Neonatal Jaundice: From Problems to Solutions

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Panelists

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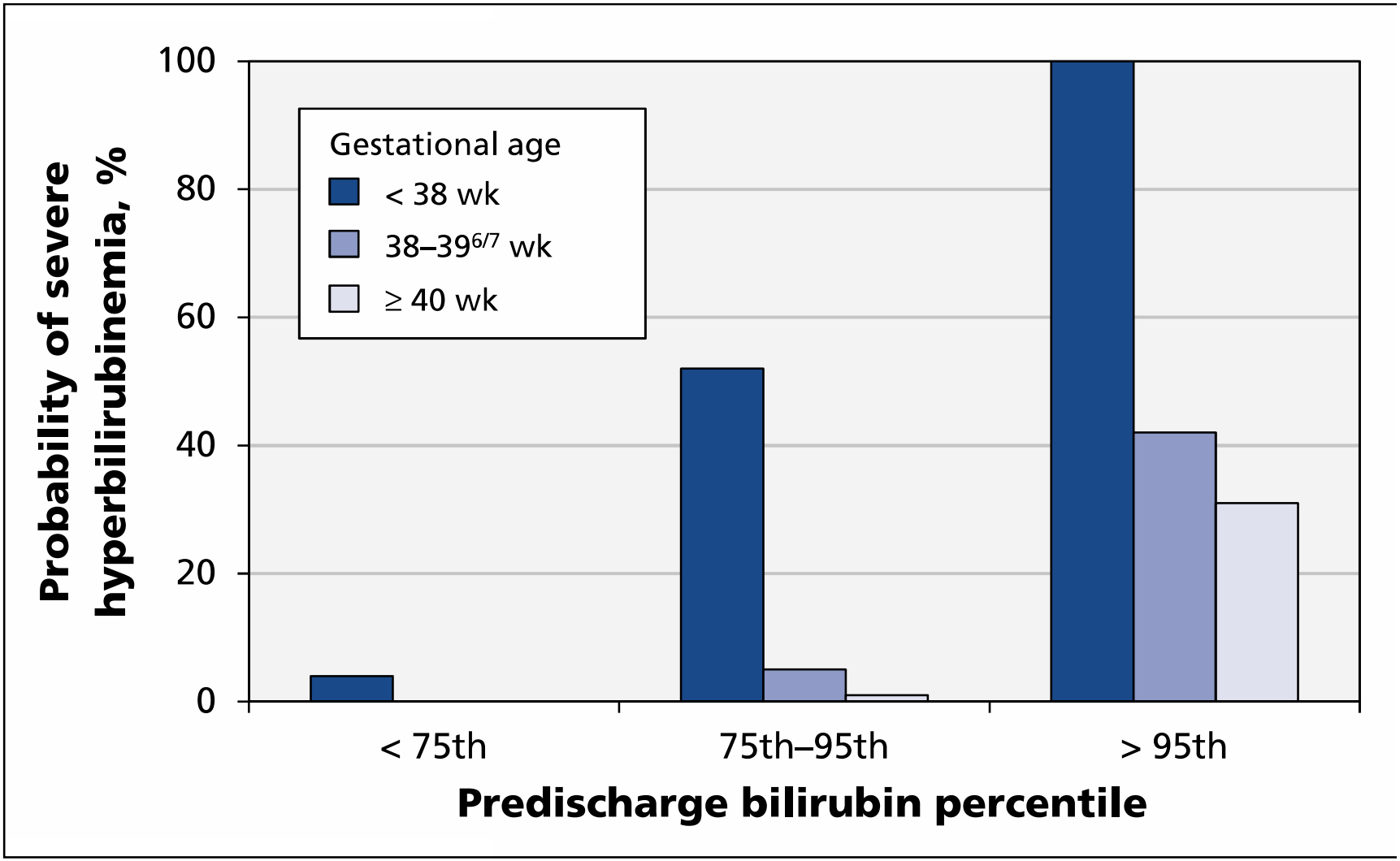
What are the risk factors for severe Jaundice and BIND ?

Risk factors

- Severe Jaundice
  - Cephalhematoma
  - Early gestational age
  - Exclusive breastfeeding
  - Weight loss >8%
- BIND
  - Early gestational age
  - Hemolysis/G6PD
  - Sepsis/Acidosis
  - LBW/Albumin<3g/dl

Asphyxia
SGA


Probability of severe hyperbilirubinemia, %
100
80
60
40
20
0
Gestational age
< 38 wk
38–39^6/7 wk
≥ 40 wk
< 75th
75th–95th
> 95th
Predischarge bilirubin percentile

Is it necessary for Pre-discharge screening of all newborns?

What are the available approaches?

Universal Screening versus Targeted approach

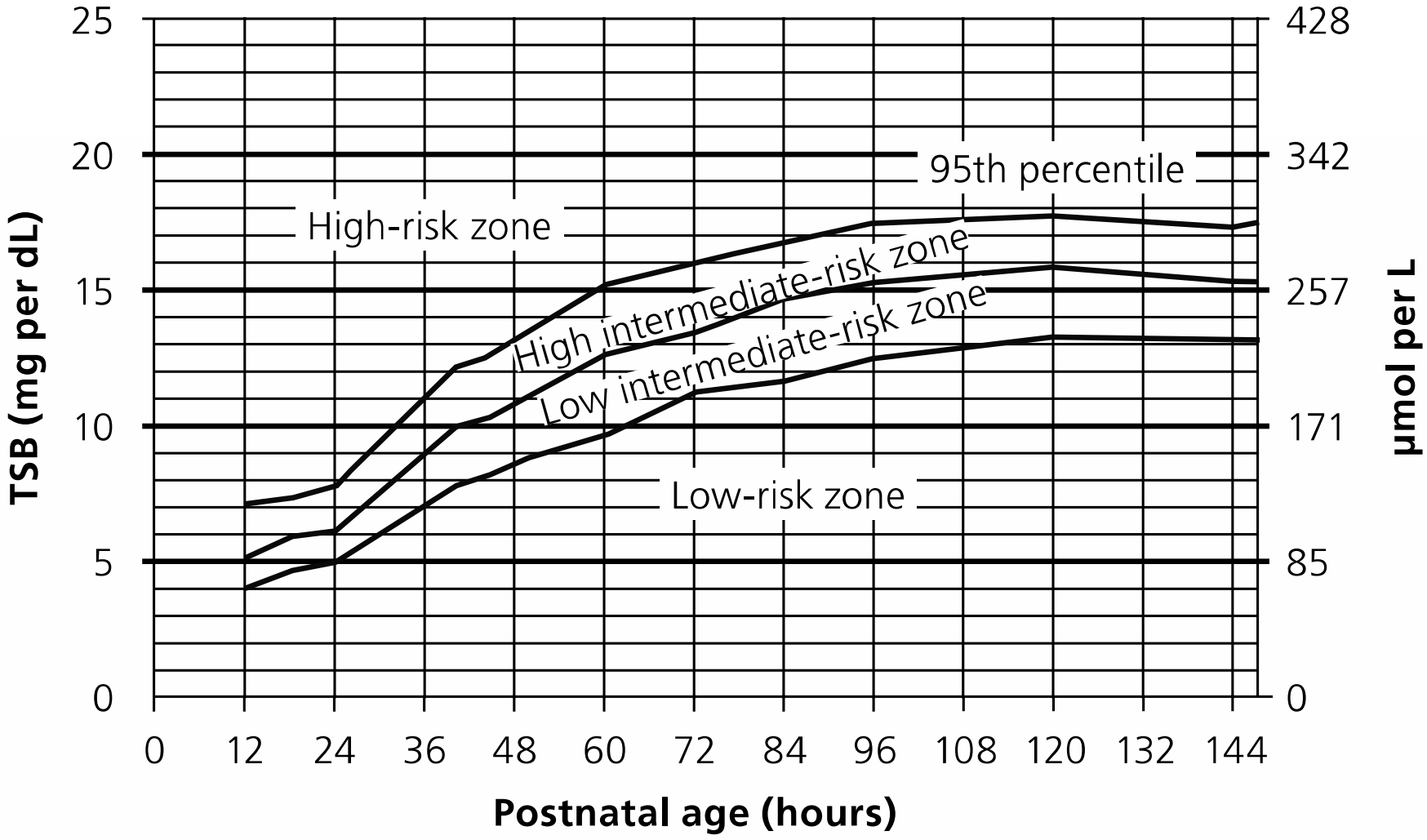
- Universal Screening with TSB or TcB
  - Increased phototherapy rates
  - Decreased readmission for jaundice
- Risk factor based approach
  - As effective as screening with TcB or TSB
- Any approach only for infants with clinical jaundice

