incorporated into clinical practice as an alternative to heel stick for screening jaundice in the newborn nursery.

This has the potential to **reduce the incidence of heel stick** by 40–60% and to **reduce potential serious, albeit rare, complications** of blood collection, including infection and osteomyelitis.

use of TcB measurements **decreases TSB measurements** and **saves money**.

The combination of peak predischarge TcB with two clinical risk factors for pathologic hyperbilirubinemia, exclusive breastfeeding and gestational age, improves prediction of subsequent hyperbilirubinemia meriting treatment.

Significant TcB levels (>14 mg/dL) should prompt measurement of a TSB level for confirmation.

■ استفاده از دستگاه transcutaneous bilirubinometer از سالیان قبل به لحاظ داشتن مزایایی از جمله کاهش خون گیری و به دنبال آن کاهش درد ناشی از نمونه گیری و نیز کاهش هزینه های آزمایشگاهی مورد توجه قرار گرفته است. در این راستا دستگاه های متعددی برای اندازه گیری میزان بیلی روبین از طریق پوست ساخته شده است.

■ در مورد تشخیص، درمان و پیگیری ایکتر نوزادی با استفاده از دستگاه transcutaneous bilirubinometer باید موارد زیر مورد توجه قرار گیرد:

1. دستگاه transcutaneous bilirubinometer میزان بیلی روبین در بافت های سطحی پوست را اندازه می گیرد نه میزان بیلی روبین موجود در گردش خون و به این دلیل تنها به عنوان وسیله غربالگری جهت تصمیم گیری برای ارسال بیلی روبین سرمی کاربرد دارد و از این طریق میزان ارسال آزمایشات سرمی بی مورد را کم می کند.

2. دستگاه transcutaneous bilirubinometer به دلیل غیر تهاجمی بودن می تواند مکرر استفاده شود و میزان افزایش بیلی روبین و تصمیم گیری برای ارسال آزمایشات سرمی را مشخص سازد.

3. با توجه به اختلاف هایی که در دستگاه های مختلف وجود دارد بایستی قبل از استفاده، دقت دستگاه با نتایج به دست آمده به روش آزمایشگاهی در آن مرکز مقایسه شود.

4. در مواردی که عدد دستگاه transcutaneous bilirubinometer بالاتر از 14 باشد باید میزان بیلی روبین به روش آزمایشگاهی تایید شود.

5. استفاده از دستگاه transcutaneous bilirubinometer جهت غربالگری در نوزادان ترم و نزدیک ترم (term & late preterm) کاربرد دارد و در مورد استفاده از آن برای نوزادان پره ترم اتفاق نظر وجود ندارد.

6. از پیشانی و یا استرنوم جهت قرار دادن پروب دستگاه و اندازه گیری بیلی روبین استفاده شود.

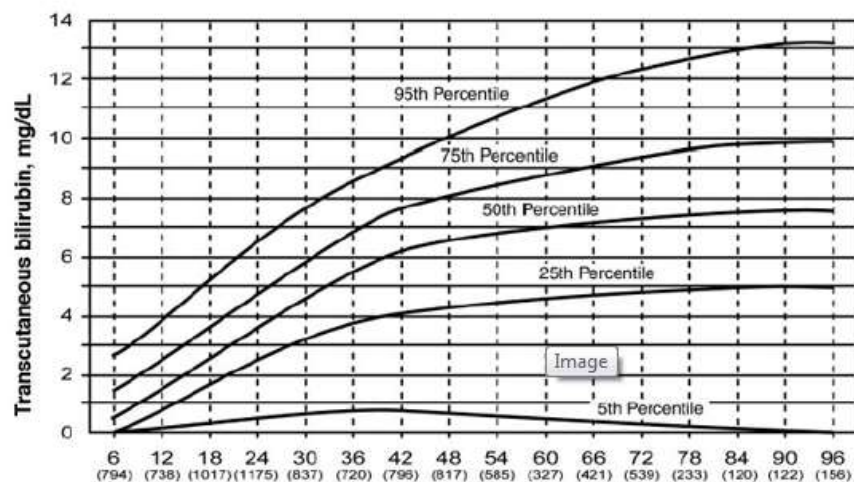
7. در صورتی که نوزاد تحت فوتوتراپی قرار گیرد استفاده از دستگاه transcutaneous bilirubinometer به منظور بررسی کاهش بیلی روبین قابل استفاده است. در این مورد باید از نواحی پوشیده شده پوست مانند ناحیه زیر پد چشمی اندازه گیری انجام شود. قطع فوتوتراپی باید براساس نتایج آزمایشگاهی صورت گیرد.

8. به دلیل این که در مقادیر بالای بیلی روبین سرمی، دستگاه transcutaneous bilirubinometer معمولا عدد بیلی روبین را کمتر از حد واقعی نشان می دهد توصیه می شود در موارد زیر حتما مقدار بیلی روبین به روش سرمی ارسال و اندازه گیری شود:

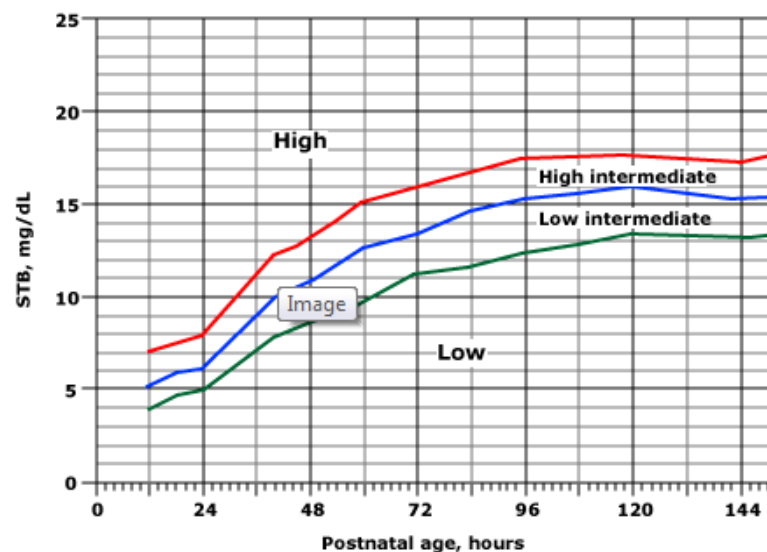
A confirmatory TB should be measured in the following settings:

1. When TcB exceeds the 75th percentile on the TB nomogram for phototherapy (graph in R).
2. When the TcB exceeds the 95th percentile on the TcB nomogram (graph in L).
3. At follow-up after discharge, the TcB > 13 mg/dL.
4. When therapeutic intervention is being considered. Therapy should be initiated while awaiting confirmatory results.
5. If the management plan would be altered by considering the TB to be equal to TcB + 3 mg/dL.
6. The TcB value is at 70% of the TSB level recommended for the use of phototherapy.

Nomogram of hour-specific transcutaneous bilirubin measurements (mg/dL) for healthy fullterm newborns



Nomogram of hour-specific serum total bilirubin (STB) concentration in healthy term and near-term newborns

