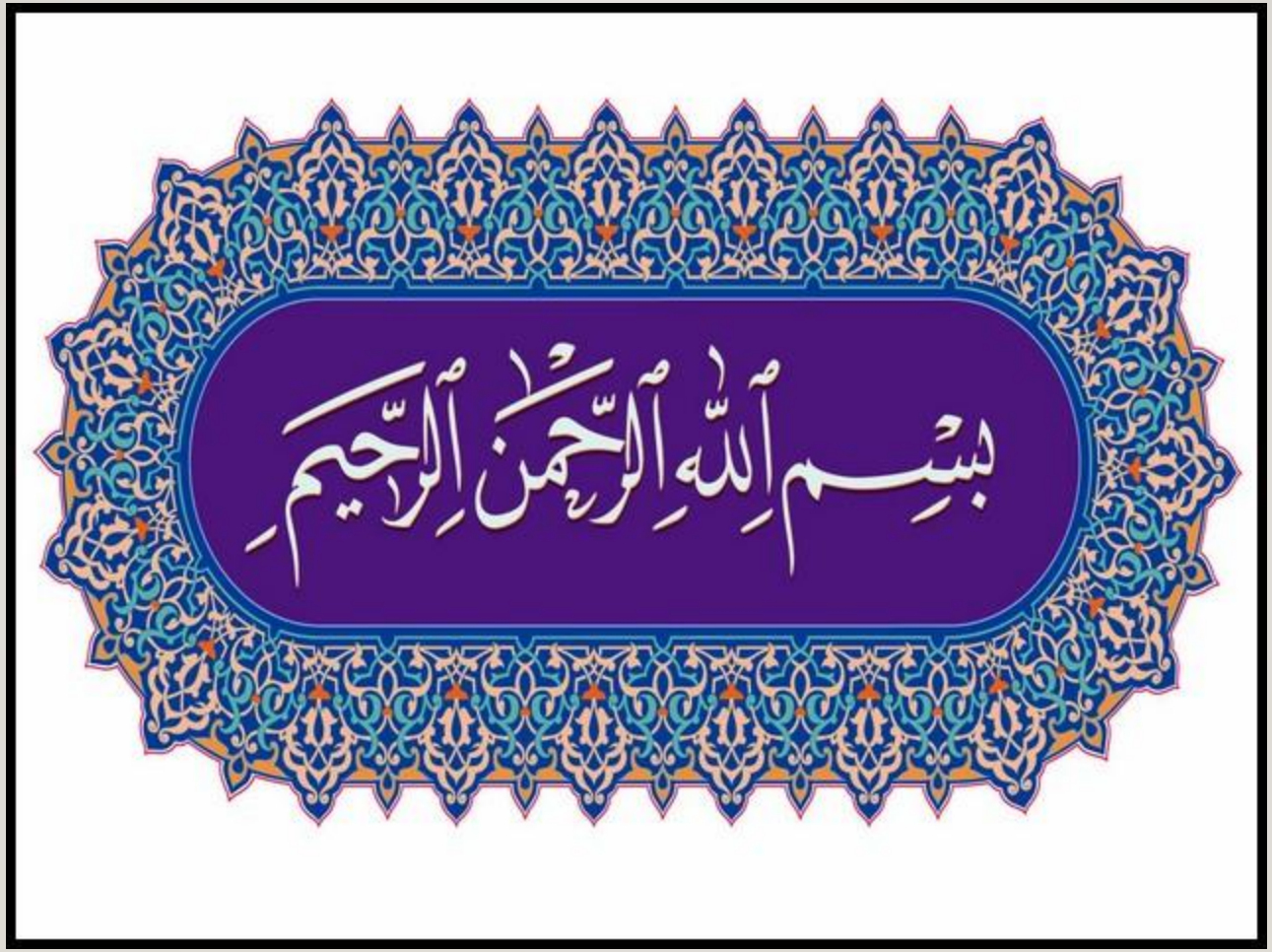
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چالش های زردی نوزادی

NEONATAL JAUNDICE CHALLENGES

- Dr. kh.s. Najib
  - Neonatologist
  - Associate professor of SUMS

CASE 1

- نوزادی ترم (سی و نه هفته)با وزن تولد ۳۱۰۰ در۱۶ ساعت اول تولد بیلی روبین ۸ دارد. حال عمومی خوب و در معاینه نرمال است.چه اقدامی انجام می دهید؟

الف-بدون ریسک فاکتور نوروتوکسیک

ب - با ریسک فاکتور نورو توکسیک

CASE 2

- نوزادی در ۳۰ ساعت بعد از تولد هنگام ترخیص از بیمارستان بیلی روبین ۸ دارد که تا آستانه شروع فوتو بر اساس منحنی مربوطه ۵ واحد کمتر است . توصیه شما برای پیگیری چیست؟