Table 1. Risk Score for Neonatal Hyperbilirubinemia

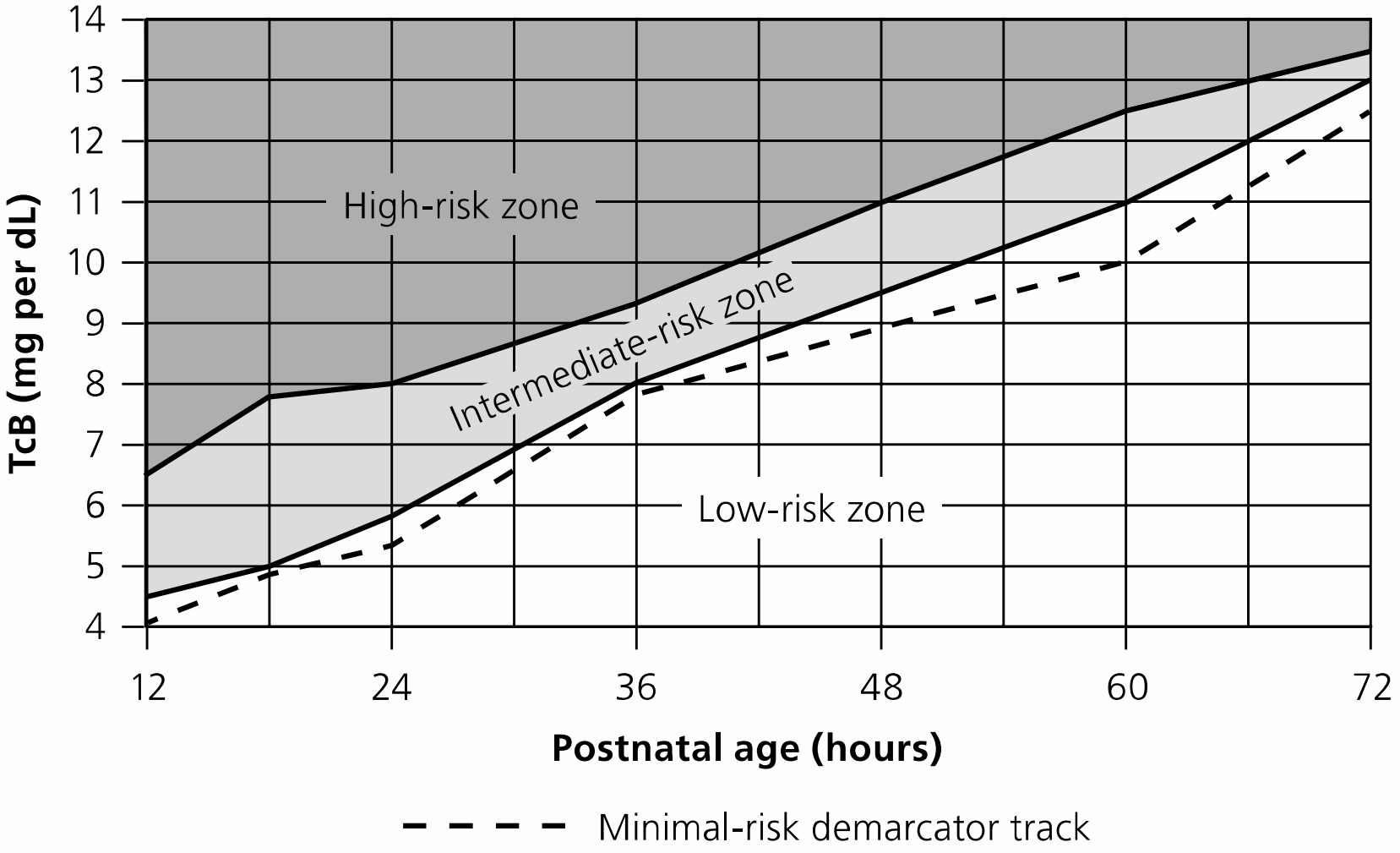
Variable	*Score*
Birth weight:	
2,000 to 2,500 g (4 lb, 7 oz to 5 lb, 8 oz)	0
2,501 to 3,000 g (5 lb, 8 oz to 6 lb, 10 oz)	3
3,001 to 3,500 g (6 lb, 10 oz to 7 lb, 11 oz)	6
3,501 to 4,000 g (7 lb, 11 oz to 8 lb, 13 oz)	9
4,001 to 4,500 g (8 lb, 13 oz to 9 lb, 15 oz)	12
4,501 to 5,000 g (9 lb, 15 oz to 11 lb, 1 oz)	15
Oxytocin (Pitocin) used during delivery	4
Vacuum-assisted delivery	4
Breast and bottle feeding	4
Exclusive breastfeeding	5
Gestational age < 38 weeks	5

