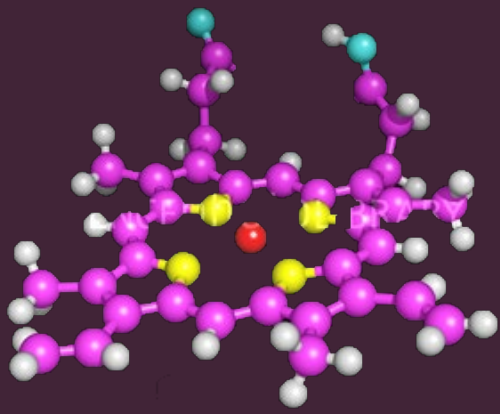


# Breast Feeding and Neonatal Hyperbilirubinemia

AAP CHAPTER WEBINAR: September 9, 2021

VINOD (Vinny) K. BHUTANI, Professor Emeritus (Active),

Department of Pediatrics, Division of Neonatal-Perinatal Medicine,

Stanford University School of Medicine, Stanford, CA

No Conflicts to declare

# Disclosure

- Neither I nor any member of my immediate family has a financial relationship or interest (currently or within the past 12 months) with any proprietary entity producing health care goods or services consumed by, or used on, patients related to the content of this CME activity.

- I do not intend to discuss an unapproved/investigative use of a commercial product/device.

# LEARNING OBJECTIVES

At the conclusion of this presentation, you should be able to:

1. Know the actual relationship between breast feeding and neonatal hyperbilirubinemia.
2. Use the hour-specific bilirubin nomogram
3. Restore Systems Integrity
4. Resolve immediate hurdles to effective phototherapy
5. Foster benign outcomes for neonatal hyperbilirubinemia.

# SCREEN & PREVENT

NURSE

PHYSICIAN

BREAST FEEDING

LIGHT

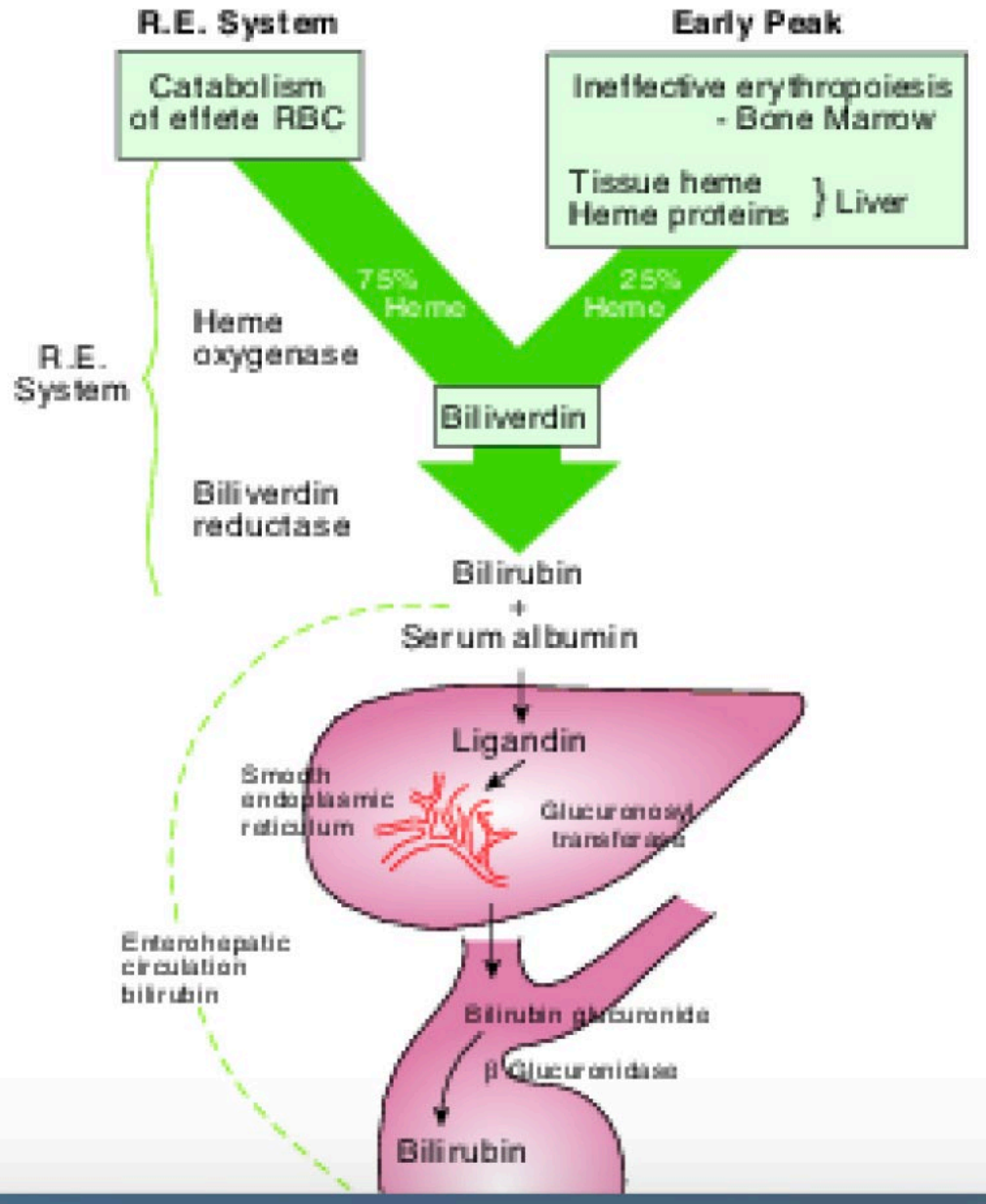
BIOENGINEER

HEALTH SYSTEM

FAMILIY

# BILIRUBIN METABOLISM

TB (at any given time)
**EQUALS**
BILIRUBIN PRODUCTION
(hemolysis)
**PLUS**
REABSORBED BILIRUBIN
(GA, weeks)
**MINUS**
BILIRUBIN ELIMINATION



**Old:** physiologic or pathological jaundice

**New:** Benign or Adverse Hyperbilirubinemia

1. Jaundice is a clinical sign
2. This condition is related to bilirubin level
3. Newborn jaundice is not a clinical diagnosis
4. We need to rely on bilirubin level and,
5. We modulate its magnitude for age (hours), prematurity (days) and assess bilirubin production.