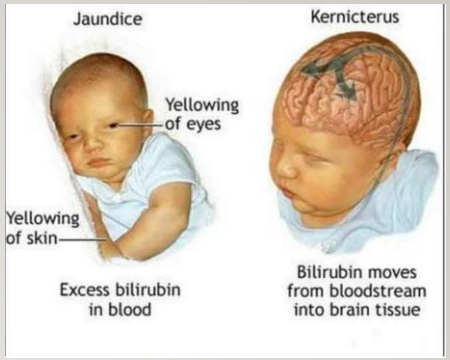
CASE 3

- نوزادی چهار روزه به علت زردی با بیلی روبین ۲۰مراجعه کرده است که بر اساس سن حاملگی و ریسک فاکتورها عدد تعویض خون ۲۲ دارد. چه اقداماتی باید فورا انجام گردد؟

CASE 4

- نوزاد ۵ روزه، ۳۷ هفته به علت زردی (TCB=13) مراجعه کرده است معاینه فیزیکی نرمال می باشد. اقدام بعدی کدام است؟

DEFINITIONS



- **Benign neonatal hyperbilirubinemia** is a transient and normal increase in bilirubin levels occurring in nearly all newborn infants. It has also been referred to as "physiologic" jaundice.
- **Severe neonatal hyperbilirubinemia** is defined as a total serum or plasma bilirubin (TSB) >25 mg/dL. It is associated with an increased risk for developing bilirubin-induced neurotoxicity.

DEFINITIONS

- **Extreme neonatal hyperbilirubinemia** is defined as a TSB >30 mg/dL. It is associated with a higher risk for developing bilirubin-induced neurologic dysfunction (BIND).
- **Bilirubin-induced neurologic disorders** **(BIND)** result from selective brain damage from free (unbound) bilirubin crossing the blood-brain barrier and binding to brain tissue

PEAK TSB

- TSB levels peak at 48 to 96 hours of age, though in newborns of East Asian ancestry, the peak typically occurs between 72 and 120 hours of age.

- Mean peak TSB values typically range from 8 to 14 mg/dL. The 95 percentile is approximately 18 mg/dL

Total serum or plasma bilirubin

- **Total serum or plasma bilirubin (TSB)** — TSB can be measured in the laboratory or with a point-of-care analyzer.
- Both methods can be performed on small-volume blood samples (≤0.3 mL), which are obtainable via a heel-stick.

Transcutaneous bilirubin
ACCURACY

- **Device used**
- **Skin pigmentation**

TcB generally overestimates TSB in newborns with darker skin pigmentation and underestimates TSB in newborns with lighter pigmented skin

- **Exposure to sunlight or phototherapy**

WHEN TO CONFIRM WITH TSB

TcB measurements should be confirmed with TSB measurements in the following situations :

- When therapeutic interventions are being considered (phototherapy or exchange transfusion); however phototherapy can be initiated while awaiting confirmatory TSB results.
- If TcB is within **3 mg/dL** of the **phototherapy threshold**
- If TcB is **>15 mg**/dL .
- If the TcB device displays an "error" message or if there is any question regarding the validity of the TcB measurement.

OTHER METHODS

- **Color comparison charts and plastic ictometers** – In resource-limited settings, color comparison charts or rulers (ictometers) are a low-cost alternative to TcB
- **Smart phone applications** – There are a growing number of direct-to-consumer applications that have been developed for smart phones and other devices to assess newborn jaundice.
- Most of these applications assess how yellow the newborn's sclerae or skin are using the smart phone's digital camera.
- Further validation of these devices is needed before they can be recommended for routine use.

Published online 2019 February 2. Research Article

Detection of Neonatal Jaundice by Using an Android OS-Based Smartphone Application

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Abstract

Background: Neonatal jaundice resulting from raised blood bilirubin levels is one of the most common clinical conditions that needs medical attention. To initiate appropriate management that can both prevent and treat severe neonatal jaundice, screening methods that measure bilirubin level are warranted.
Methods: In this study, we present an Android OS-based application for detecting neonatal jaundice. We used the application to detect jaundice in 113 neonates. Our smartphone-based estimation of bilirubin levels depends on a smartphone, a color calibration card, and a 100X zoom microscope clip. Our application was designed to acquire images of the newborn's forehead skin in a standardized manner, estimate the average R, G, B scores of the images that have been taken from the forehead skin and calibration card, and then convert them to hue, saturation, intensity (HSI) parameters. All these are performed offline; in this application, we used offline machine learning and regression techniques for analysis
Results: Our smartphone-based estimation of bilirubin levels had a sensitivity of 68% and specificity of 92.3% for estimating the bilirubin levels of less than 10 mg/dL and sensitivity of 82.1% and specificity of 100% for estimating the bilirubin levels of less than 15 mg/dL. Our application-based estimation of bilirubin levels had the correlation of 0.479 with the total serum bilirubin values.
Conclusions: Our results suggest that our smartphone-based application can serve as a promising screening tool for neonatal jaundice, and it can aid in determining neonates requiring a blood draw for measuring total serum bilirubin level.