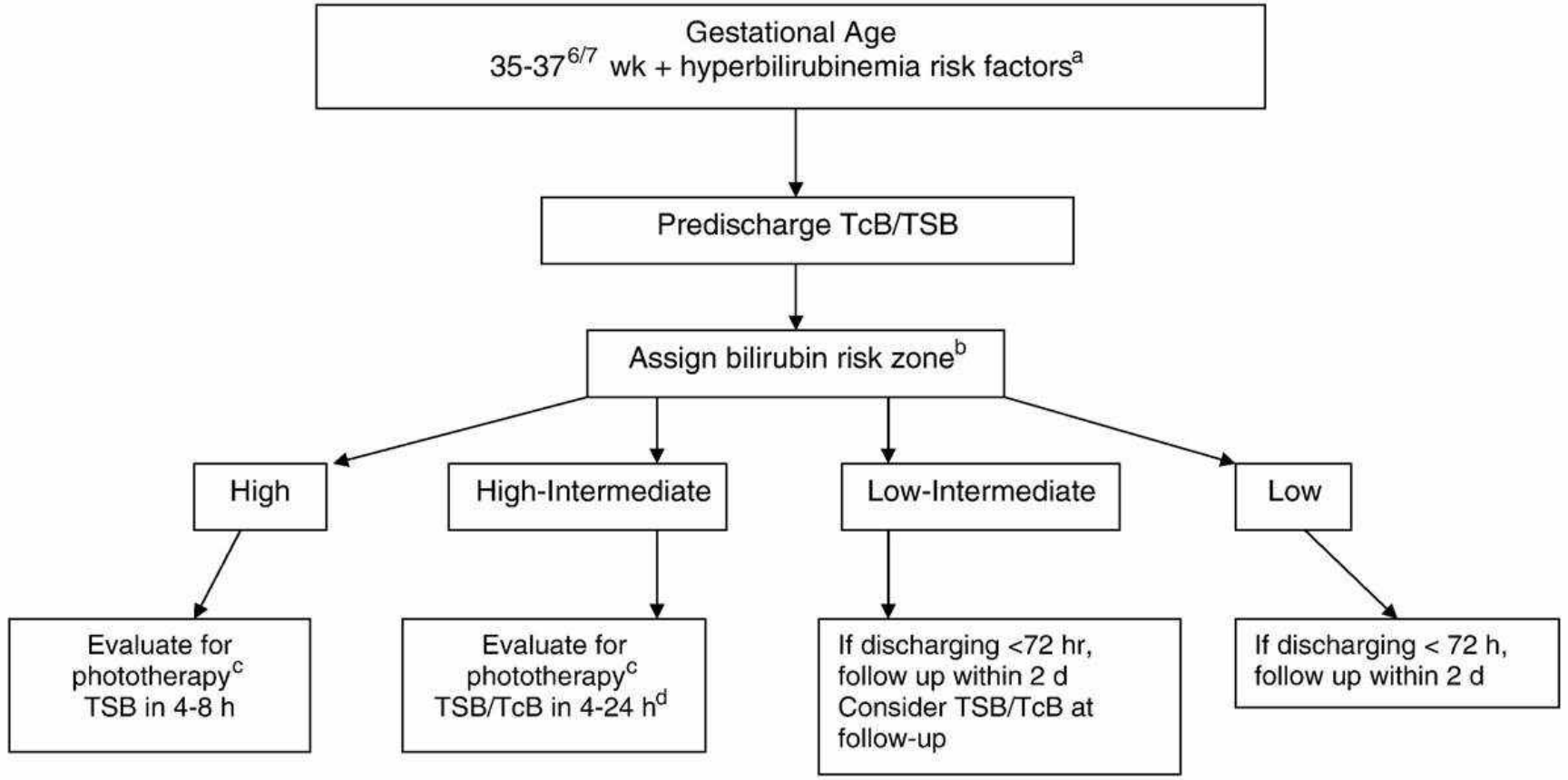
NOTE: *A total score of 8 or more suggests an increased risk of hyperbilirubinemia; total serum bilirubin or transcutaneous bilirubin level should be obtained.*

Risk Assessment for Hyperbilirubinemia Using TSB



Risk Assessment for Hyperbilirubinemia Using TcB




Gestational Age
35-37 6/7 wk + hyperbilirubinemia risk factors a
Predischarge TcB/TSB
Assign bilirubin risk zone b
High
High-Intermediate
Low-Intermediate
Low
Evaluate for phototherapy c TSB in 4-8 h
Evaluate for phototherapy c TSB/TcB in 4-24 h d
If discharging <72 hr, follow up within 2 d Consider TSB/TcB at follow-up
If discharging < 72 h, follow up within 2 d

What is the role of TcB in preterm Infants?

TcB and Preterm Infants

- < 37 weeks
- 22 studies in the meta-analysis
- Pooled estimate of r=0.83 (similar for <32 weeks)
- Forehead as good as sternum
- Bilicheck as good as JM 103

Preterm And TcB

Bhutani 2000	0.90 (0.87–0.93)	6.4%
De Luca 2007	0.79 (0.74–0.83)	7.1%
Knupfer 2001	0.73 (0.66–0.78)	6.8%
Namba 2007	0.83 (0.79–0.86)	7.1%
Nanjundaswamy 2005	0.86 (0.78–0.91)	5.2%
Sanpavat 2007	0.79 (0.74–0.83)	6.8%
Siu 2010	0.81 (0.74–0.87)	5.9%
Stillova 2007	0.85 (0.74–0.92)	4.3%
Stillova 2009	0.81 (0.64–0.90)	3.6%
Szabo 2004 (bilicheck) F	0.67 (0.55–0.76)	5.9%
Tan 1988	0.78 (0.75–0.81)	7.4%
Willems 2004	0.86 (0.80–0.91)	5.7%
Yasuda (JM102) 2003	0.85 (0.80–0.91)	5.3%
Yasuda (JM103) 2003	0.93 (0.89–0.96)	5.3%
Total	**0.83 (0.80–0.86)**	**100%**
Sternum		
Donzelli 2000	0.89 (0.83–0.93)	8.2%
Karen 2009	0.39 (0.17–0.57)	8.0%
Karolyi 2004	0.68 (0.60–0.74)	8.9%
Palmer 1982	0.82 (0.65–0.91)	6.6%

Preterm AND TcB

Study Title	*r* (95% CI)	Weight
Forehead		
Ahmed 2010	0.90 (0.87–0.92)	6.6%
Badiee 2012	0.82 (0.72–0.89)	5.0%
Bhardwaj 1989	0.82 (0.74–0.88)	5.6%
Bhutani 2000	0.90 (0.87–0.93)	6.4%
De Luca 2007	0.79 (0.74–0.83)	7.1%
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Sternum		