# How common is the problem: Benign vs Adverse

- Jaundice: 80-84% of all term and late preterm newborns

BENIGN:

- Hyperbilirubinemia: TB <40$^{th}$ percentile for age in hours
- ADVERSE: Mild: Use of phototherapy, Severe: Use of Exchange transfusion
- ADVERSE: USA risk of Kernicterus ~1.4 per 100,000 live-births
- Risk of Kernicterus in USA/CANADA/UK/EUROPE:

- TB <25 mg/dL: when confounded by sepsis and high NMR
- TB 25-30 mg/dL: 1 in 17
- TB 31-35 mg/dL: 1 in 12
- TB >35 mg/dL: Nearly all

# Changes you may wish to make in practice

1. Know your screening set-up and systems.
2. Promote breast feeding
3. Drill the team's responsiveness to urgency
4. Develop institutional guidelines for management.

# Case 1: healthy baby with adverse outcomes

Term baby is being discharged from Well Baby Nursery

- Breast feeding
- Alert and normal; may have icterus, noted night before
- TcB was done at discharge
- Assess bilirubin risk
- Follow-up is arranged.

# PRE-DISCHARGE SCREENING

# Assess Risk of Neonatal Hyperbilirubinemia.

- How do you assess risk?, for bilirubin >10, 15, 20 or 25 mg/dL?
- Clinical factors: prematurity, gender, race, ethnicity, age (hours)
- Bilirubin: adjust TB to age in hours & percentile risk zones
- Process. TcB, TB. Plot value on a bilirubin nomogram
- Project  (measure) TB rate of rise (ROR)
- Know signs for ABE (acute bilirubin encephalopathy)

# How to use the Nomogram?

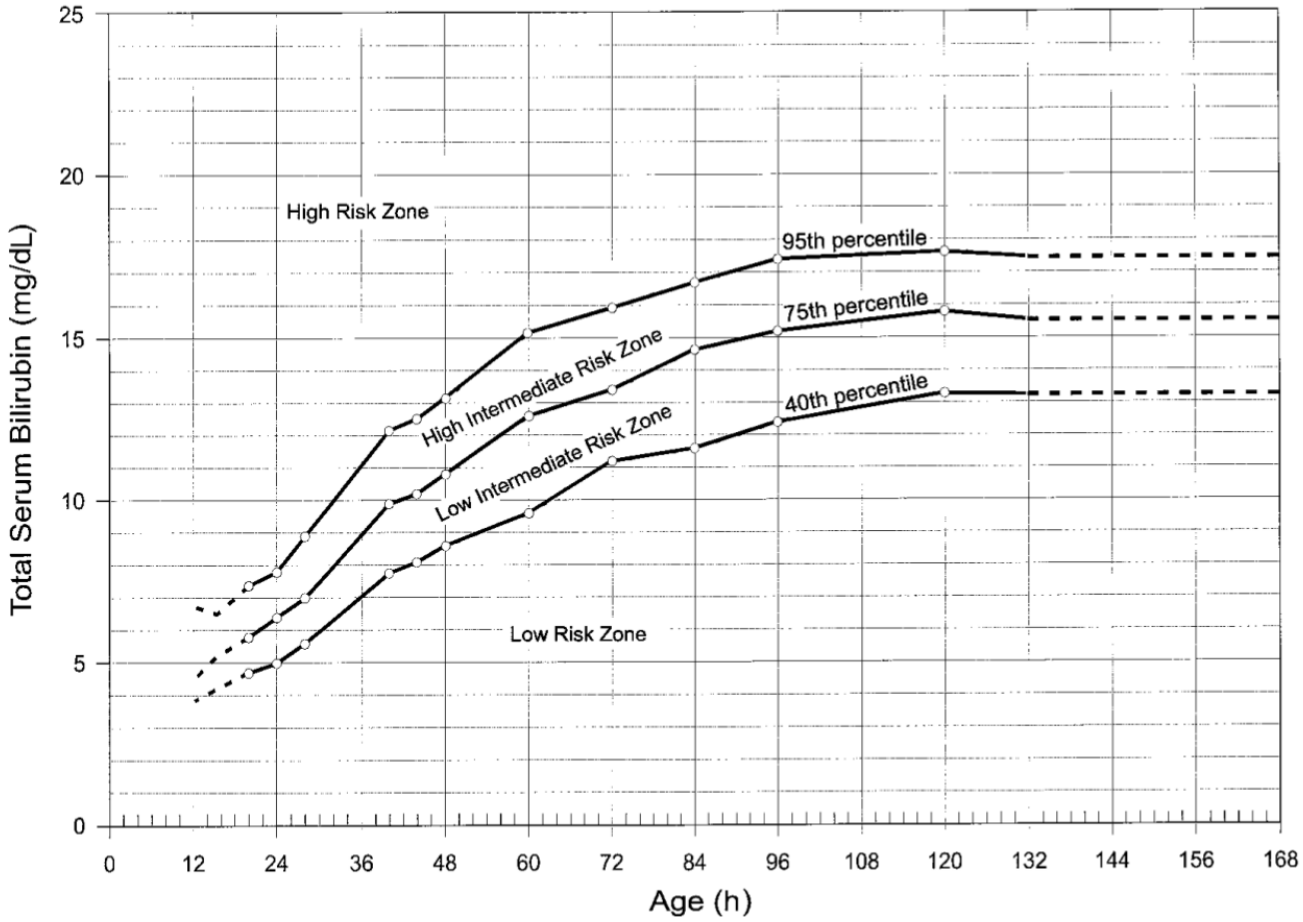
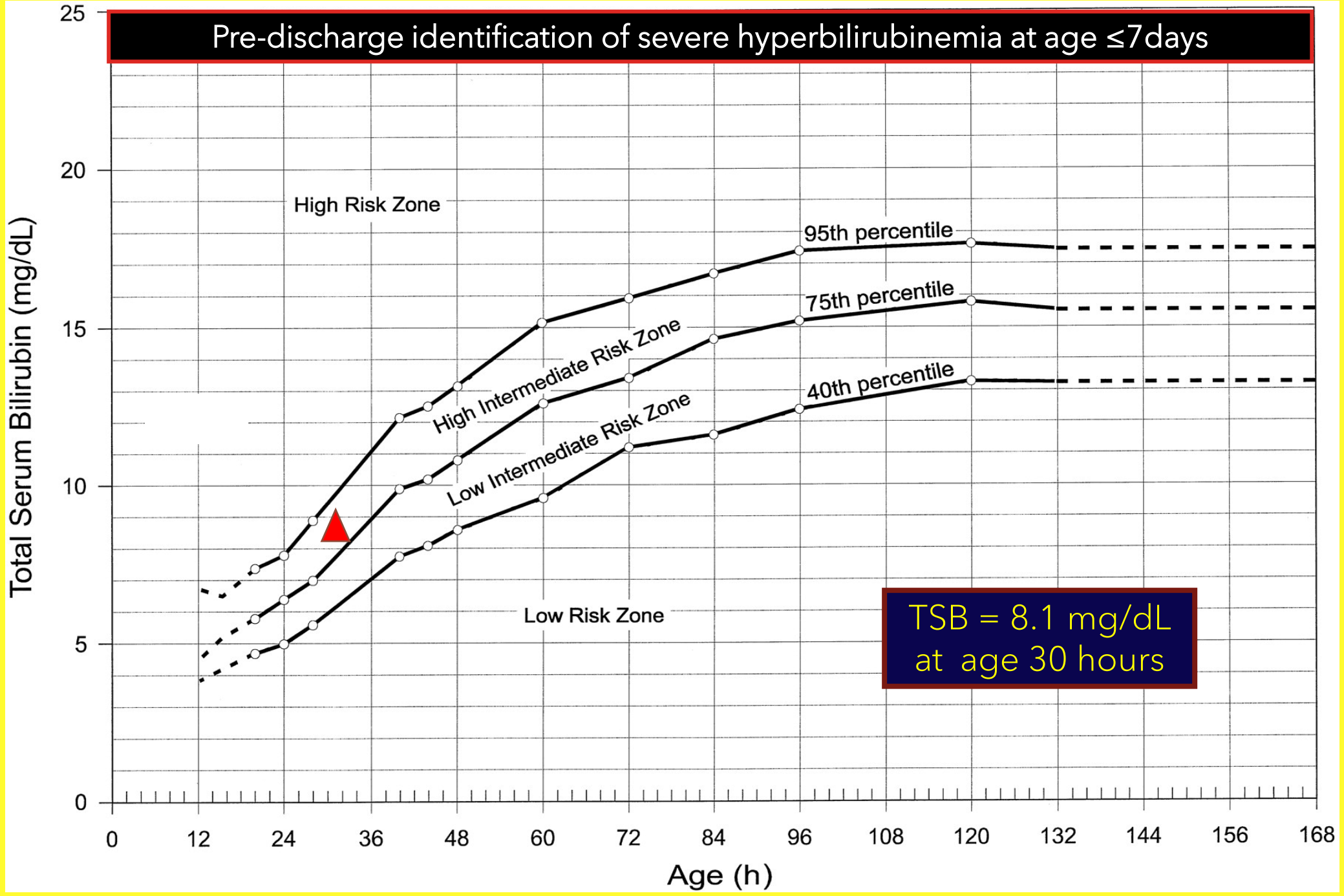