Keywords: Neonatal Jaundice, Machine Learning, Bilirubin, Screening, Smartphone, Image Processing

MANAGEMENT GOALS

- The goals of managing neonatal hyperbilirubinemia are to prevent severe hyperbilirubinemia and bilirubin-induced neurologic disorders (BIND) while avoiding unnecessary intervention which can interfere with successful initiation of breastfeeding and parent/caregiver bonding with the newborn

SUPPORTIVE CARE

- Newborns with hyperbilirubinemia should receive adequate nutritionand oral hydration since this enhances bilirubin elimination
- For breastfed infants with inadequate intake, excessive weight loss (>10 percent of BW), and/or who evidence of hypovolemia, supplemental feeds should be provided with human milk, either expressed maternal milk (preferred) or pasteurized donor milk

INTRAVENOUS HYDRATION

- Most newborns with hyperbilirubinemia do **not** require IV hydration since oral feeding with or without supplementation generally provides adequate hydration.
- However, for newborns with dehydration, hypovolemia, and/or hypernatremia due to inadequate oral intake, IV hydration may be necessary.
- In addition, we suggest IV hydration for newborns who require an escalated level of care (ie, those who have TSB levels at or approaching the threshold for exchange transfusion), as discussed separately.

INTRAVENOUS HYDRATION

- Initial correction of hypovolemia consists of a 10 to 20 mL/kg bolus of isotonic fluids (eg, **normal saline**).
- If required, ongoing IV hydration consists of crystalloid fluid (typically 10 percent dextrose with one-quarter normal saline) at a maintenance rate (ie, 60 to 80 mL/kg per day for newborns <48 hours old; 80 to 100 mL/kg per day for those ≥48 hours old).
- Subsequent adjustments are based on measurement of serum electrolytes.

THRESHOLDS FOR TREATMENT
SYMPTOMATIC PATIENTS

- Newborns with elevated total serum or plasma bilirubin (TSB) levels in association with signs of acute bilirubin encephalopathy (ABE) generally require escalation of care and exchange transfusion. Signs and symptoms of ABE include lethargy, hyper- or hypotonia, poor suck, high-pitched cry, recurrent apnea, opisthotonos, retrocollis, seizures .

- Symptomatic newborns require escalation of care even if the TSB level is not above the threshold for exchange transfusion. Phototherapy should be provided while preparations are made to perform exchange transfusion.

THRESHOLDS FOR TREATMENT
SYMPTOMATIC PATIENTS

- In newborns with signs of encephalopathy in the setting of TSB levels that are well below the treatment threshold, other etiologies should also be considered sepsis, hypoglycemia).
- ABE is unusual at TSB levels <20 mg/dL ; most reported cases of ABE have occurred at TSB levels ≥30 mg/dL
- Thus, neurologic abnormalities (lethargy, poor tone, seizures, apnea) in a newborn with TSB <20 mg/dL are more likely to becaused by other conditions rather than ABE.

THRESHOLDS FOR TREATMENT
ASYMPTOMATIC PATIENTS

- **TSB at or above treatment threshold**
- **TSB near threshold** – Newborns with TSB levels that are <2 mg/dL below the phototherapy threshold are at high risk of subsequently needing treatment
- We suggest initiating phototherapy early (ie, at near-threshold TSB values rather than waiting for TSB to cross the treatment threshold) if the newborn has any of the following:

➢ Early-onset jaundice (within first 24 hours after birth)

➢ Alloimmune hemolytic disease or other hemolytic process

➢ Rapidly rising bilirubin levels (ie, increasing by ≥0.3 mg/dL per hour in the first 24 hours or ≥0.2 mg/dL per hour thereafter)

➢ Significant bruising or cephalohematoma

THRESHOLDS FOR TREATMENT

ASYMPTOMATIC PATIENTS

- For newborns with near-threshold TSB levels without any of these risk factors, treatment should be individualized depending on parent/caregiver preference.
- The use of subthreshold phototherapy in this setting may reduce the risk of readmission, but could also result in unnecessary exposure to phototherapy, impede newborn-parent/caregiver bonding, and prolong birth hospitalization.
- Home phototherapy is an option for some newborns with near-threshold TSB levels if there are no clinical risk factors and additional criteria are met.