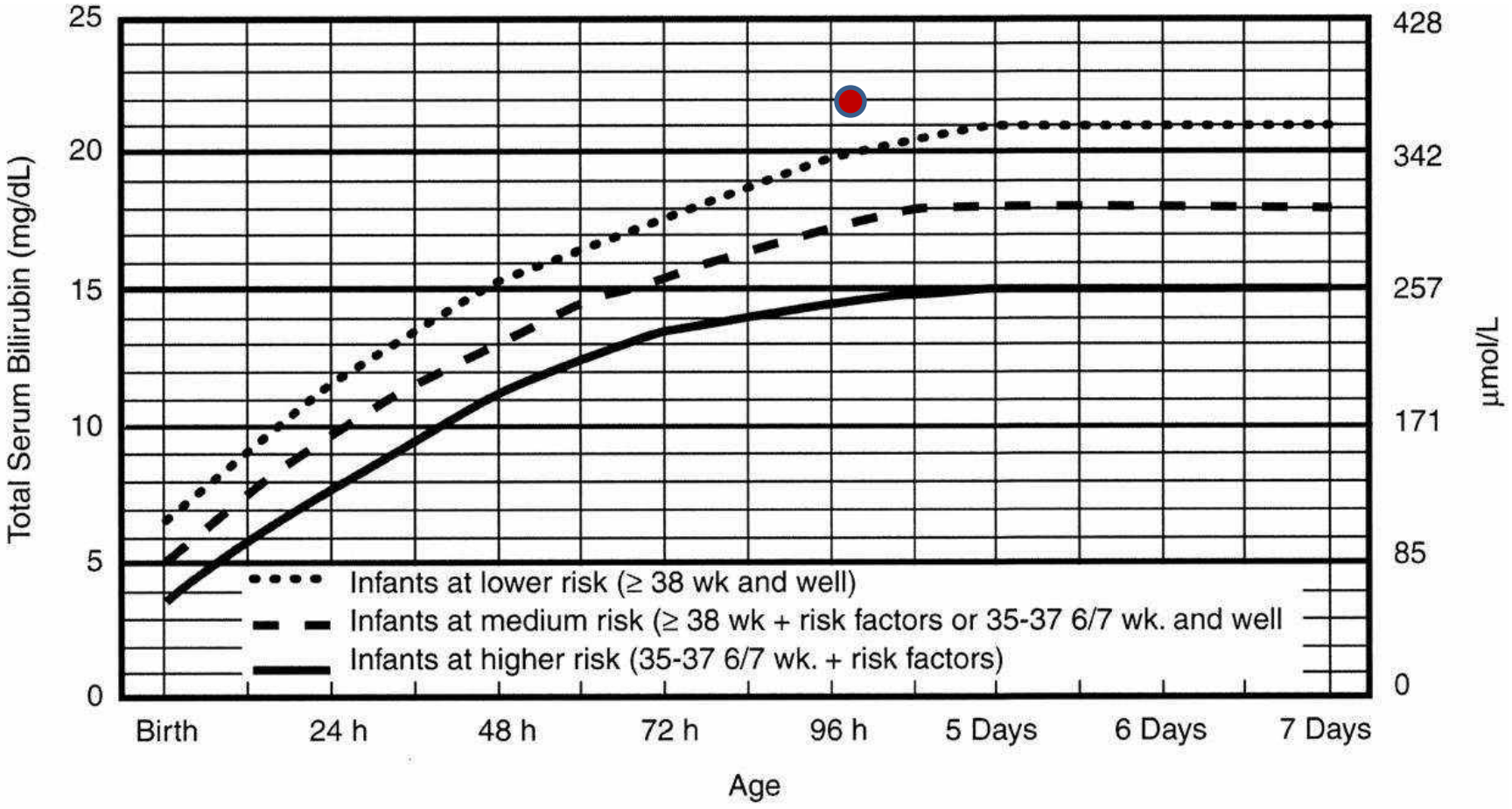
TcB- Current stand

- **For assessment** of Hyperbil use TcB as **first** line
  - GA > 35 wks and >24 hrs
- If TcB value >15 mg%: Use serum bilirubin
- For subsequent measurements: TcB can be used if photo-occlusive pad is used.
- Use **for prediction** (pre discharge): If >75th centile, take TSB
- Use Serum Bil: GA < 35 wks, < 24hrs

NICE guidelines

If a newborn requires phototherapy which guidelines to follow Term and Preterm ?

AAP charts - Phototherapy



Category of Jaundice and PT

1. Infants at low risk: Gestation ≥38 weeks and well
2. Infants at medium risk: Gestation ≥38 weeks and risk factors* OR 35-37+^{6} weeks and well
3. Infants at low risk: Gestation 35-37+^{6} weeks and risk factors*

*Isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin <3 g/dL

Phototherapy AND Preterm

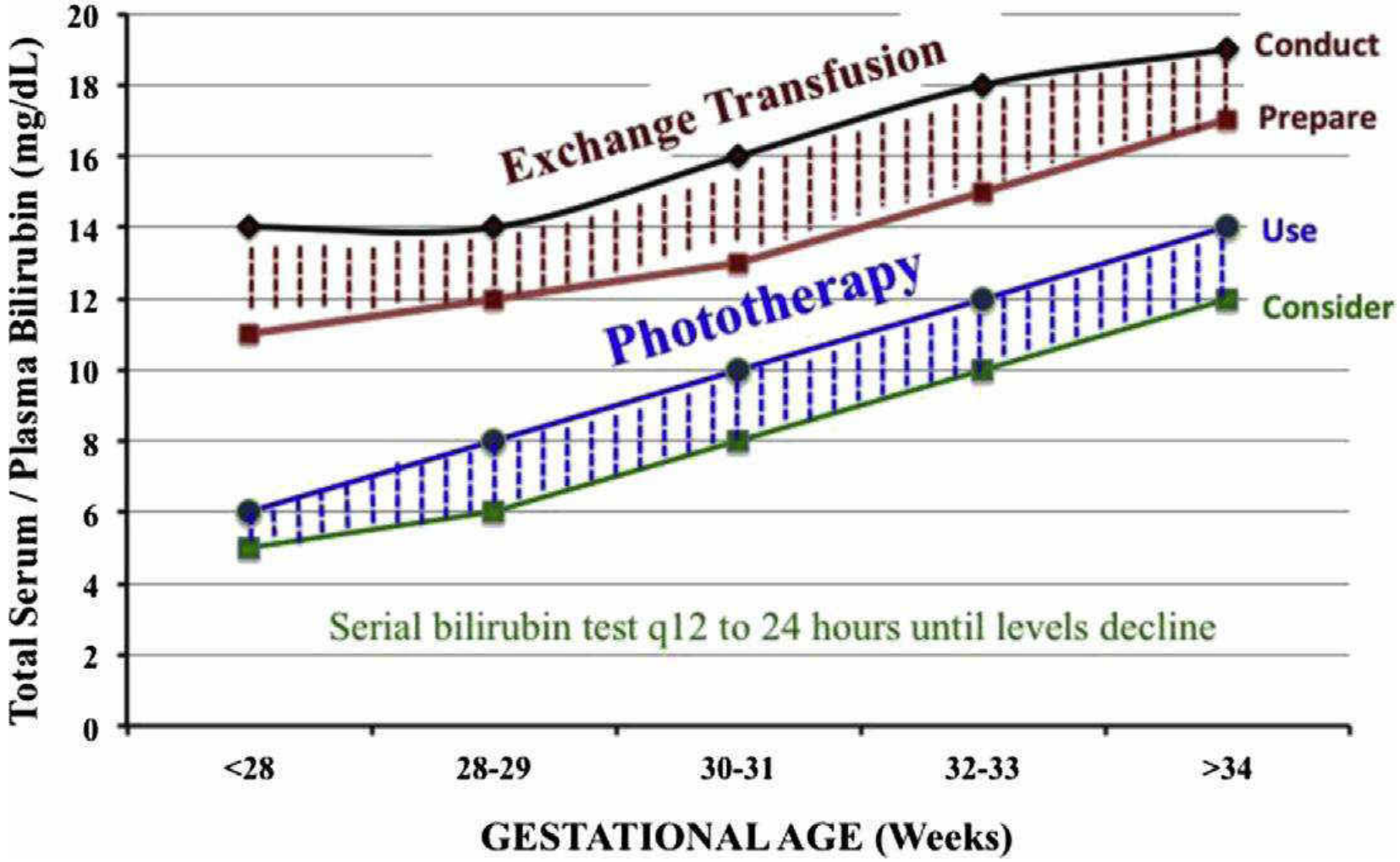
Table 3: Indications for PT and BET in LBW babies

Birth Weight (grams)	Guidelines for PT* (mg/dL)		Consider BET (mg/dL)
	Healthy Infant	Sick Infant	
<1000	5-7	4-6	10-12
1000-1500	7-10	6-8	12-15
1501-2000	10-12	8-10	15-18
2001-2500	12-15	10-12	18-20

*Martin & Fanaroff. Neonatal-Perinatal Medicine, 8th Edition p1450

NNF Guidelines

Operational total bilirubin thresholds to manage moderately preterm infants



J Perinatol 2012;32(9):660–4;

What is Intensive Phototherapy ?