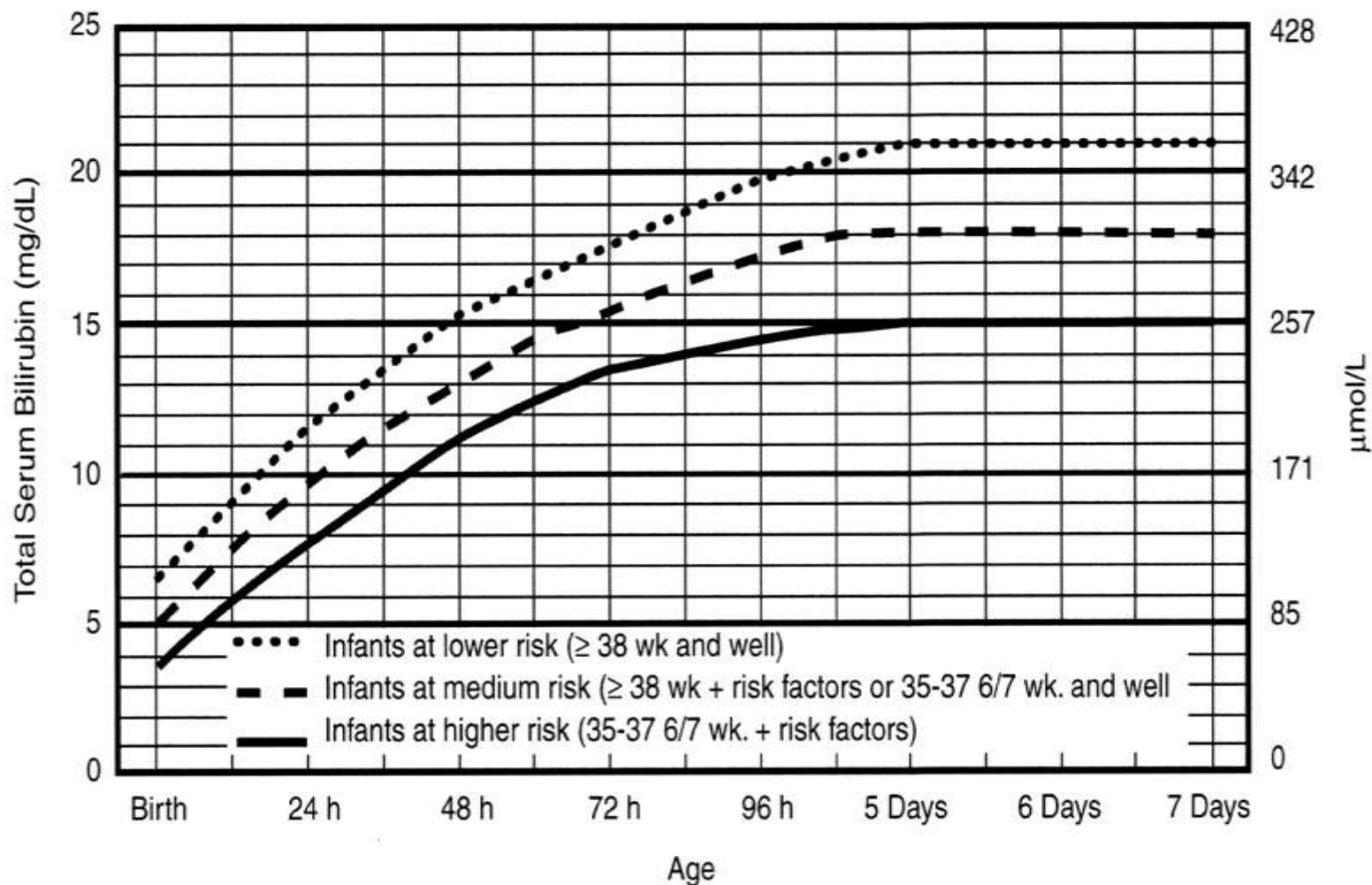


WHEN WE START PHOTOTHERAPY?



- The recommended treatment for hyperbilirubinemia is phototherapy. Exchange transfusion is recommended for the treatment of extreme hyperbilirubinemia. *(USPSTF, 2009; AAP, 2004)*
- The initiation of phototherapy should be based on the AAP guidelines, taking into account the infant's postnatal age in hours and the risk for bilirubin neurotoxicity. *(AAP, 2004)*
- Neurotoxic risk factors include:
isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis and albumin <3 g/dL

Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation



Subcommittee on Hyperbilirubinemia, *Pediatrics* 2004;114:297-316

TABLE 32.25**Suggested Use of Phototherapy and Exchange Transfusion in Preterm Infants <35 Wk of Gestational Age**

	Phototherapy	Exchange Transfusion
Gestational Age (Week)	Initiate Phototherapy Total Serum Bilirubin (mg/dL)	Total Serum Bilirubin (mg/dL)
<28 0/7	5–6	11–14
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34 0/7–34 6/7	12–14	17–19

- This table is modified from Maisels et al.⁵¹ and reflects the authors' recommendations for operational or therapeutic TSB thresholds—bilirubin levels at, or above which, treatment is likely to do more good than harm.⁵² They are not based on good evidence.
- Use total bilirubin. Do not subtract direct-reacting or conjugated bilirubin from the total.
- For infants ≤26 weeks gestation, it is an option to use phototherapy prophylactically starting soon after birth.
- Measure irradiance at regular intervals with an appropriate spectroradiometer.
- Measure the serum albumin level in all infants <35 weeks gestation.
- Use the lower range of the listed TSB levels for infants at greater risk for bilirubin toxicity, for example, those with rapidly rising TSB levels, suggesting hemolytic disease, those with serum albumin levels <2.5 g/dL and those who have one or more of the following: (a) blood pH <7.15; (b) capillary or arterial PCO₂ >50 mm Hg; (c) blood culture positive sepsis; (d) apnea and bradycardia requiring bagging or intubating; (e) hypotension requiring pressor treatment; and (f) mechanical ventilation at the time of blood sampling.
- Use post-conceptual age for phototherapy, for example, when a 29 0/7 week infant is 7 days old, use the TSB level for 30 0/7 weeks.
- In the NICHD, Neonatal Research Network there was a 5% increase in mortality observed in infants <750 g who received intensive phototherapy. This observation and the evidence in neonatal rats of an increase in oxidative injury with increasing irradiance⁵³ suggest that it is prudent to use less intensive levels of irradiance in these infants. In VLBW infants, phototherapy is almost always prophylactic—it is used to prevent a further increase in the TSB, and TSB levels can usually be controlled by phototherapy that is less intensive. Thus, although there are no studies that show a significant increase in mortality in infants <1500 g, the trends toward a possible increase^{19,36,38} suggest that it is reasonable in infants <1500 g to start phototherapy at irradiance levels of about 15 μW/cm² per nm. If the TSB continues to rise, additional phototherapy should be provided by increasing the surface area exposed (phototherapy above and below the infant, reflecting material around the incubator). If the TSB, nevertheless, continues to rise, the irradiance should be increased by switching to a higher-intensity setting on the device or by bringing the overhead light closer to the infant. Fluorescent and LED light sources can be brought closer to the infant, but this cannot be done with halogen or tungsten lamps because of the danger of a burn.

Operational TB Thresholds to Manage Moderately Preterm Infants

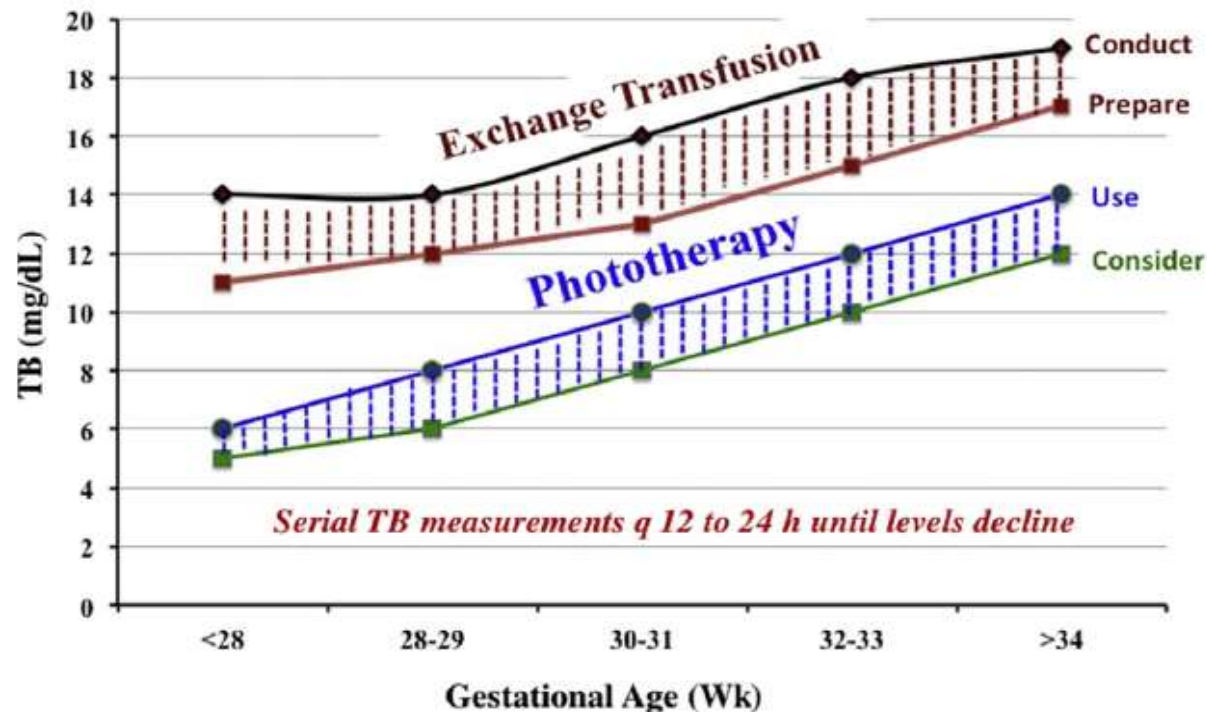



Fig. 1. Suggested use of phototherapy and exchange transfusion in preterm infants less than 35 weeks GA. The operational thresholds have been demarcated by recommendations of an expert panel. The shaded bands represent the degree of uncertainty. Recommended thresholds to prepare for exchange transfusion assume that these infants are already being managed by effective phototherapy. Increase in exposure of body surface area to phototherapy may inform the decision to conduct an exchange transfusion based on patient response to phototherapy. (Adapted from Maisels MJ, Watchko JF, Bhutani VK, et al. An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation. *J Perinatol* 2012;32:660–4; with permission.)