**Fig 2.** Risk designation of term and near-term well newborns based on their hour-specific serum bilirubin values. The high-risk zone is designated by the 95th percentile track. The intermediate-risk zone is subdivided to upper- and lower-risk zones by the 75th percentile track. The low-risk zone has been electively and statistically defined by the 40th percentile track. (Dotted extensions are based on <300 TSB values/epoch).

# Pre-discharge identification of severe hyperbilirubinemia at age ≤7days



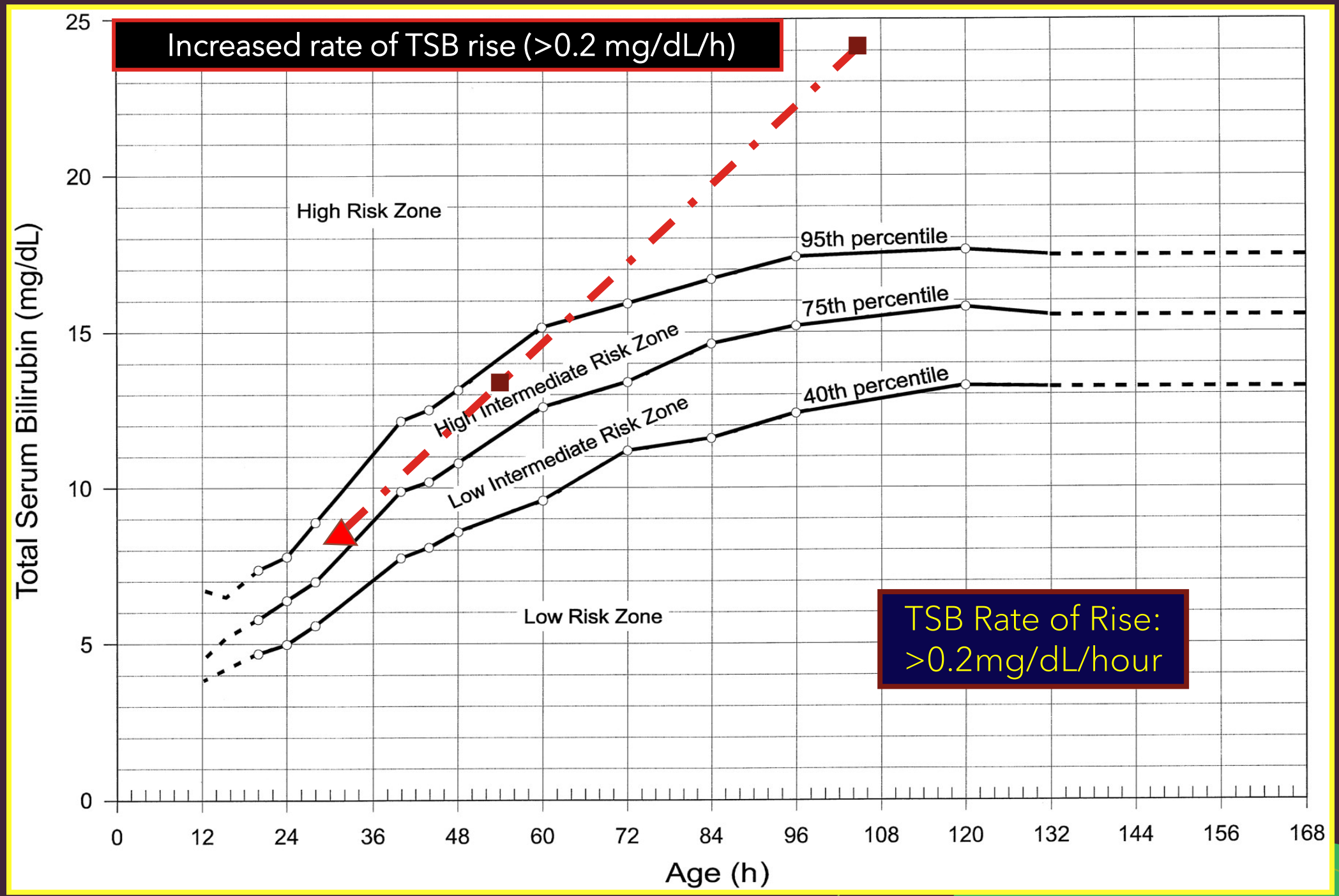
# WHY DO YOU SCREEN?