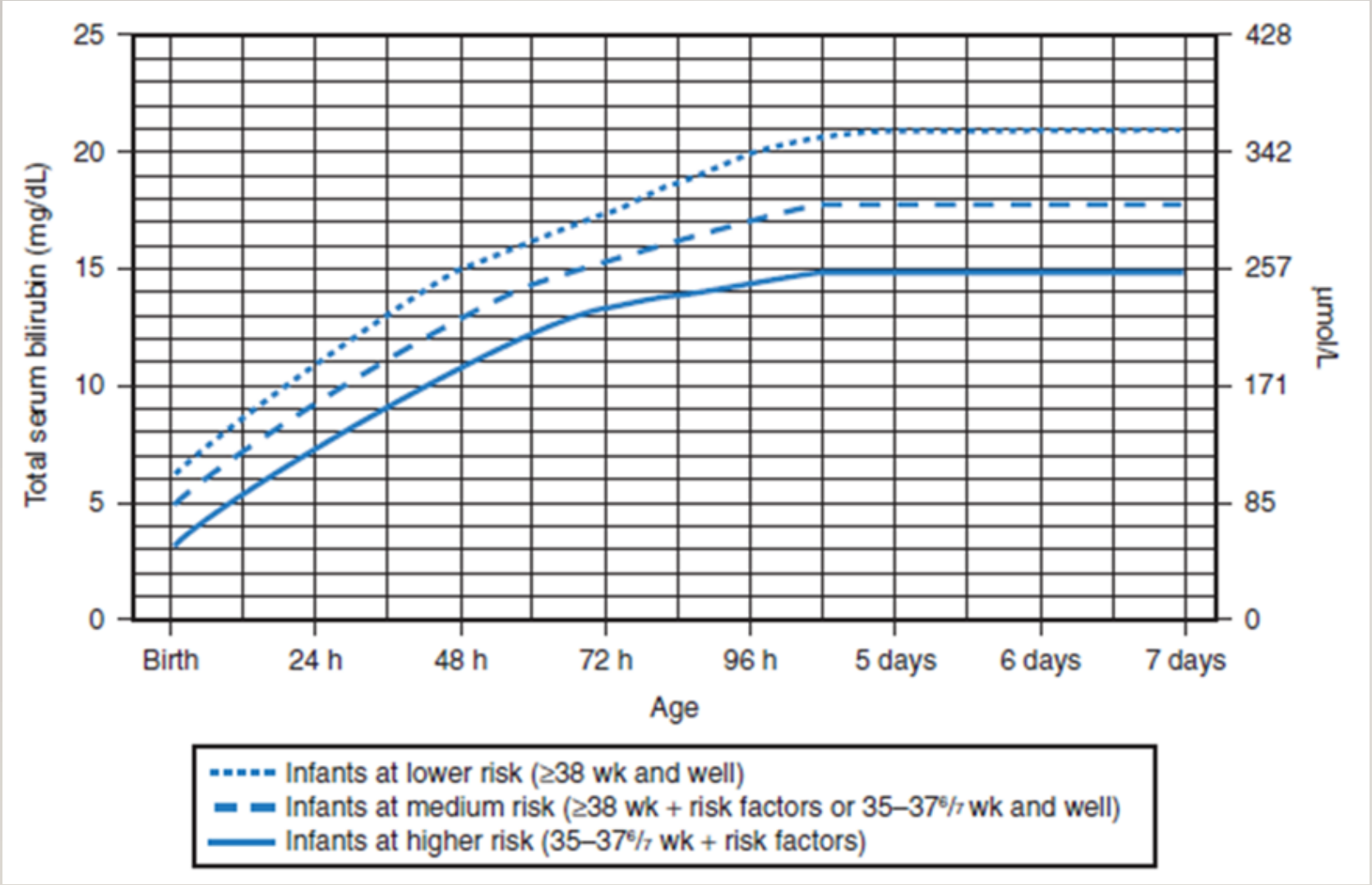
NEUROTOXICITY RISK FACTORS

- Gestational age<38 weeks (this risk increases with the degree of prematurity)
- Serum Albumin less than 3 gr
- Isoimmune hemolytic anemia, G6PD deficiency or other hemolytic disease
- Sepsis
- Significant clinical instability in the previous 24 hours

NEUROTOXICITY RISK FACTORS

- Although there were insufficient data for the committee to recommend measuring the albumin concentration of all newborn infants,

- measuring albumin is recommended as part of escalation of care.