- How phototherapy came to be is a fascinating story, one with a nurse at its center
- Sister Jean Ward, the nurse in charge of the Premature Unit at Rochford General Hospital in Essex, England, firmly believed in the restorative powers of fresh air and sunshine (Fig)

Jean Ward in 1956, with one of the first infants given phototherapy at Rochford General Hospital.

Photograph courtesy of BMJ Publishing Group. With permission



- 
- On sunny days, she wheeled the infants outdoors into the hospital courtyard, returning them to the nursery just before the doctors—who were not as keen on this practice— arrived for ward rounds.
 - One day in 1956, Sister Ward showed the physicians an undressed infant whose skin was pale except for a triangular area that appeared much more yellow than the rest of its body.
 - Dr. RH Dobbs asked whether she had painted the infant's skin with iodine. She said she had not; what she held in her arms was a jaundiced infant whose color had faded except in an area that had been covered by the corner of a sheet

- Subsequently, physicians and scientists at Rochford Hospital discovered that the levels of bilirubin pigment in tubes of blood left in the sun also dropped dramatically.

Serum from jaundiced babies was collected and taped to the window in direct sunlight. After only 24 hours in the sun, the bright yellow jaundiced serum had turned green, indicating the conversion of bilirubin to biliverdin.

Bilirubin concentrations were also measured over the following days and it was shown that there was a significant decrease in the bilirubin concentration even at day 1

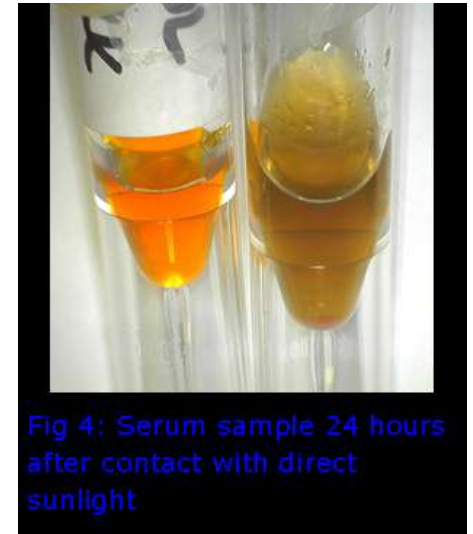


Fig 4: Serum sample 24 hours after contact with direct sunlight

- Putting these 2 observations together, the idea of phototherapy for neonatal jaundice was born.

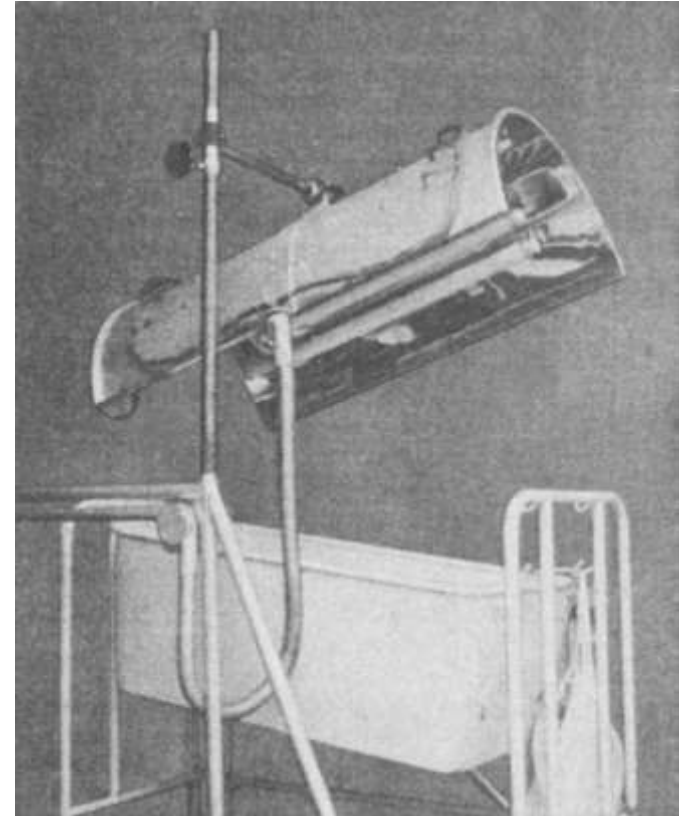
- The very first phototherapy unit incorporating an artificial light source instead of natural sunlight was devised and tested by Dr. RJ Cremer and colleagues at Rochford Hospital, and the results were reported in 1958.

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 8 24-inch lightblue 40-watt fluorescent tubes spaced 2 inches apart.

A cot can be wheeled under the reflector, and the lights can be switched on separately to vary the amount of power delivered.

*Reprinted from Cremer RJ, Perryman PW, Richards DH.
Influence of light on the hyperbilirubinaemia of infants.
Lancet. 1958;1:1094-1097. With permission.*



- Phototherapy was not used in the United States until the landmark study of Lucey et al was published a decade later.
- This randomized controlled trial demonstrating the effectiveness of phototherapy led to its acceptance as a simple, inexpensive, and relatively safe way to prevent hyperbilirubinemia in premature infants (*Lucey J, Ferriero M, Hewitt J. Prevention of hyperbilirubinemia of prematurity by phototherapy. Pediatrics. 1968;41:1047-1054.*)