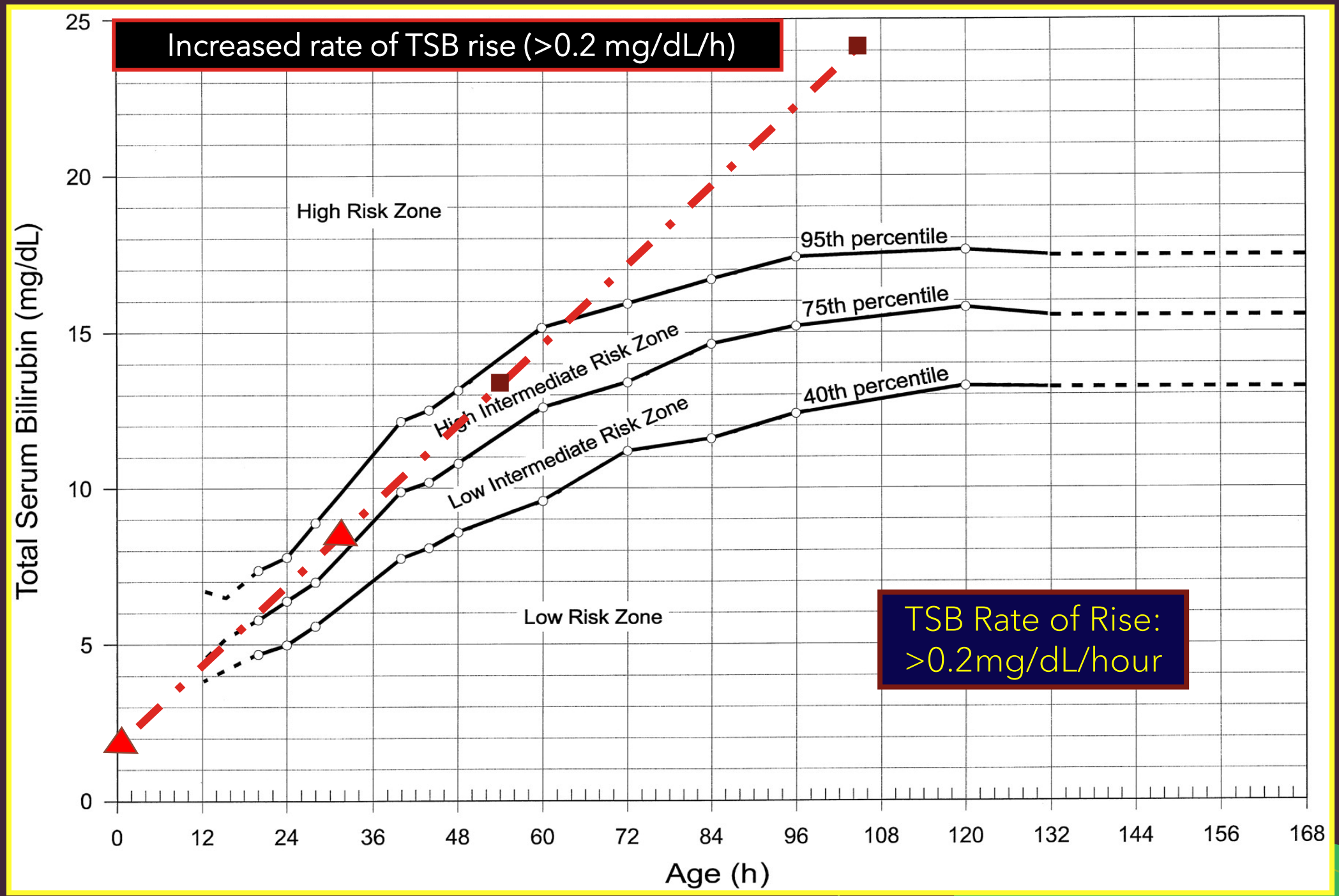
# Your baby has hyperbilirubinemia, because

- First, TB >75$^{th}$ %ile, (high risk zone) as plotted
- Next, assess room you have before harm ensues.
- Next, project the rate of rise to reach neurotoxicity (time when it reaches to PhotoRx threshold or harm.
- **The margin** could be narrow and dangerous unless you measure the rate of bilirubin rise.

# Myth: There is a specific bilirubin level at which injury occurs

1. **Not true**
2. Depends on bilirubin rate of rise
3. Depends on biology: prematurity/illness
4. Relies on albumin-binding of bilirubin.


Increased rate of TSB rise (>0.2 mg/dL/h)
Total Serum Bilirubin (mg/dL)
25
20
15
10
5
0
High Risk Zone
High Intermediate Risk Zone
Low Intermediate Risk Zone
Low Risk Zone
95th percentile
75th percentile
40th percentile
0
12
24
36
48
60
72
84
96
108
120
132
144
156
168
Age (h)
TSB Rate of Rise:
>0.2mg/dL/hour


Increased rate of TSB rise (>0.2 mg/dL/h)
Total Serum Bilirubin (mg/dL)
25
20
15
10
5
0
High Risk Zone
High Intermediate Risk Zone
Low Intermediate Risk Zone
Low Risk Zone
95th percentile
75th percentile
40th percentile
0
12
24
36
48
60
72
84
96
108
120
132
144
156
168
Age (h)
TSB Rate of Rise:
>0.2mg/dL/hour