NNT of PT to prevent Exchange?

Intensive Phototherapy

- Intensity atleast 30 Microwt/cm2/nm at center of baby
- Blue green Spectrum (460 to 490 nm)
- As much surface area exposed as possible

LED Phototherapy

Good Phototherapy

- Irradiance
- Spectrum of Light
- Surface area of Exposure
- Feeding of the baby

NNT of PT

- NNT for 36 week and <24 hours
    - 10 (95% CI 6–19)
- NNT for 41 weeks, day 3 or more, female
    - 3041 (95% CI 888– 11 096)

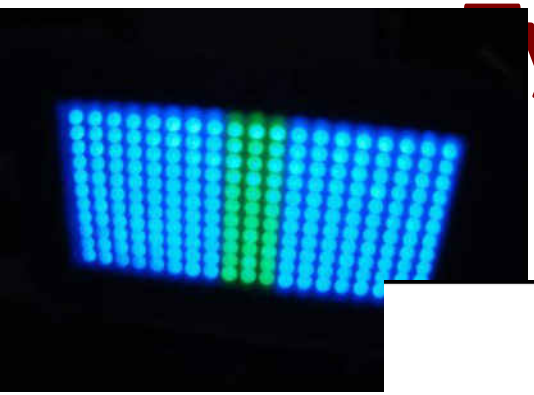
Table 2. Adverse Effects of Neonatal Phototherapy

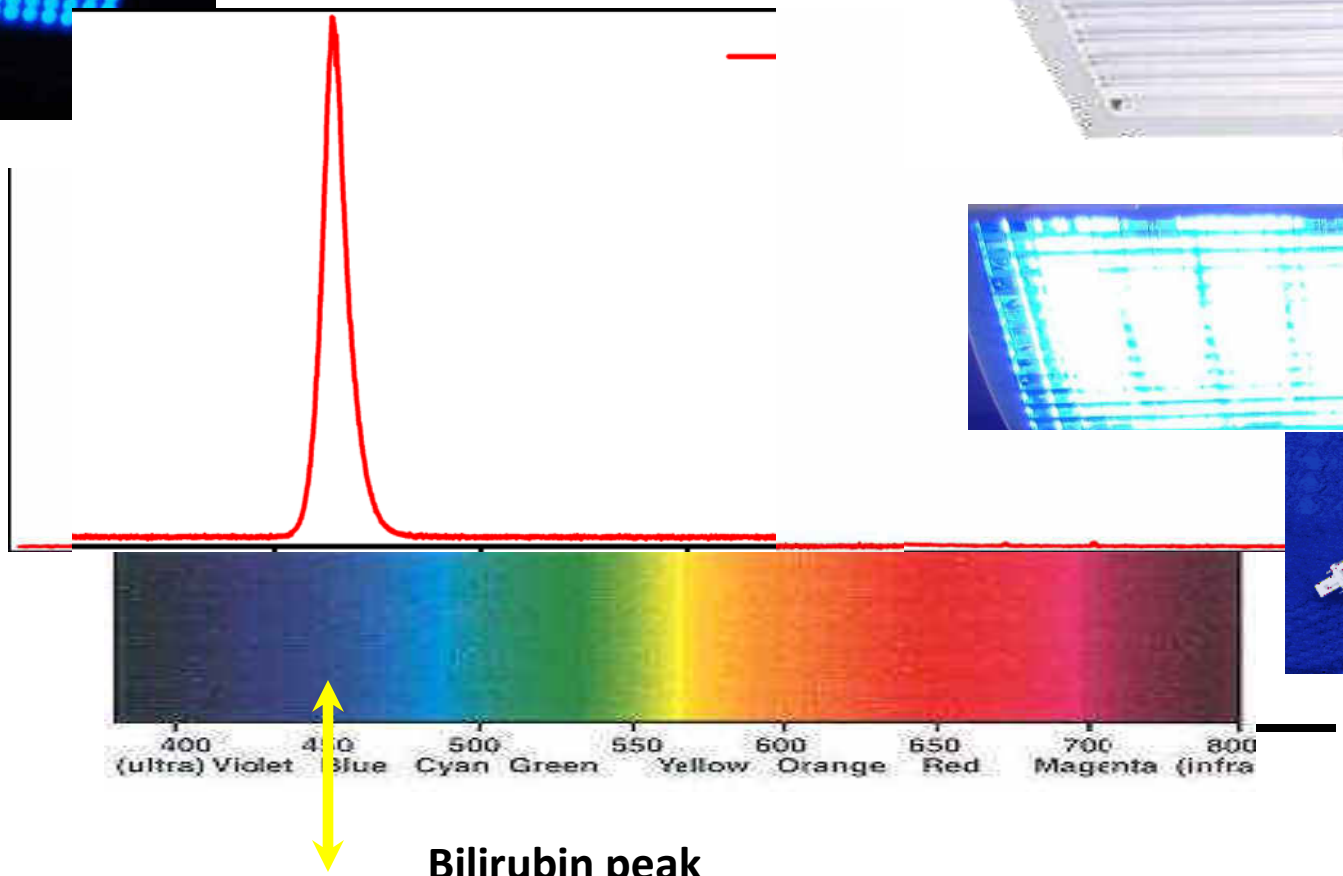
Short-term
Diarrhea
Interference with maternal–infant bonding
Intestinal hypermotility
Temperature instability
Long-term
Increased risk of childhood asthma (odds ratio = 1.4)
Increased risk of type 1 diabetes mellitus (odds ratio = 3.79)

Information from references 5, 22, and 24 through 27.

Comments on Super LED and Sunlight PT?

ype of phototherapy





Bilirubin peak
absorption spectrum

LED And Super LED

- CFL → LED → Super LED → intelligent super LED

- Advantages
  - High irradiance
  - Long shelf life
  - Low power consumption (0.1W/LED)
  - Environmental friendly
  - Does not produce heat

SUPER LED Phototherapy

FILTERED SUNLIGHT FOR NEONATAL JAUNDICE

- Safe, low-tech treatment
- Nigeria Study: Filtered sunlight was efficacious on 93% of treatment days, as compared with 90% for conventional phototherapy, and had a higher mean level of irradiance (40 vs. 17 µW/ cm^2/ nm, P<0.001)

Slusher et al. Safety and efficacy of filtered sunlight in treatment of jaundice in African neonates. Pediatrics. 2014; 133(6): e1568-74.
Slusher et al. A Randomized Trial of Phototherapy with Filtered Sunlight in African Neonates. NEJM. 2015; 373(12): 1115-24

Filtered sunlight

Can be a option in resource poor setting, need to be evaluated further

Any role for Home PT or Day Care PT?