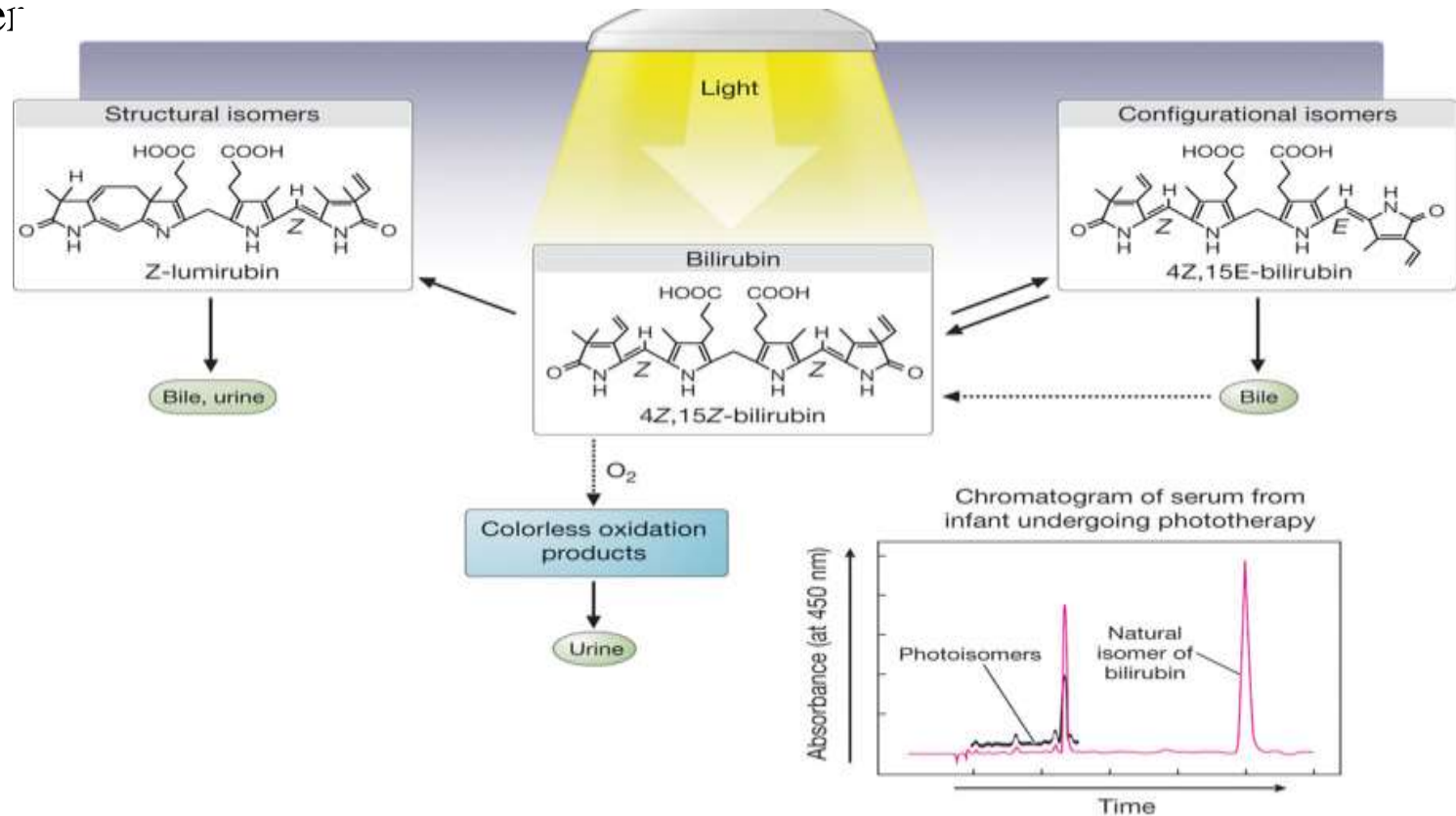


- Maisels, a noted bilirubin expert, suggests that phototherapy is much like a percutaneous drug.



- When phototherapy illuminates the skin, an infusion of discrete photons of energy, like molecules of a drug, are absorbed by bilirubin in the same way that a drug molecule binds to a receptor. Bilirubin molecules in skin exposed to light undergo relatively quick photochemical reactions— configurational isomerization, structural isomerization, and photo-oxidation— to form nontoxic, excretable isomers.

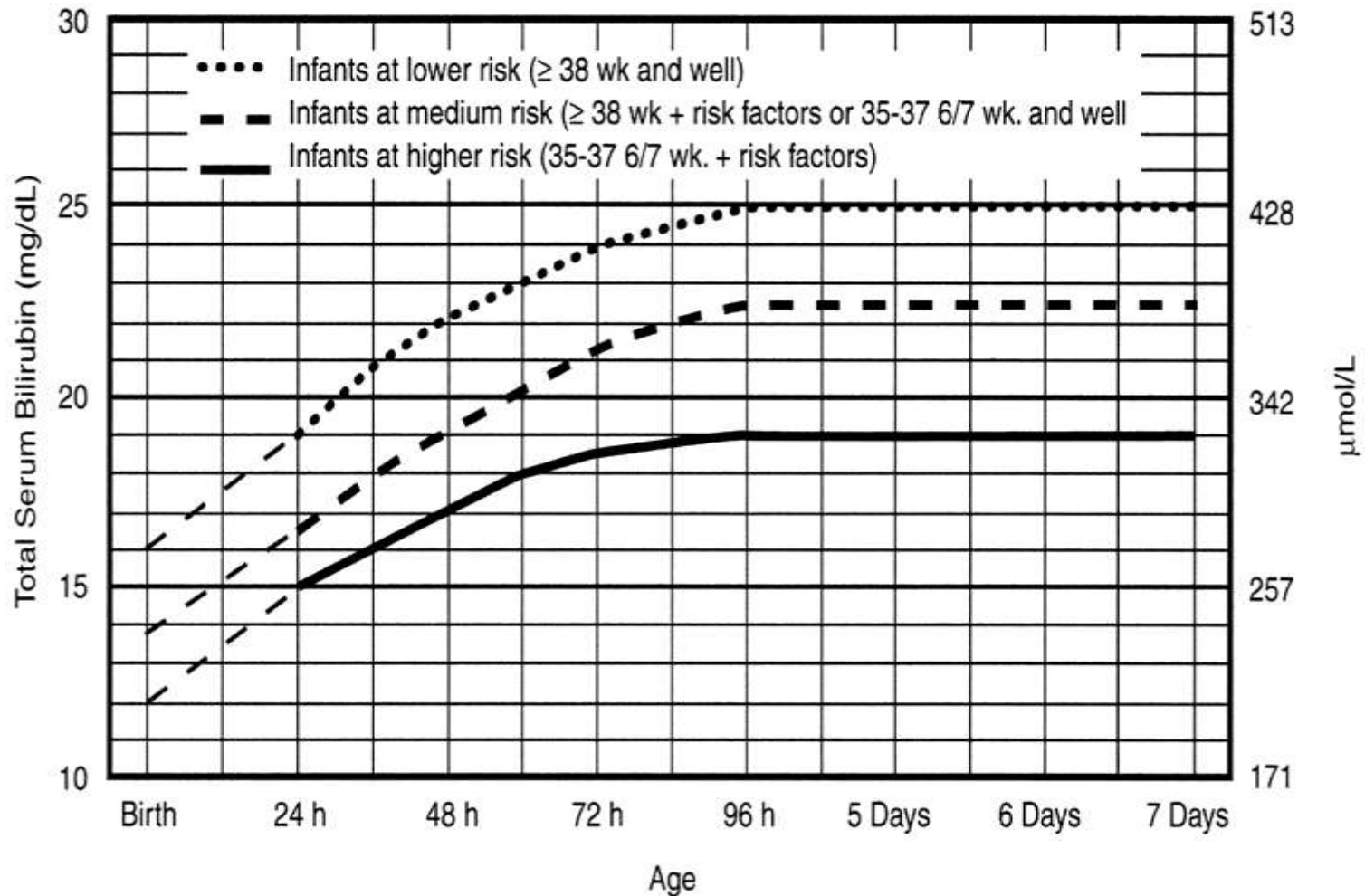
- Phototherapy is the use of visible light for the treatment of hyperbilirubinemia in the newborn.
- This relatively common therapy lowers the serum bilirubin level by transforming bilirubin into water-soluble isomers that can be eliminated without conjugation in the liver





B-barekataan ,Neonatologist

Guidelines for exchange transfusion in infants 35 or more weeks' gestation



Subcommittee on Hyperbilirubinemia, Pediatrics 2004;114:297-316

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Operational TB Thresholds to Manage Moderately Preterm Infants