PEDS. 1999

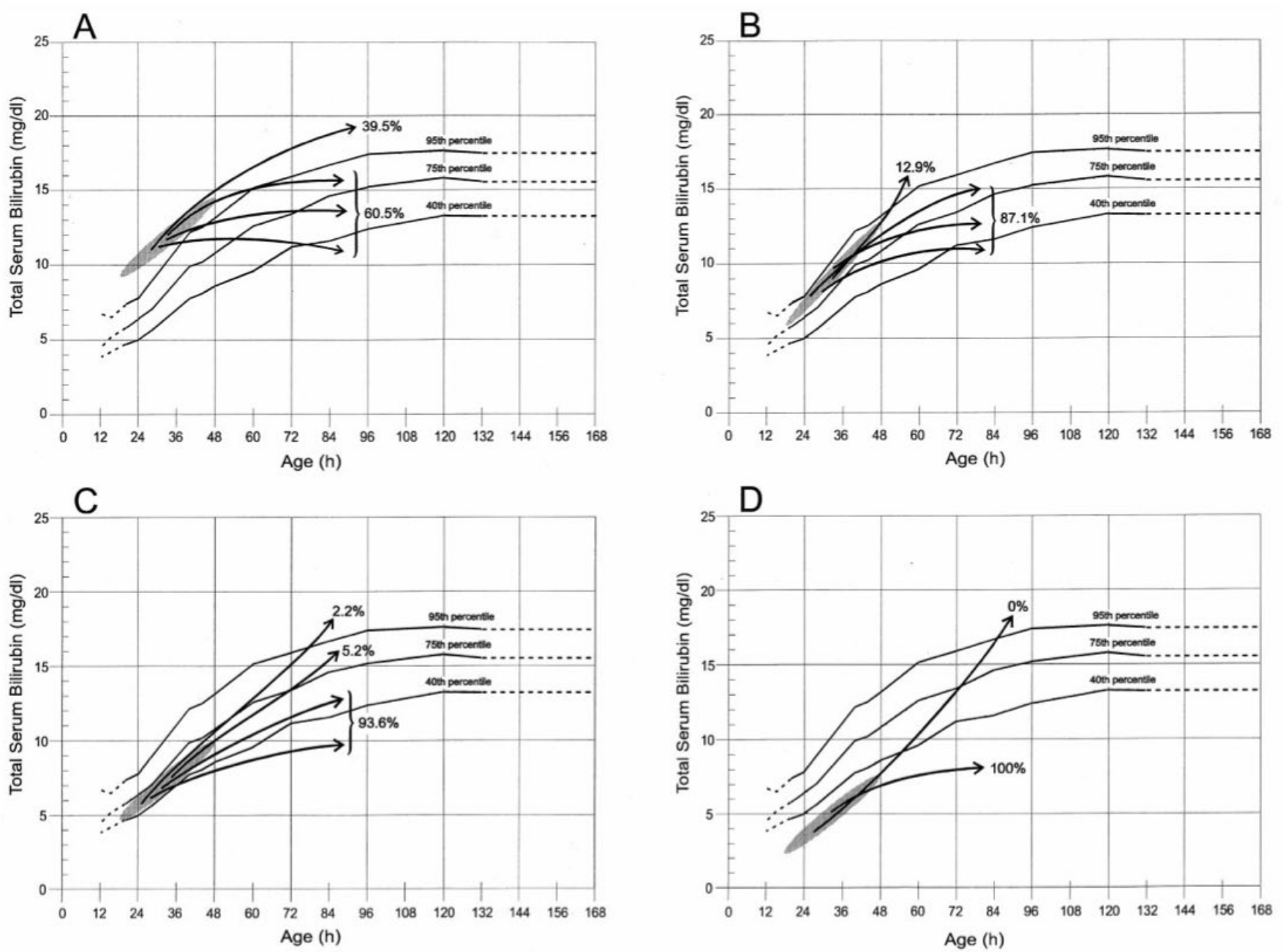



**Fig 4.** Outcome of newborns as defined by the percentage that remains or moves up to the high-risk zone after their risk assessment with the predischarge bilirubin value (represented by the shaded area). A, Outcome for newborns designated in the high-risk zone ($n$ = 172); B, outcome of newborns in upper intermediate-risk zone ($n$ = 356); C, outcome of newborns in the lower intermediate-risk zone ($n$ = 556); D, outcome of newborns in the low-risk zone ($n$ = 1756).

PEDS. 1999

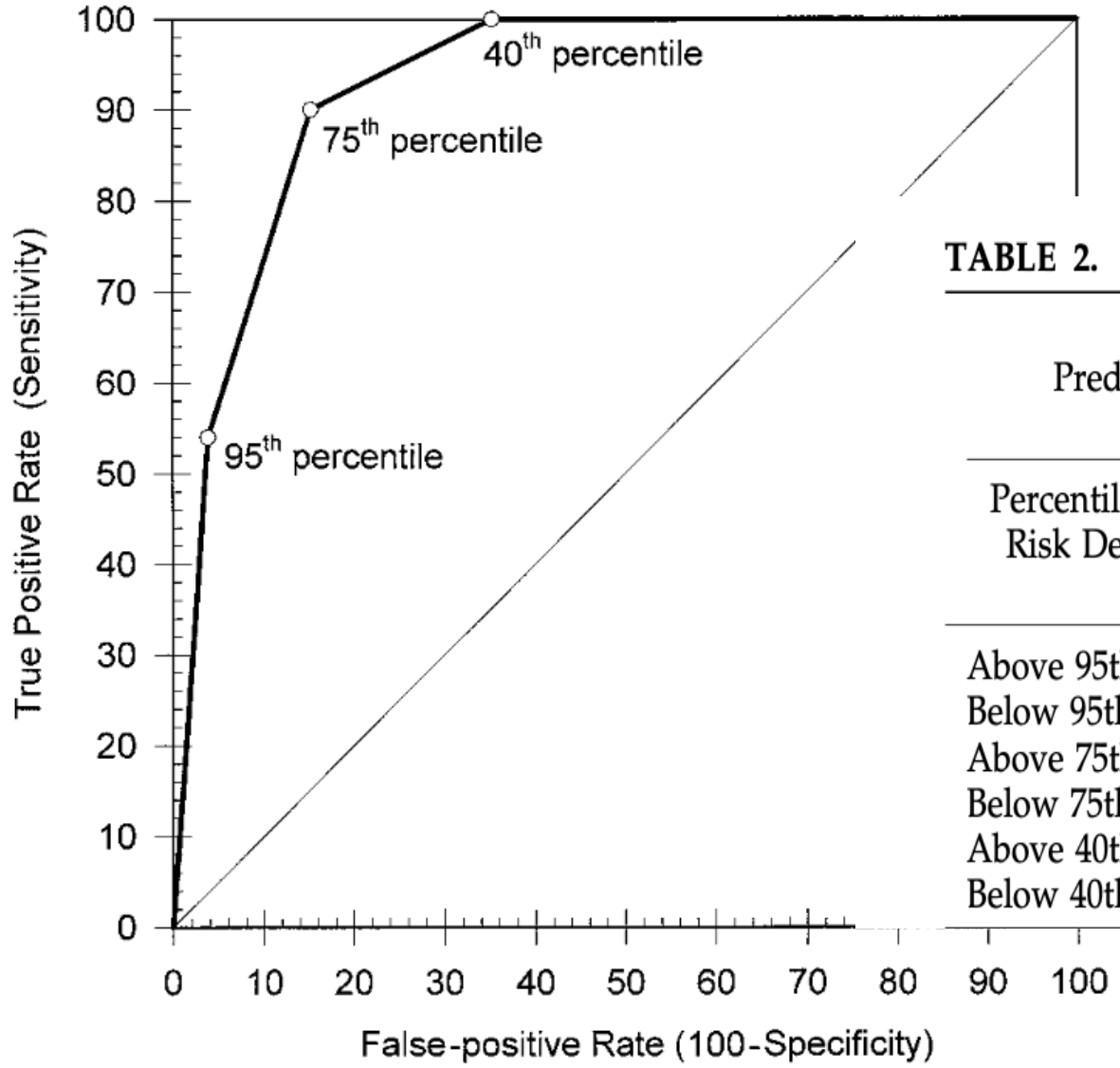



**Fig 3.** The ROC curve for the predictive abilities of the 40th, 75th, and the 95th percentile-based risk zones and their false-positive and false-negative rates (%). (Its location in the upper left corner is indicative of the usefulness of the risk zones).