Eur J Pediatr
DOI 10.1007/s00431-014-2373-8

ORIGINAL ARTICLE

Intermittent versus continuous phototherapy for the treatment of neonatal non-hemolytic moderate hyperbilirubinemia in infants more than 34 weeks of gestational age: a randomized controlled trial

Monica Sachdeva & Srinivas Murki & Tejo Pratap Oleti & Hemasree Kandraju

Subjects

- Healthy late preterm (> 34 weeks) and term neonates
- Neonatal hyperbilirubinemia under phototherapy (AAP-2004)
- Minimum 8 hours PT
- TSB <18mg/dl

At Enrollment Characteristics

Variable	Intermittent PT Group (n=36)	Continuous PT Group (n=39)	P Value
	2 (5.6%)	5 (12.8%)	0.28
Maternal Oxytocin	12 (33.3%)	9(23.1%)	0.32
Previous sibling jaundice	ABO setting	10(25.6%)	0.39
Average Weight loss	6.2(± 4.6)	6.1 (±4.2%)	0.97
TSB at admission, (mg/dl)	16.9 (± 1.6)	17.3 (± 2.1)	0.43
TSB at enrolment	14.9 (± 1.5)	15.1 (± 1.6)	0.35
Age at randomization in hours	103 (± 44)	99 (± 38)	0.73

Outcomes

Variable	Intermittent PT Group (n=36)	Continuous PT Group (n=39)	P Value
Rate of fall of bilirubin (mg/dl/hour)	0.18 (0.12 – 0.28)	0.13 (0.09 – 0.17)	0.001
Max Bilirubin (mg/dl)	15.2 (± 1.4)	15.4 (± 1.6)	0.34
Duration of PT in hours	24 (12 - 24)	30 (24 - 42)	0.001
Mean Duration of hospitalization in hours	33 (± 11.5)	33 (± 19.1)	0.83
Readmission for rebound	2 (5.6)	1 (2.6)	0.23

What is the role of Fluids for Infants under PT to prevent Exchange?

A Randomized Controlled Trial of Fluid Supplementation in Term Neonates With Severe Hyperbilirubinemia

Fluid supplementation in term neonates presenting with severe hyperbilirubinemia decreased the rate of exchange transfusion (RR = 0.30; 95% CI= 0.14 to 0.66) and duration of phototherapy (52 ± 18 hours versus 73 ± 31 hours, p = .004)

The Journal of Pediatrics
Volume 147, Issue 6 , Pages 781-785, December 2005

Role of Albumin to prevent Exchange Transfusion or ND abnormalities?

Nabaneeta Dash, Praveen Kumar, Venkataseshan Sundaram and Savita Verma Attri

From Department of Pediatrics, Advanced Pediatrics Centre, PGIMER, Chandigarh, India.

TABLE III *Comparison of Outcome Between Intervention and Control Groups*

Characteristics	Albumin group; n=23	Saline group; n=27	P
Duration of post-ET phototheraphy (h)	29 (24, 48)*	33 (24, 43)*	0.76
Total mass of bilirubin removed during ET (mg)	34 (28-46)*	33 (27-38)*	0.46
Bilirubin removed/kg birth weight (mg/kg)	12.5 (3.6)	12.1 (3.4)	0.69
TSB at the end of ET (mg/dL)	11.9 (3.9)	13.1 (4.3)	0.31
Maximum TSB post- ET (mg/dL)	18.5 (2.8)	17.9 (2.9)	0.50
Hours post- ET maximum TSB	6 (2-12)*	6 (2-12)*	0.50
Need for second ET	2 (9) #	2 (7.5) #	1.00

*ET:exchange transfusion, TSB: total serum bilirubin. All values are represented as mean (SD) except *Median (IQR)and #number (%).*

What is BIND Scoring?

Condition	1 point	2 points	3 points
Mental Status	Sleepy, poor feeding	Lethargy, irritability, very poor feeding	Semicoma, seizures, apnea
Muscle Tone	Slight decrease	Moderate hyper- or hypotonia depending on arousal state, mild arching, posturing, bicycling	Severe hyper- or hypotonia, opisthotonus, fever
Cry	High-pitched	Shrill and frequent or too infrequent	Inconsolable or only with stimulation

Total score:	1-3 points	Stage IA: minimal signs of encephalopathy
	4-6 points	Stage IB: progressive, but reversible with treatment
	7-9 points	Stage II: advanced, largely irreversible, but severity decreased with treatment

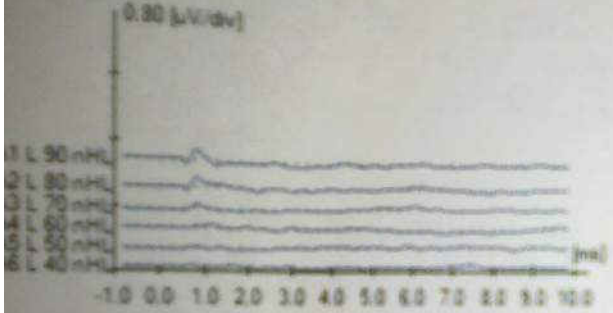
Which babies with jaundice require Long term follow up and How?

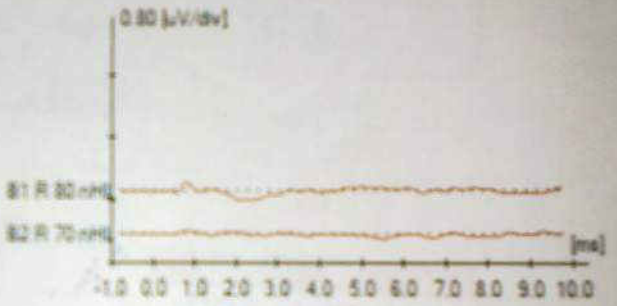
BIND and Kernicterus

- TSB > 25mg/dl in term and late preterm infants no difference in
  - Cognitive scores
  - Neurological exam
  - Or neurological diagnosis at 2 years
- If DCT positive
  - Lowe IQ scores (less by & points)
- Canadian Study
  - Increased risk of ADHD if TSB >19mg/dl(OD 1.9, 1.1 3.3)

At discharge

- Neurological examination
  - Hypotonia
  - Poor suck
  - Persistent ATNR
- BERA at 1 month of age
- Development follow up till 18 months of age