Total serum bilirubin (mg/dL)
25
20
15
10
5
0
428
342
257
171
85
0
μmol/L
Birth
24 h
48 h
72 h
96 h
5 days
6 days
7 days
Age
Infants at lower risk (≥38 wk and well)
Infants at medium risk (≥38 wk + risk factors or 35–37⁶/₇ wk and well)
Infants at higher risk (35–37⁶/₇ wk + risk factors)

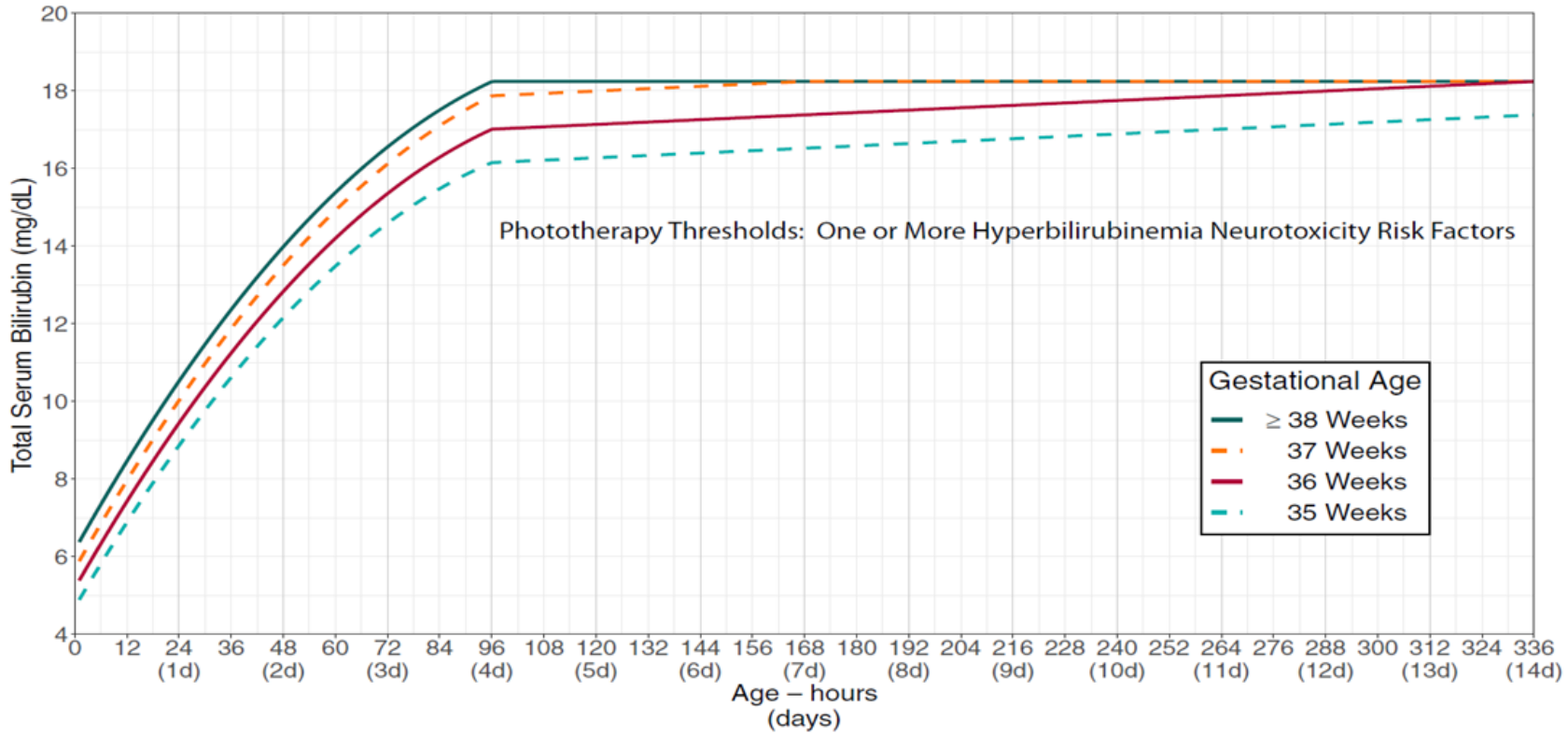
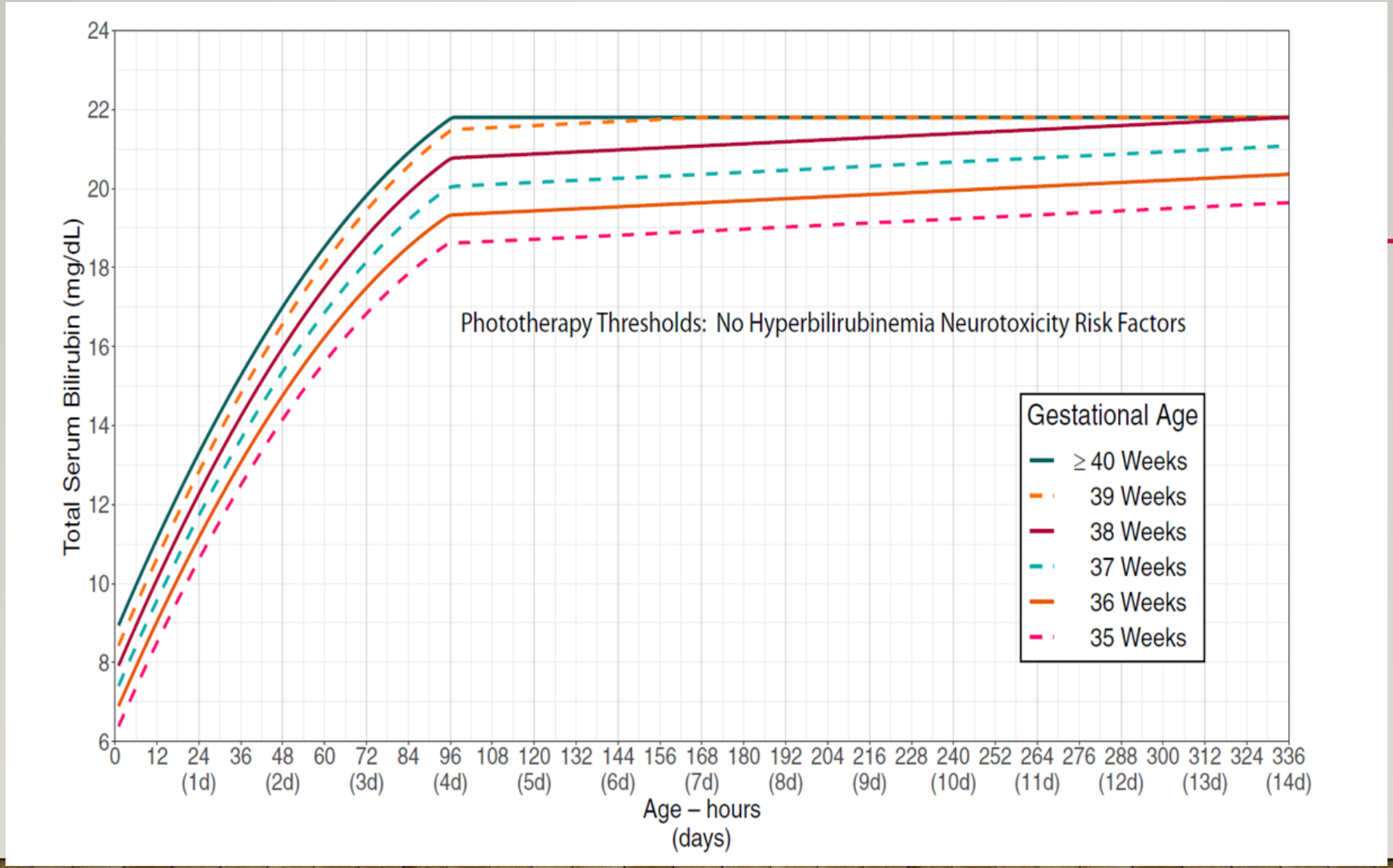
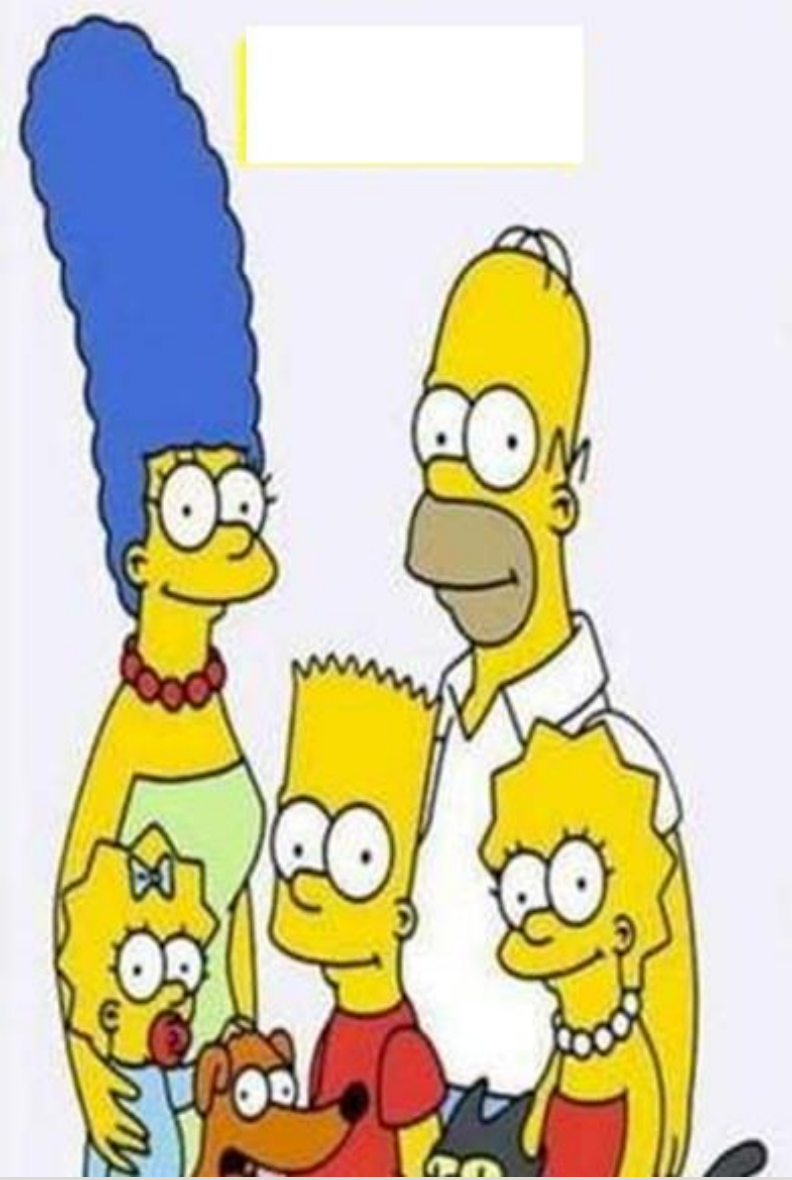