**TABLE 2.** Predictive Characteristics of Percentile Tracks as Risk Demarcators f

| Location of Predictive Predischarge TSB Vector | | Outcome: Subsequent Significant Hyperbilirubinemia | |
|---|---|---|---|
| Percentile Track as Risk Demarcator | Number of Newborns (Total = 2840) | Present (Total = 126) | Absent (Total = 2714) |
| Above 95th percentile | 172 | 68 | 104 |
| Below 95th percentile | 2668 | 58 | 2610 |
| Above 75th percentile | 528 | 114 | 414 |
| Below 75th percentile | 2312 | 12 | 2300 |
| Above 40th percentile | 1084 | 126 | 958 |
| Below 40th percentile | 1756 | 0 | 1756 |

# Thus, when you plot of TB for risk status

1. You assess TB rate of rise (ROR) >0.2 mg/dL/hour
2. You can assess how soon the TB reaches a level of 20 or, at the time of next visit, what is the likely TB.
3. You can guestimate TB ROR from birth (cord blood).
4. You can decide when to schedule the first follow-up visit.
5. You may reassure the family if TB (<40$^{th}$ percentile).

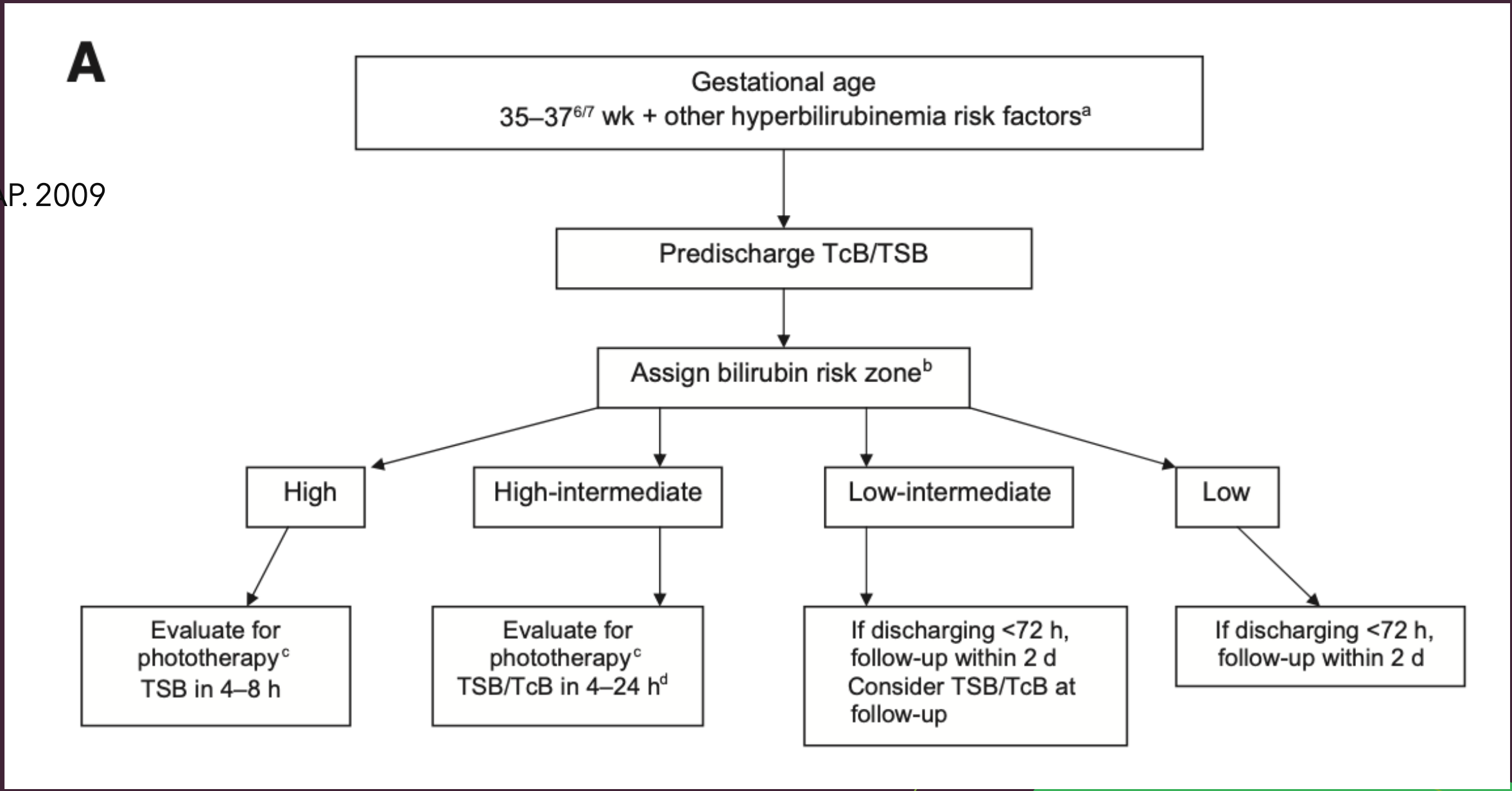
# Major Reasons for Increased TB ROR

Rhesus disease
ABO incompatibility (regardless of DAT)
Bruises and hematomas
G6PD enzyme deficiency
Inherited RBC disorders
Unusual bilirubin elimination disorders.