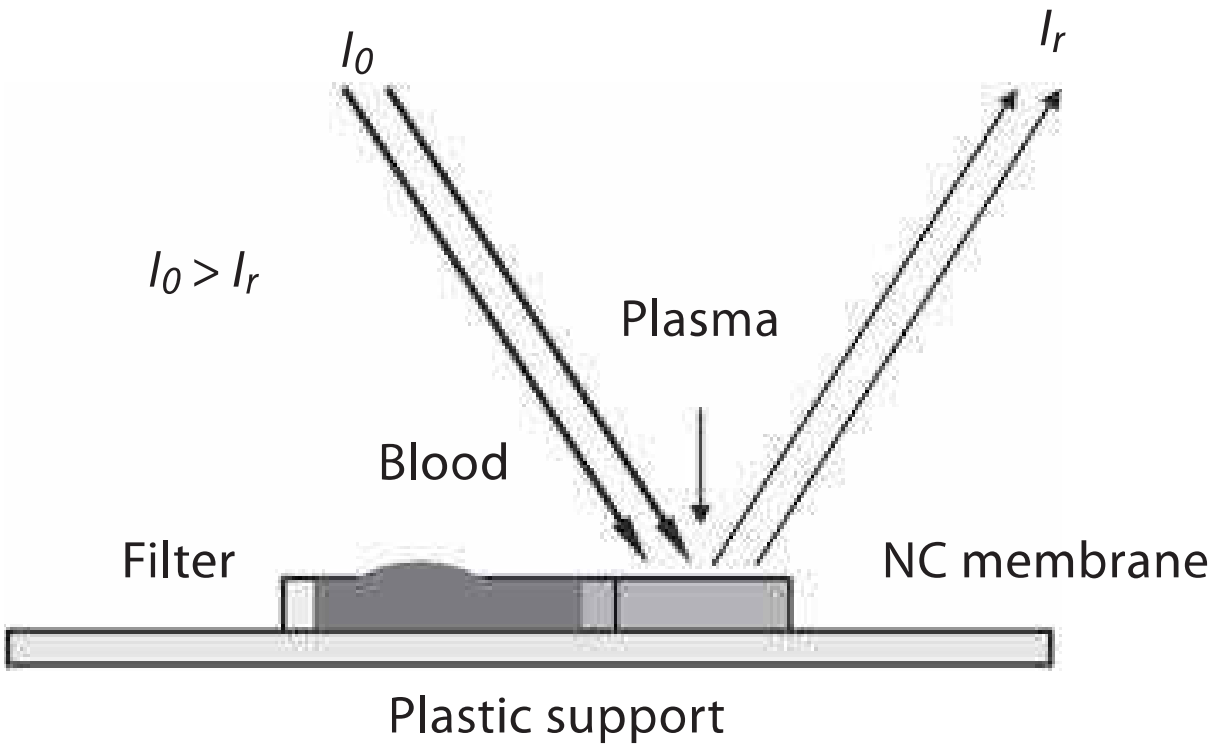


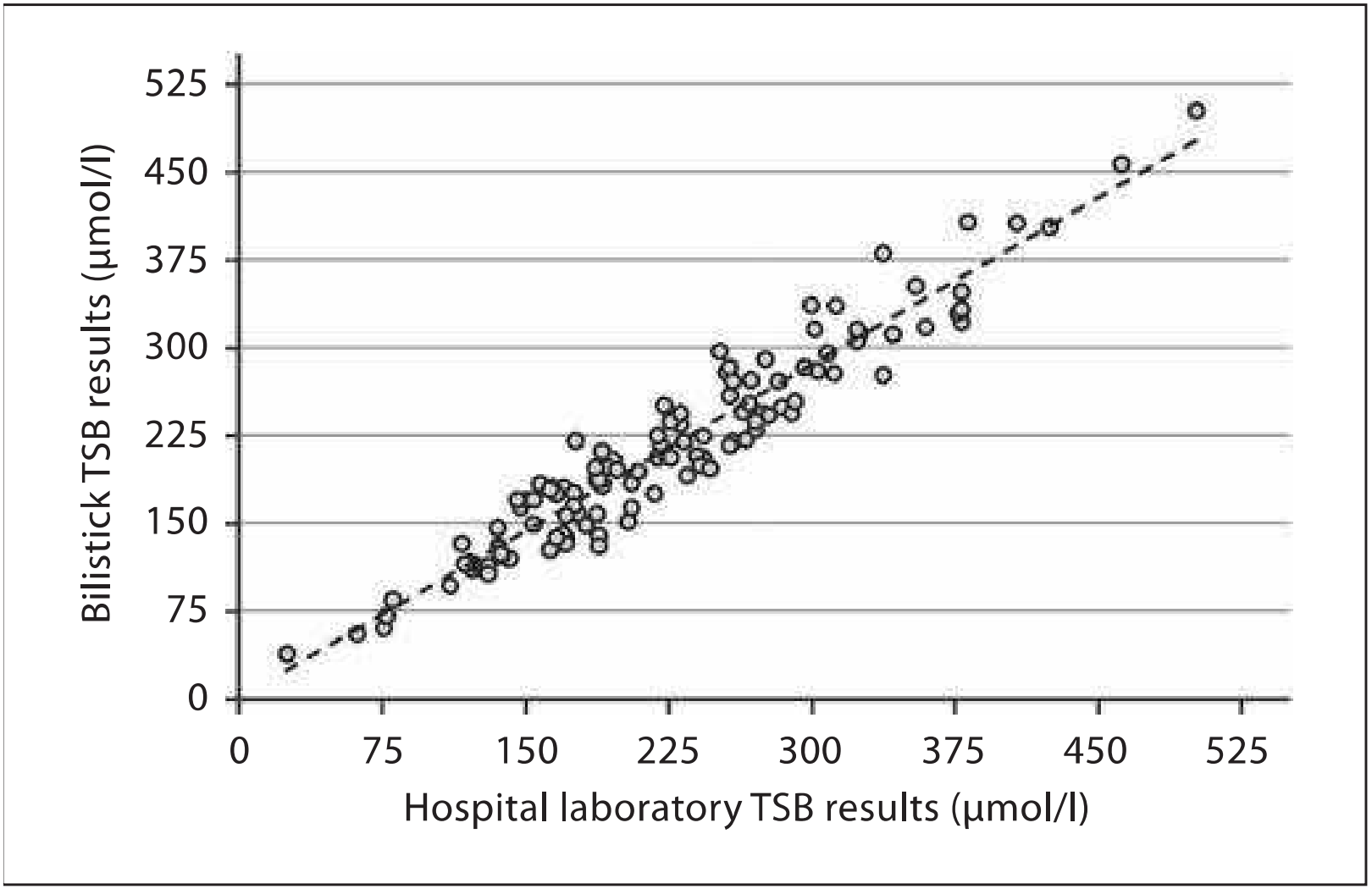
Collection Parameters					Latencies (ms)					Interlatencies (ms)		
Transducer	Ear	Intensity	Type	Frequency	I	II	III	IV	V	I-III	III-V	I-V
Insert Earphones	Left	90dB nHL	Click	N/A								
Insert Earphones	Left	80dB nHL	Click	N/A								
Insert Earphones	Left	70dB nHL	Click	N/A								
Insert Earphones	Left	60dB nHL	Click	N/A								
Insert Earphones	Left	50dB nHL	Click	N/A								
Insert Earphones	Left	40dB nHL	Click	N/A								
Insert Earphones	Right	80dB nHL	Click	N/A								
Insert Earphones	Right	70dB nHL	Click	N/A								

BERA observation :-

... usiva click as

Newer POCT for Bilirubin?


I_0
I_r
$I_0 > I_r$
Plasma
Blood
Filter
NC membrane
Plastic support



25 microml and 100 Seconds

Who are target newborns to reduce BIND?

Target Newborns

- Rh Negative and O positive mothers
- G6PD endemic areas
- Late preterm Infants
- Babies on Exclusive Breastfeeds

Breastfeeding Jaundice

- TSB >12 gmd/dl : 3 times higher risk
- TSB>15mg/dl: 6 times higher risk
- Presence of Jaundice : stoppage of BF (NNH Is 4)
- Interruption of BF for Jaundice (NNH for stoppage of BF at 1 month NNH is 4)