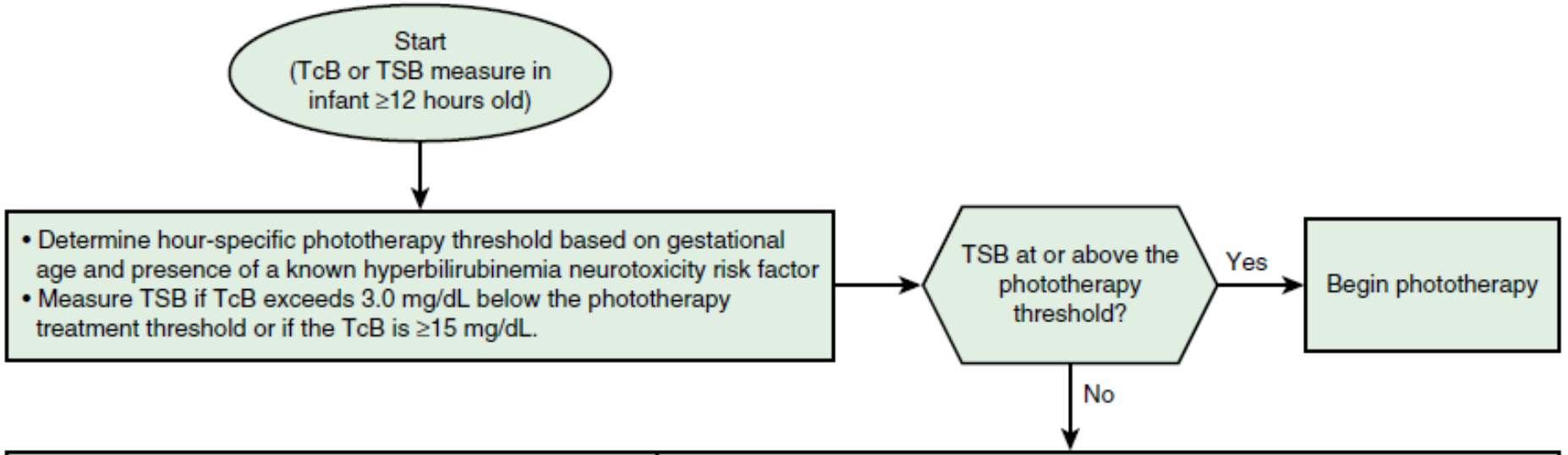
FIGURE 3

Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract the direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 2.