# SCREEN TO GUIDE FOLLOW-UP

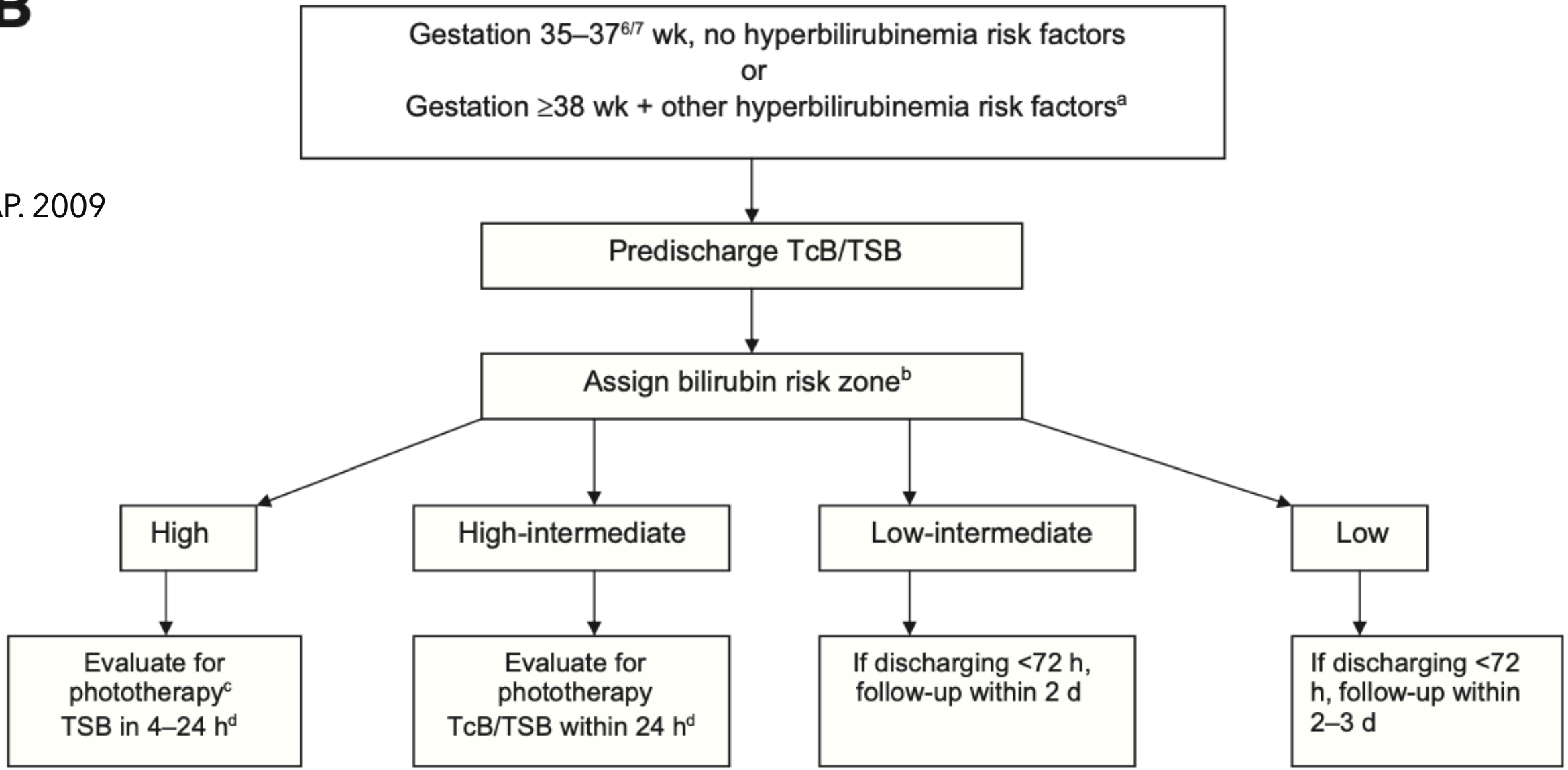
# Follow-Up (Pediatrics, 2009).

AAP. 2009



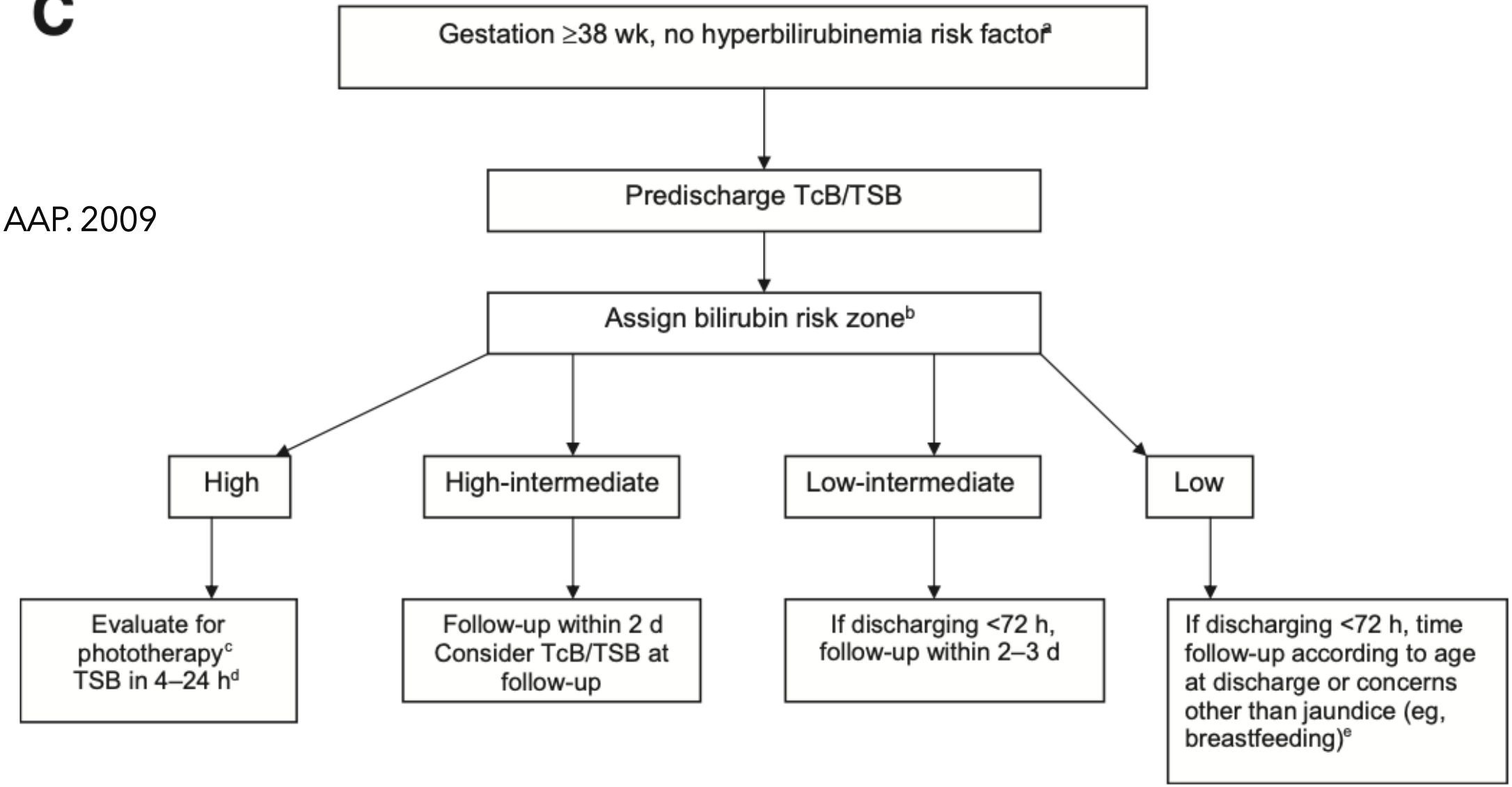
**B**

AAP. 2009


Gestation 35–37[6/7] wk, no hyperbilirubinemia risk factors
or
Gestation ≥38 wk + other hyperbilirubinemia risk factors[a]
Predischarge TcB/TSB
Assign bilirubin risk zone[b]
High
High-intermediate
Low-intermediate
Low
Evaluate for phototherapy[c] TSB in 4–24 h[d]
Evaluate for phototherapy TcB/TSB within 24 h[d]
If discharging <72 h, follow-up within 2 d
If discharging <72 h, follow-up within 2–3 d