Breastfeeding and Jaundice

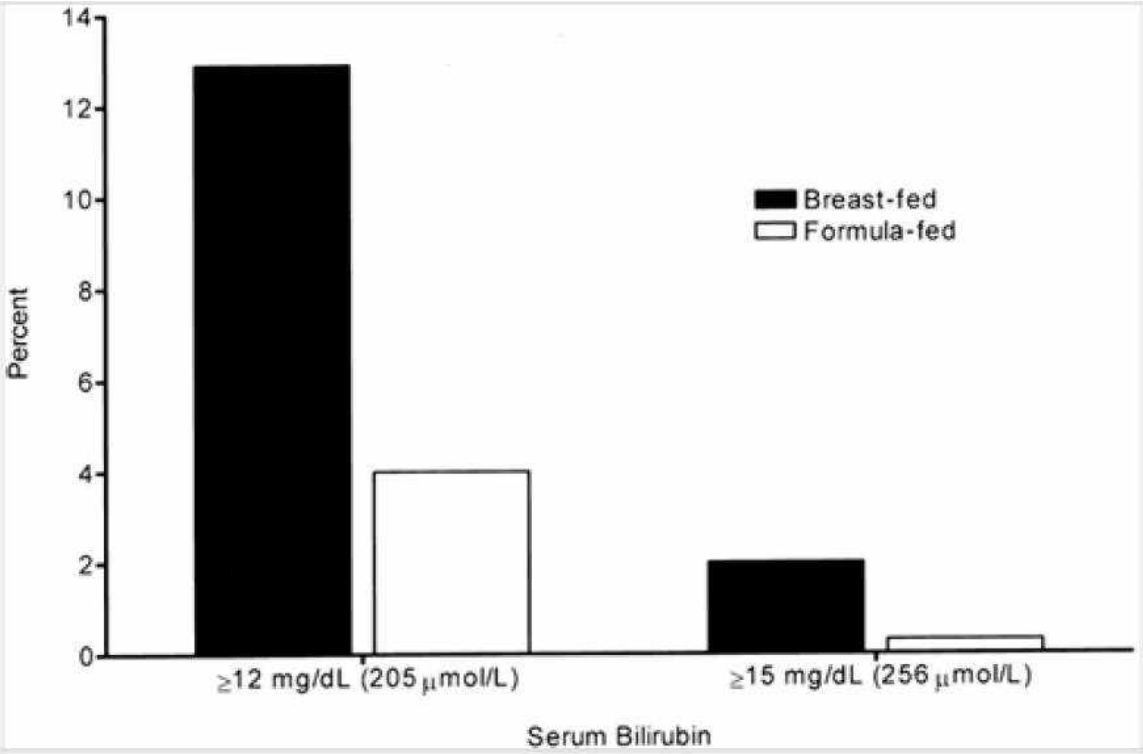


Figure 35-14 Pooled analysis of 12 studies showing the percent of newborns with serum bilirubin levels ≥12mg/dL (205 μmol/L) in breast-fed and formula-fed newborns and, in 6 of the 12 studies, the percent of newborns with serum bilirubin levels ≥15 mg/dL (256 μmol/L) (From Schneider AP. Breast milk jaundice in the newborn. A real entity. *JAMA* 1986;255:3270-3274, with permission.)

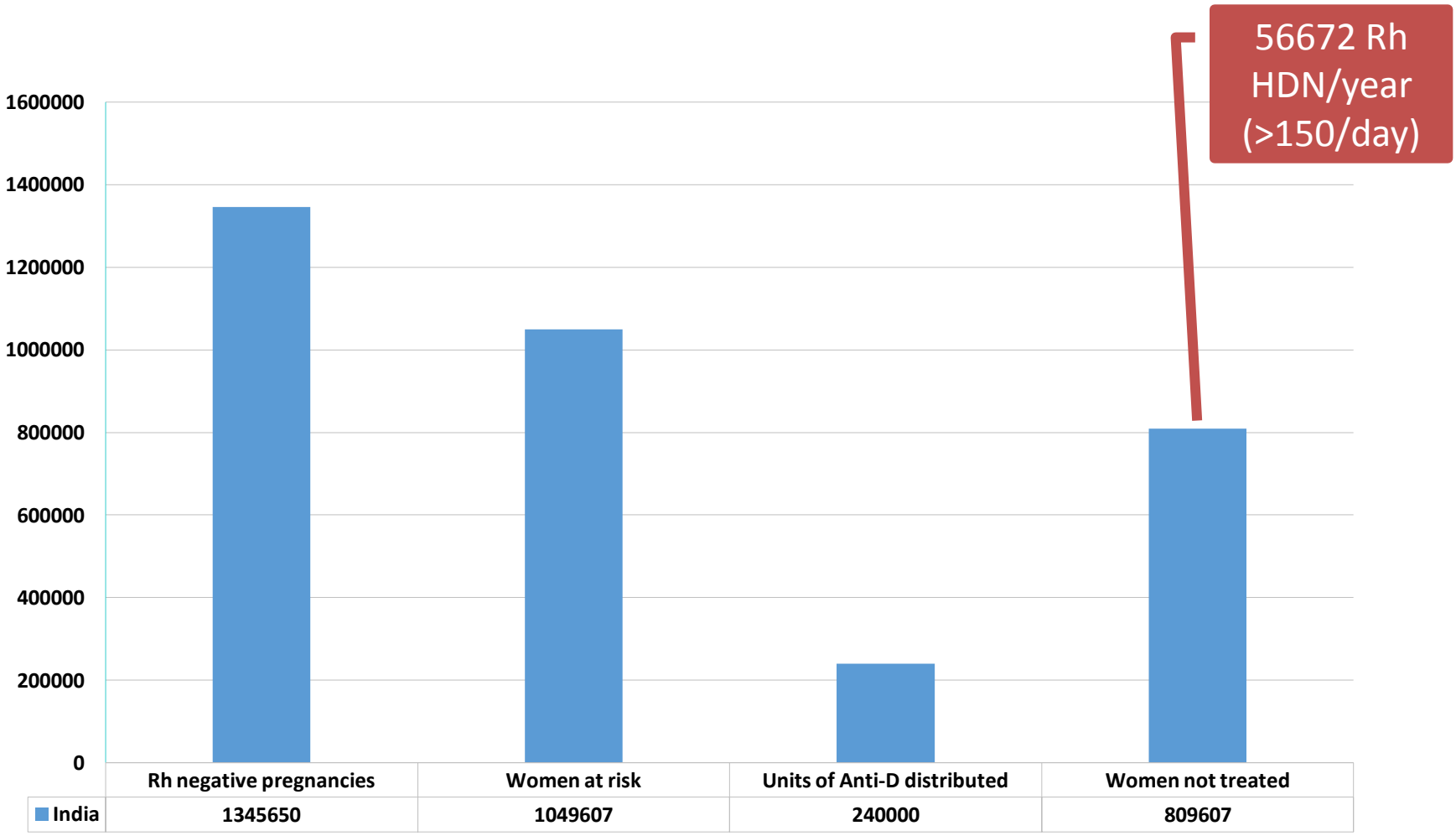
Jaundice in late Preterms

- 57% of late preterm infants have Jaundice
- 36% have bilirubin >15mg/dl
- Mean age of onset is day 3
- Risk factors
  - Lower gestation
  - LGA
  - Birth trauma
  - Previous sibling jaundice

Predictors of Significant Jaundice in Late Preterm Infants

Rh Jaundice: Prenatal Diagnosis, Prevention

Prevent Rh isoimmunization



Arch Dis Child Fetal Neonatal Ed 2011 96: F84-F85

Prevent Rh Isoimmunization

- Screening all mother at Booking
  - 7% incidence of Rh-Negative
- If Fetus un affected (Group, TSB, Cord DCT)
  - Anti-D within 72 hours 300IU

Summary

- Risk based approach for TcB
- TcB for preterm
- AAP guidelines and preterm guidelines
- Intensive PT, LED or CFL
- Day care PT only for select babies
- BIND newborns to follow up till 18 to 24 months
- Prevent Rh, Closer monitor Late preterm, BF