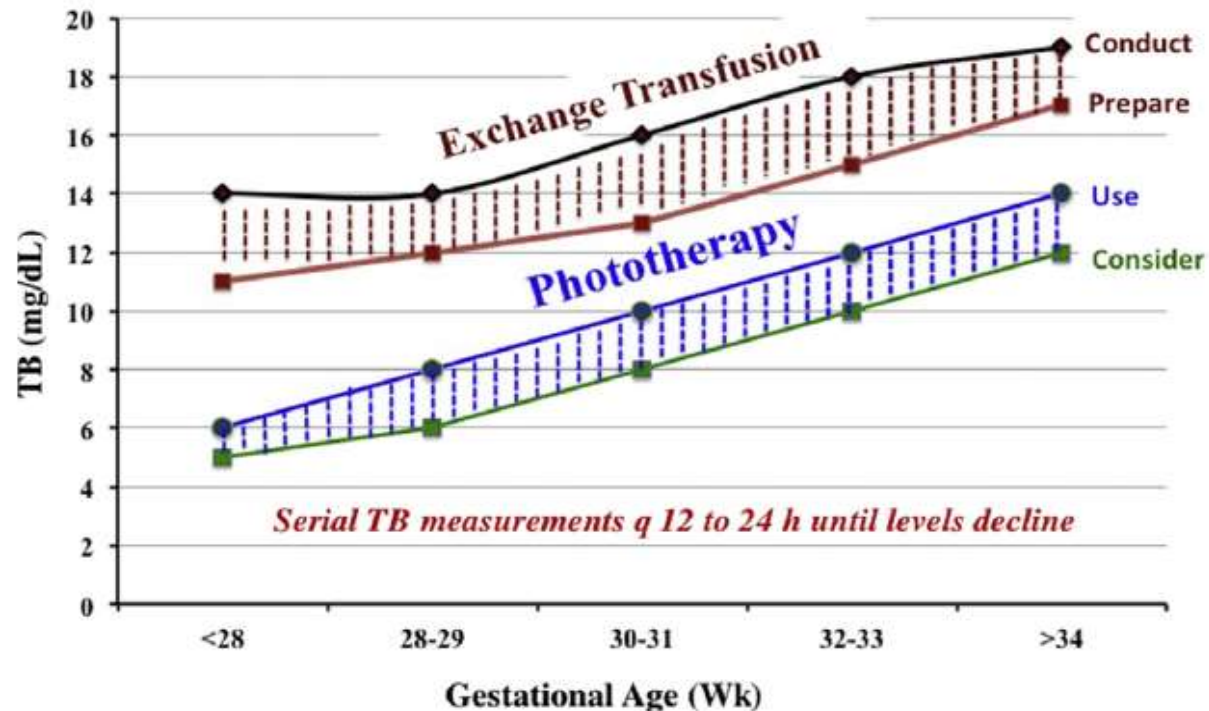


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Home Phototherapy

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™




pediatrics.aappublications.org January 6, 2012

Equipment designed for delivering phototherapy in the home has become available.

Home phototherapy for neonatal hyperbilirubinemia has been suggested as an alternative means of providing care for selected infants while saving much of the cost of continued or added hospitalization.



B-barekatain ,Neonatologist




A **physician** who considers the use of home phototherapy should limit its use to infants with the following characteristics:


- (1) term infants, older than 48 hours, otherwise healthy;
- (2) serum bilirubin concentration greater than 14 mg/dL but less than 18 mg/dL;
- (3) no elevation in direct-reacting bilirubin concentration; and
- (4) diagnostic evaluation (described below) negative.



Prior to therapy, a diagnostic evaluation should include:

- (1) history and physical examination;*
- (2) hemoglobin concentration or hematocrit;*
- (3) WBC count and differential count;*
- (4) blood smear for red cell morphology platelets;*
- (5) reticulocyte count;*
- (6) total and direct-reacting bilirubin concentration;*
- (7) maternal and infant blood typing and Coombs test;* *and*
- (8) urinalysis including a test for reducing substances.*

- 
- The physician should estimate the rate of rise of the serum bilirubin concentration with laboratory determinations at least **four hours** apart before home phototherapy is initiated.
 - If the concentration of bilirubin is rising too sharply (more than 1 mg in three to four hours) or if there is no rise in serum bilirubin concentration at all in the absence of phototherapy, then home phototherapy is not advisable.



A candidate for home phototherapy should have **home caretakers** who, in the judgment of the pediatrician, are capable of following instructions.

The infant should be full term and otherwise **meet the criteria for discharge** from the hospital or for continuing care at home.

Arrangements must be made to measure the infant's serum bilirubin concentration at least **every 12 to 24 hours** depending on the previous concentration and the rate of rise.



The **supervising physician** should be in contact with the family daily during the period of treatment.

Parents should sign a **consent form** that explains the risks (including the possibility that displaced eye patches may occlude the infant's airway) and benefits of the procedure.

This form should also outline **the roles** of the physician, the equipment provider, and the parents in the subsequent care of the infant.




The parents should be taught **how to use the equipment**.

They should also be instructed to provide **adequate hydration** during phototherapy, to apply the eye patches correctly, and to report problems promptly.

Infants should be **removed from phototherapy** during feedings and diaper changes and when the parents are asleep.

Only **equipment** designed specifically for providing bilirubin reduction should be used for home phototherapy.



Home phototherapy should be discontinued once the serum bilirubin concentration falls below 14 mg/dL.

The serum bilirubin concentration should be remeasured 12 to 24 hours after cessation of phototherapy to look for a rebound in bilirubin concentration.

The infant should be rehospitalized if he/she shows signs of illness or side effects, or when the serum bilirubin concentration exceeds 18 mg/dl.

Prolonged jaundice



Persistent jaundice in the neonate is defined as jaundice that lasts longer than 14 to 21 days.

It can occur in up to 15% of all newborns.

The vast majority of these neonates have benign unconjugated hyperbilirubinemia but one in 2500 live births has cholestatic liver disease.

The difficult task facing primary care providers is discriminating between serious conjugated hyperbilirubinemia and benign unconjugated jaundice because in the early stage, the infants can look very well except for their jaundice.

Early identification of infants with cholestatic liver disease is critical so that a correct diagnosis is made and the appropriate therapy is instituted.

Causes of unconjugated hyperbilirubinaemia

Breast Milk Jaundice

Haemolysis

Blood group incompatibilities (ABO & Rhesus)

Polycythaemia

Extravasated Blood

Increased Enterohepatic Circulation

Pyloric stenosis

Bowel obstruction

Endocrine/Metabolic (also cause conjugated hyperbilirubinaemia)

Hypothyroidism

Galactosaemia

Sepsis (UTI)



The **first** test is measurement of Direct reacting bilirubin

Appropriate **further** investigations in prolonged unconjugated hyperbilirubinemia should include:

- *Full blood count, including reticulocytes*
- *Examination of blood film*
- *Thyroid function tests*
- *G6PD*
- *Urine culture*



By far, the most common cause of prolonged jaundice is so called 'breastmilk jaundice' (BMJ).

These babies can be managed effectively with continuation of breastfeeding and phototherapy even if TSB exceeds 20 mg/dl in a term baby.

It is important that one does not stop breastfeeding routinely in these babies, which is of immense benefit for the infant.

Stopping of breastfeeding, even for short duration, will result in anxiety and consequent suppression of lactation in the mother and many babies may not go on to exclusive breastfeeds again.

In addition, this spreads a wrong message about the breast-feeding.



Risk Factors for the Development of Hyperbilirubinemia

■ Risk Factors for the Development of Hyperbilirubinemia in Infants of 35 or More Weeks Gestation

**Elevated predischARGE TSB or TcB level*

**Jaundice observed in the first 24 h or prior to discharge*

**Blood group incompatibility with positive direct antiglobulin test,*

** other known hemolytic disease (e.g., G6PD deficiency, hereditary spherocytosis)*

**Decreasing gestational age*

**Previous sibling with jaundice or who received phototherapy*

**Vacuum extraction delivery, cephalohematoma, or significant bruising*

**Exclusive breastfeeding, particularly if nursing is not going well and weight loss is excessive*

**East Asian race*

**Macrosomic infant of a diabetic mother*

**Maternal age ≥ 25 years*

**Male gender*

MAJOR RISK FACTORS

- PredischARGE TB or TcB level in the high-risk zone (see Figure 100-9)
- Jaundice observed in the first 24 hours
- Blood group incompatibility with positive DAT, other known hemolytic disease (e.g., G6PD deficiency)
- Gestational age 35 to 36 weeks
- Previous sibling received phototherapy
- Cephalohematoma or significant bruising
- Exclusive breastfeeding, particularly if nursing poorly and weight loss is excessive
- East Asian race

MINOR RISK FACTORS

- PredischARGE TB or TcB in the high intermediate-risk zone
- Gestational age 37 to 38 weeks
- Jaundice observed before discharge
- Previous sibling with jaundice
- Macrosomic infant of diabetic mother
- Maternal age ≥ 25 years
- Male sex

FACTORS ASSOCIATED WITH DECREASED RISK OF SIGNIFICANT JAUNDICE*

- TB or TcB in the low-risk zone (see Figure 100-9)
- Gestational age ≥ 41 weeks
- Exclusive bottle feeding
- Black race
- Discharge from hospital after 72 hours

RISK FACTORS FOR DEVELOPMENT OF SEVERE HYPERBILIRUBINEMIA IN INFANTS ≥ 35 WEEKS OF GESTATION

From American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114:297.