C

AAP. 2009


Gestation ≥38 wk, no hyperbilirubinemia risk factor[a]
Predischarge TcB/TSB
Assign bilirubin risk zone[b]
High
High-intermediate
Low-intermediate
Low
Evaluate for phototherapy[c] TSB in 4–24 h[d]
Follow-up within 2 d Consider TcB/TSB at follow-up
If discharging <72 h, follow-up within 2–3 d
If discharging <72 h, time follow-up according to age at discharge or concerns other than jaundice (eg, breastfeeding)[e]

# THE OFFICE CRISIS

# Case 2: healthy babies with adverse outcome

Late preterm, @36 weeks, is having a rough morning,

1. You ask: “what happened?”
2. You check for any neurologic signs?
3. Where would you manage this baby?
4. What is the risk of bilirubin neurotoxicity?

# Case 2: Assess for risk of bilirubin neurotoxicity

- History and physical exam (neurologic)
- Assess for sub-optimal breastfeeding
- Check Bilirubin level and TB ROR
- Track response to phototherapy
- Quality Measure: timeliness (drill and practice)

# Bilirubin Reduction Strategies

1. **Assess bilirubin risk status**
2. Assess for hemolysis
3. **Promote enteral feeds.**
4. Consider natural resolution with age.
5. Consider use of phototherapy

Exchange transfusion is the last resort but risky.

The American Heart Association/American Stroke Association (AHA/ASA) practice guidelines recommend Intravenous Streptokinase, is recommended for selected patients within 3 hours of ischemic stroke sign/symptom

The AAP practice guidelines recommend Effective Phototherapy is recommended for pateients with severe neonatal hyperbilirubinemia as soon as possible.

# Myth: You can use any light.

1. NO.
2. Specific Blue Light (LED): 476nm.
3. Select dose: 25-35 microwatts/cm$^2$
4. Initial dose for uninterrupted 6 hours

# Other treatments: none proven or harmful

- No Laxatives, Suppositories, Cathartics
- No known medication or chemoprevention
- Role of IVIG. Unproven
- IV fluids. None needed, only if baby is dehydrated
- Direct Sunlight. NO. NO. NO

# BILIRUBIN MINEFIELD

# The “sitting duck” syndrome

- Read AAP “fine print” about G6PD def.
- Know: it occurs in 12.2% of AA male
- Know: for East Asians, Hispanics and Native Americans it is ~5%.
- Know: Caucasian female: 0% incidence; unless, Italian or Greek (Med)
- Concurrent B-UGT immaturity/mutation
- Triggers are in the environment, sepsis, certain foods and drugs (in breast milk).

# Bilirubin Elimination Disorders

- Starvation: sub-optimal breast feeds
- Prematurity: each week of GA
- Illness: Urosepsis, Sepsis, Hypothyroidism, IEM
- UGT immaturity
- UGT mutation (Gilbert's disease)
- UGT defect (partial): Crigler Najjar II
- UGT absence: Crigler Najjar I

# Case 3: When is bilirubin ROR dangerous?

- Unrecognized hemolysis such as Iso-immmunization, G6PD def, inherited RBC defects, etc
- Bilirubin ROR is >0.25 mg/dL/hour or 6 mg/in 24 hours
- Associated factors: Albumin level, Altered bilirubin binding to albumin, appearance of “free bilirubin”. Infant vulnerability.

# MYTH: Exchange Transfusion Cures Kernicterus

- Exchange dramatically lowers bilirubin
- However, underlying process continues
- Bilirubin blood-brain breach not a threshold
- Breach of blood brain barrier: injury continues
- Babies manifest neurotoxicity post-exchange
- Exchange saves life; it is not brain protective.

# SWISS-CHEESE MODEL OF HEALTHCARE

# Where the seams of care are breached

1. Not knowing that the baby is hemolyzing
2. Not knowing the TB ROR
3. Not knowing worrying about prematurity
4. Not letting the baby starve
5. Not scheduling a precise follow-up visit
6. Not recognizing a dire situation in your office.
7. Not referring a distressed baby to ED.
8. Not knowing that photons act immediately
9. No one can rescue you by doing a timely ExTx.
10. Not following up an adverse event.

# Take-home messages for your practice

## KNOW YOUR SYSTEM'S INTEGRITY.

1. Mostly hyperbilirubinemia is benign and responsive
2. Systems-approach can monitor for timeliness
3. Use of effective phototherapy (should be <6%).
4. Remain vigilant for early signs of ABE
5. When needed, team acts urgently for timely interventions

# SUMMARY

- Pre-discharge screening to ensure benign outcome.
- Hyperbilirubinemia is often predictable and can be managed
- Diverse manifestations such that it may be unpredictable.
- Favism (G6PD def.) is often under-predicted.
- Direct re-admission to the NICU is the safest option.
- Most readmitted infants need immediate intervention.

# SUMMARY

- Pre-discharge screening to ensure benign outcome.
- Hyperbilirubinemia is often predictable and can be managed
- Diverse manifestations such that it may be unpredictable.
- Favism (G6PD def.) is often under-predicted.
- Direct re-admission to the NICU is the safest option.
- Most readmitted infants need immediate intervention.

PHOTOTHERAPY DELIVERS PHOTONS THAT HAVE IMMEDIATE EFFECT

# Thank You!

You may contact me at bhutani@stanford.edu

if you have any answered questions about bilirubin.

# References


- 1. AAP 2004. Guidelines. Systems Approach
- 2. AAP 2009. Clarifications (Follow-up)
- 3. AAP TECHNICAL REPORT for phototherapy (2011)
- 4. NEOREVIEW (2012). Neonatal G6PD deficiency
- 5. Cloherty and Stark: Manual of Neonatal Care (2017). Chapter 26
- 6. UPTODATE, Inc (2021). Current evidence.