Prevention and follow up of neonatal Hyperbilirubinemia

Key Elements in the AAP Guideline on Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation

- 1. Promote and support successful breastfeeding*
- 2. Establish nursery protocols for the identification and evaluation of hyperbilirubinemia*
- 3. Measure the total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) level on infants jaundiced in the first 24 h*
- 4. Recognize that visual estimation of the degree of jaundice can lead to errors, particularly in darkly pigmented infants*
- 5. Interpret all bilirubin levels according to the infant's age in hours*
- 6. Recognize that infants at less than 38 weeks gestation, particularly those who are breastfed, are at higher risk of developing hyperbillirubinemia and require closer surveillance and monitoring*
- 7. Perform a systematic assessment on all infants before discharge for the risk of severe hyperbilirubinemia*
- 8. Provide parents with written and verbal information about newborn jaundice*
- 9. Provide appropriate follow-up based on the time of discharge and the risk assessment*
- 10. Treat newborns, when indicated, with phototherapy or exchange transfusion*



■ **Predischarge Measurement of the Bilirubin Level**

We know that infants who are clinically jaundiced in the first few days and particularly those jaundiced in the first 24 hours, are much more likely to later develop significant hyperbilirubinemia.

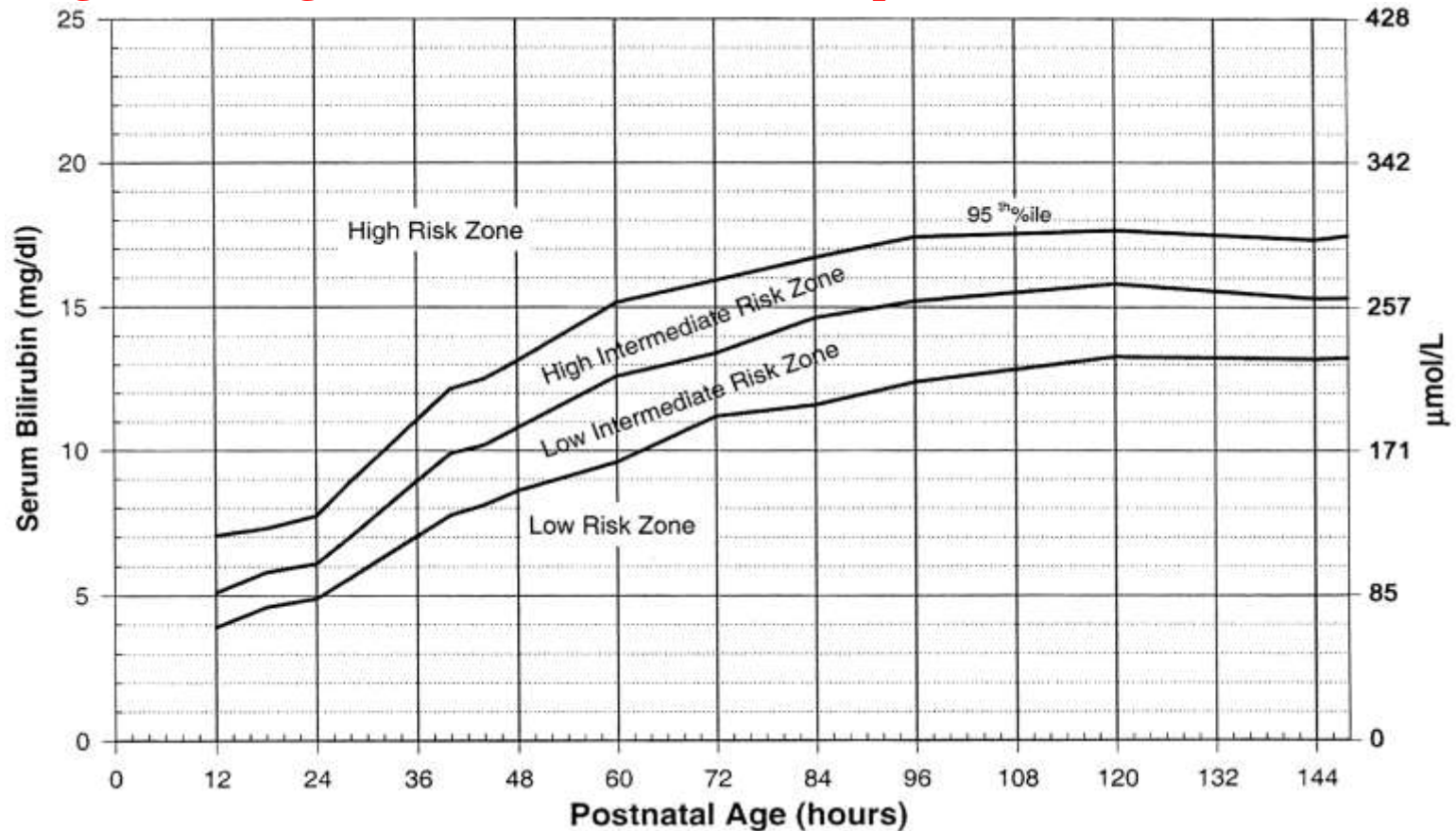
In a study that has had worldwide impact, Bhutani et al measured TSB concentrations in 13,003 infants prior to their discharge from the hospital.

In 2840 infants additional TSB levels were measured at least once in the 5–6 days following discharge.

Infants with ABO incompatibility and a positive DAT were excluded, as were Rh-sensitized infants.

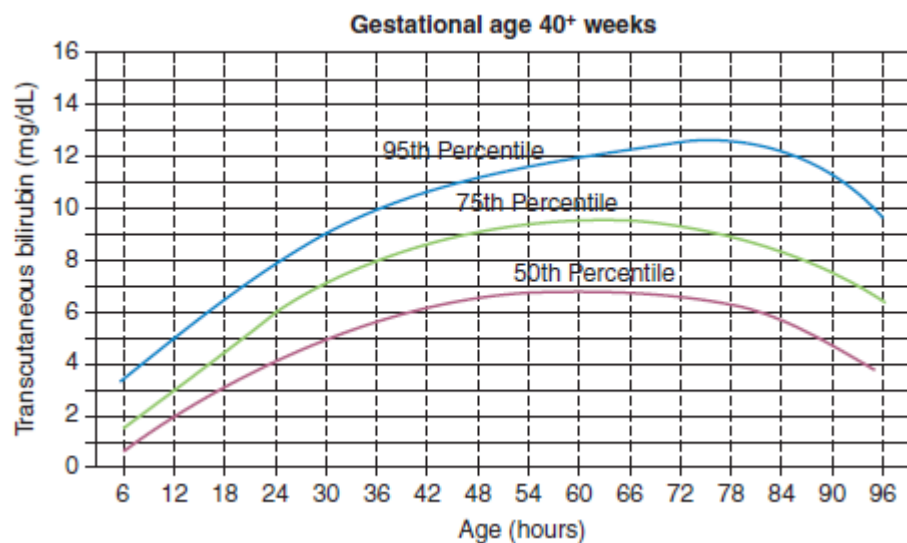
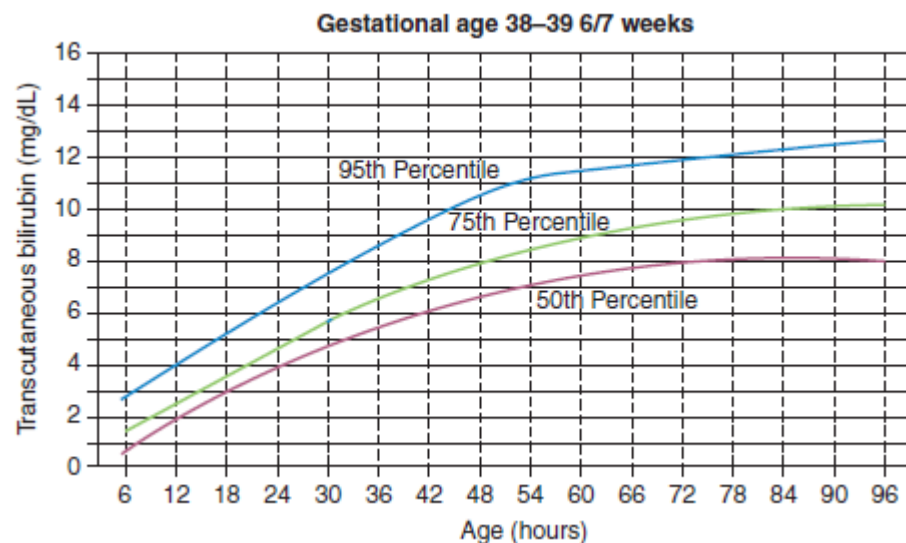
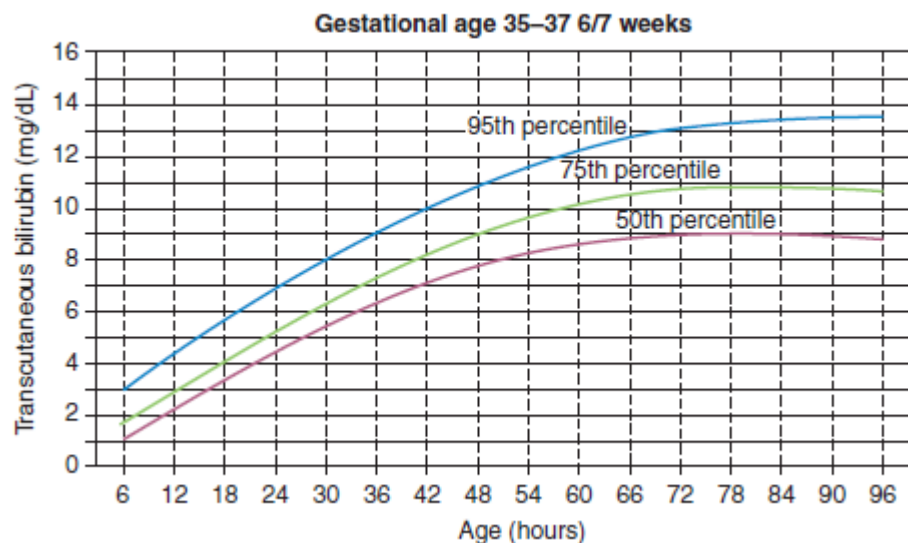
The investigators plotted the TSB levels against the infant's age in hours and created a nomogram with percentiles that defined the four risk zones illustrated in Figure

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



Subcommittee on Hyperbilirubinemia, Pediatrics 2004;114:297-316

Transcutaneous bilirubin levels in the first 96 hours in a normal newborn population of ≥ 35 weeks gestation
Pediatrics.2006;117:1169–1173, with permission. Copyright 2006 by the American Association of Pediatrics.)



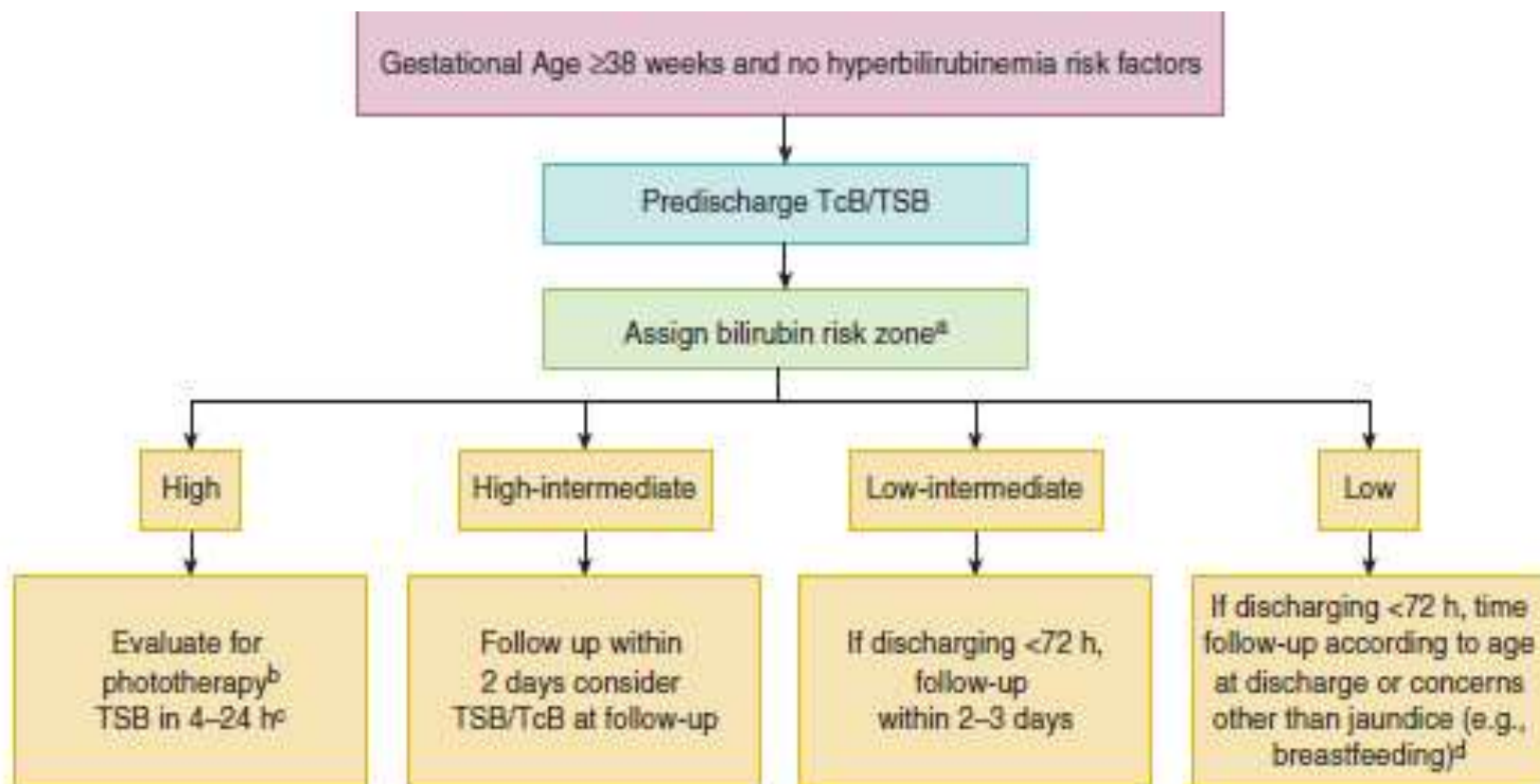


■ Combining Gestation with the Predischarge Bilirubin Level

Although studies using clinical risk factors have a predictive accuracy similar to that of the predischarge bilirubin risk zone combining the predischarge TSB or TcB with clinical risk factors improves the prediction of the risk of subsequent hyperbilirubinemia

When the predischarge TSB level was ≥ 95 th percentile on the Bhutani nomogram Newman et al found that a 40-week gestation infant had about a 10% risk of subsequently developing a TSB level > 20 mg/dL, while in a 36-week gestation infant, with a similar predischarge TSB level, the risk was about 42%.

To be helpful to the practicing physician, a prediction model should be as parsimonious as possible. Combining the predischarge TSB/TcB with the infant's gestation allows a level of positive and negative prediction that is indistinguishable from models that use additional clinical risk factors. 18



Other hyperbilirubinemia risk factors

- Exclusive breastfeeding particularly if nursing is not going well and/or weight loss is excessive (>8-10%)
- Isoimmune or other hemolytic disease (e.g., G6PD deficiency, hereditary spherocytosis)
- Previous sibling with jaundice
- Cephalohematoma or significant bruising
- East Asian race

Gestational Age 35-37 6/7 weeks and no other hyperbilirubinemia risk factors
OR
Gestational Age ≥ 38 weeks + other hyperbilirubinemia risk factors

Predischarge TcB/TSB

Assign bilirubin risk zone^a

High

Evaluate for
phototherapy^b
TSB in 4-24 h^c

High-intermediate

Evaluate for
phototherapy^b
TSB/TcB in 24 h^c

Low-intermediate

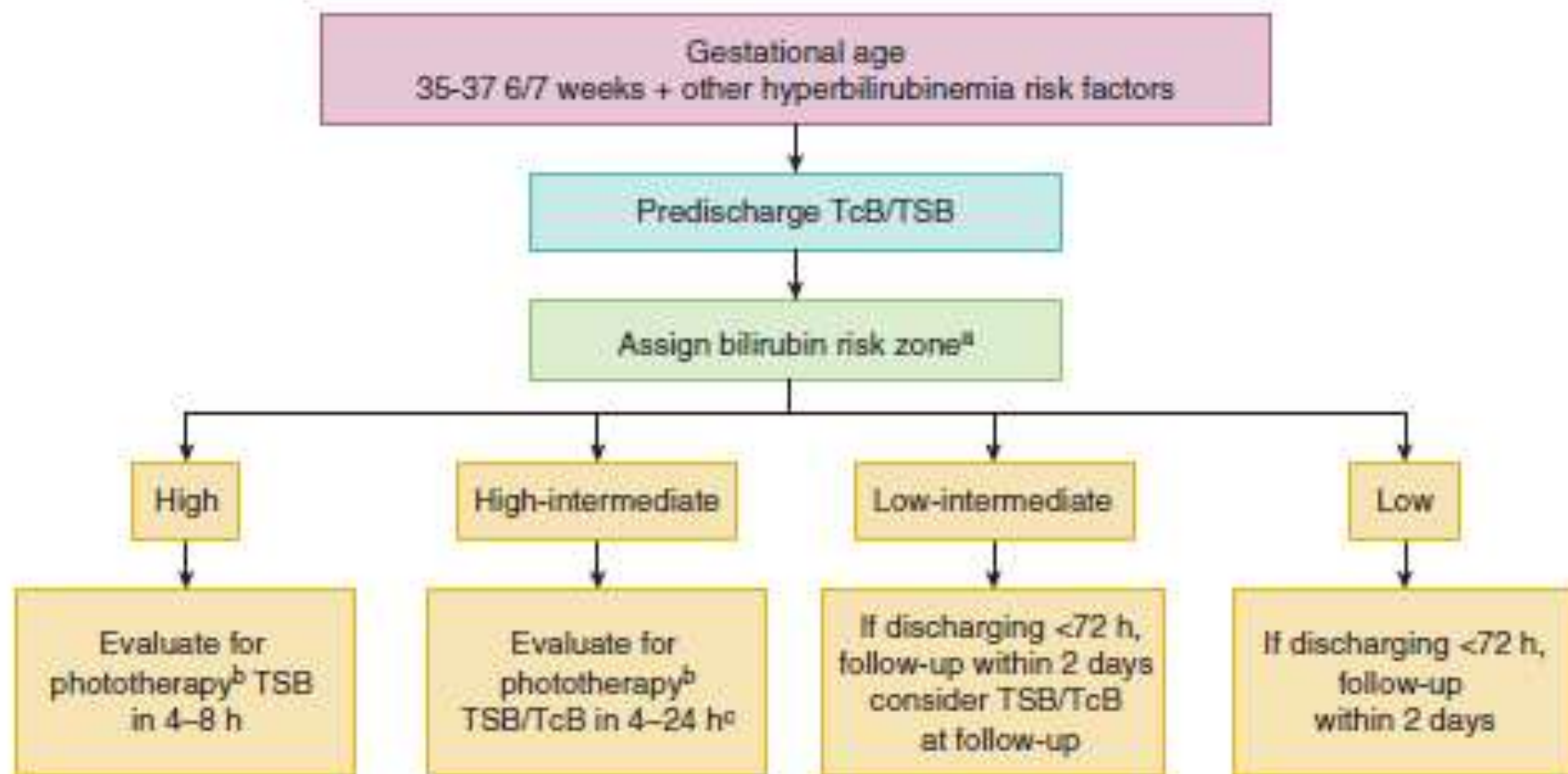
If discharging <72 h,
follow-up
within 2 days

Low

If discharging <72 h,
follow-up
within 2-3 days

Other hyperbilirubinemia risk factors

- Exclusive breastfeeding particularly if nursing is not going well and/or weight loss is excessive (>8-10%)
- Isoimmune or other hemolytic disease (e.g., G6PD deficiency, hereditary spherocytosis)
- Previous sibling with jaundice
- Cephalohematoma or significant bruising
- East Asian race



Other hyperbilirubinemia risk factors

- Exclusive breastfeeding particularly if nursing is not going well and/or weight loss is excessive (>8-10%)
- Isoimmune or other hemolytic disease (e.g., G6PD deficiency, hereditary spherocytosis)
- Previous sibling with jaundice
- Cephalohematoma or significant bruising
- East Asian race

Discharge

- Close follow-up necessary
 - Individualize based on risk
 - Weight, % change from BW, intake, voiding habits, jaundice

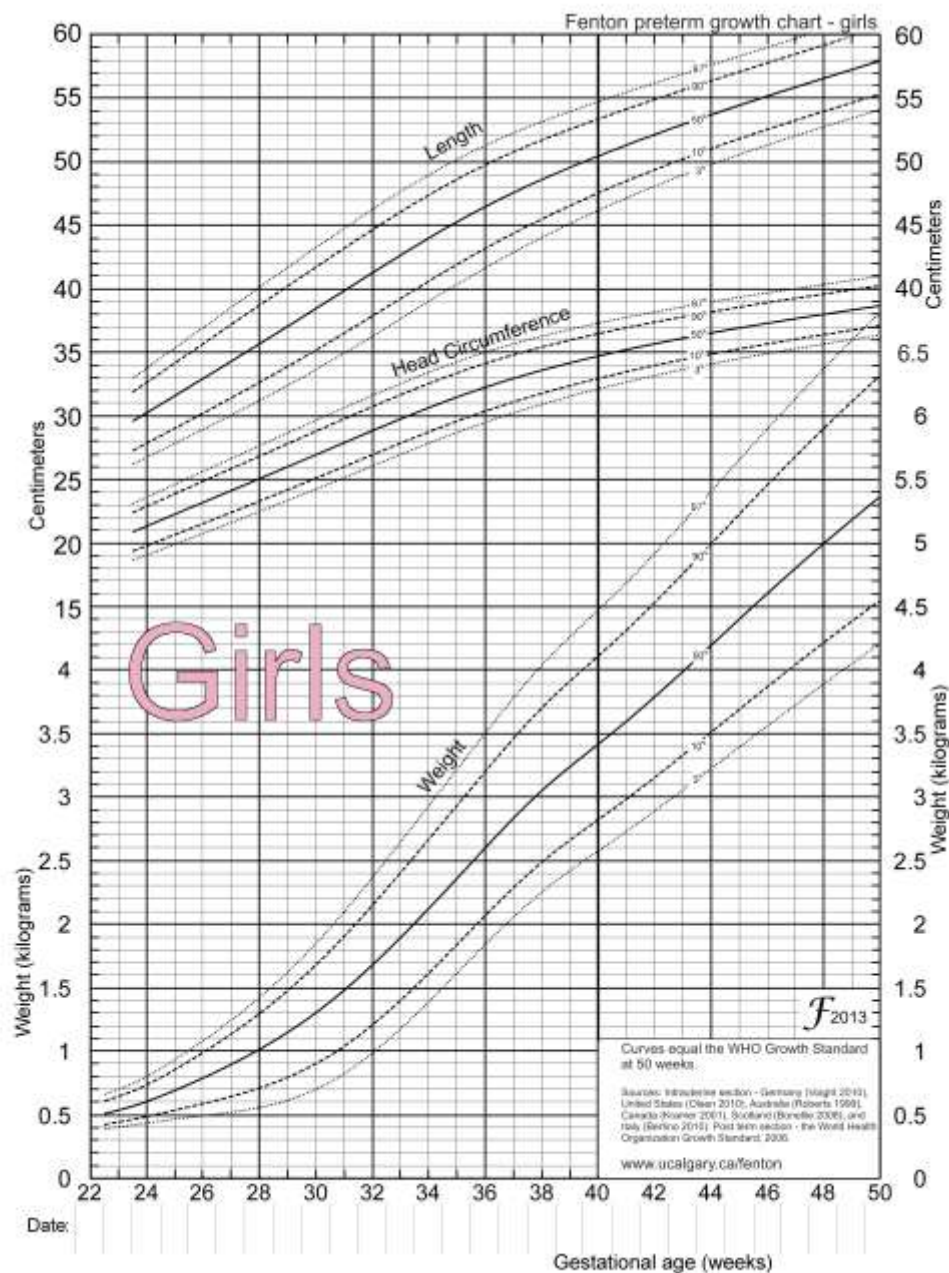
Infant Discharge	Should be Seen by
< 24 hours	72 hours
24-48 hours	96 hours
48-72 hours	120 hours



- Vit D or Multivitamin???

- Iron???

- Growth Chart in preterm newborns



The JOURNEY of a premature baby is often
ONE step forward and TWO steps back....

Photo: Lisa Nicole Imagery

Watch them breathe, watch them sleep and nourish them with

'LIQUID GOLD'. When strong enough, they will take three LEAPS
forward and NEVER look back.....