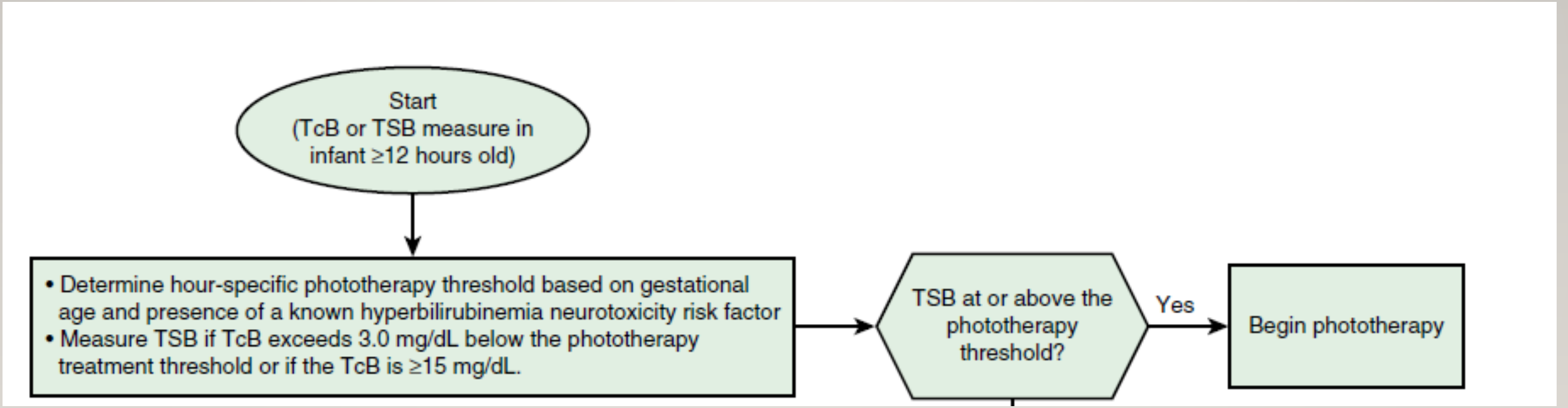

Phototherapy Thresholds: No Hyperbilirubinemia Neurotoxicity Risk Factors
Total Serum Bilirubin (mg/dL)
24
22
20
18
16
14
12
10
8
6
Gestational Age
≥ 40 Weeks
39 Weeks
38 Weeks
37 Weeks
36 Weeks
35 Weeks
0 12 24 (1d) 36 48 (2d) 60 72 (3d) 84 96 (4d) 108 120 (5d) 132 144 (6d) 156 168 (7d) 180 192 (8d) 204 216 (9d) 228 240 (10d) 252 264 (11d) 276 288 (12d) 300 312 (13d) 324 336 (14d)
Age – hours
(days)

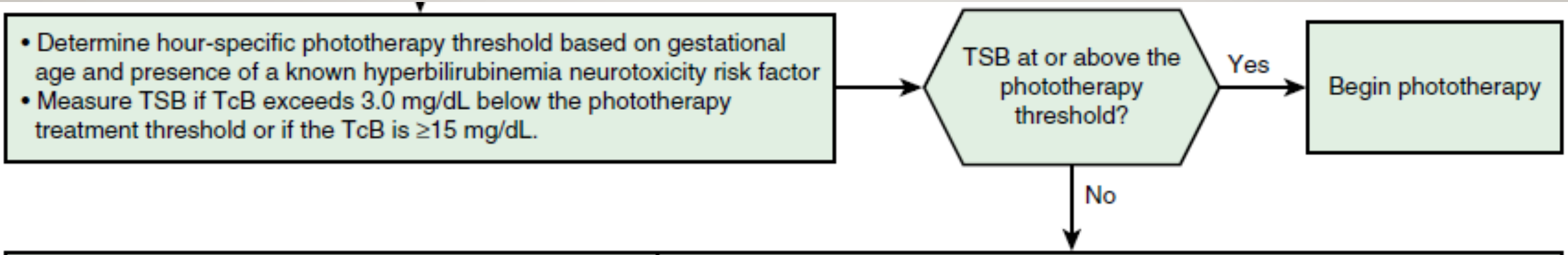


SCREENING



Phototherapy threshold minus TcB or TSDB		Discharge recommendations
0.1-1.9 mg/dL	Age <24 hours	Delay discharge, consider phototherapy, measure TSB in 4 to 8 hours
	Age ≥24 hours	Measure TSB in 4 to 24 hours[a] Options: • Delay discharge and consider phototherapy • Discharge with home phototherapy if all considerations in the guideline are met • Discharge without phototherapy but with close follow-up
2.0-3.4 mg/dL	Regardless of age or discharge time	TSB or TcB in 4 to 24 hours[a]
3.5-5.4 mg/dL	Regardless of age or discharge time	TSB or TcB in 1-2 days
5.5-6.9 mg/dL	Discharging <72 hours	Follow-up within 2 days; TcB or TSB according to clinical judgment[b]
	Discharging ≥72 hours	Clinical judgment[b]
≥7.0 mg/dL	Discharging <72 hours	Follow-up within 3 days; TcB or TSB according to clinical judgment[b]
	Discharging ≥72 hours	Clinical judgment[b]


Start
(TcB or TSB measure in infant ≥12 hours old)
• Determine hour-specific phototherapy threshold based on gestational age and presence of a known hyperbilirubinemia neurotoxicity risk factor
• Measure TSB if TcB exceeds 3.0 mg/dL below the phototherapy treatment threshold or if the TcB is ≥15 mg/dL.
TSB at or above the phototherapy threshold?
Yes
Begin phototherapy



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5.5-6.9 mg/dL	Discharging <72 hours	Follow-up within 2 days; TcB or TSB according to clinical judgment[b]
	Discharging ≥72 hours	Clinical judgment[b]
≥7.0 mg/dL	Discharging <72 hours	Follow-up within 3 days; TcB or TSB according to clinical judgment[b]
	Discharging ≥72 hours	Clinical judgment[b]

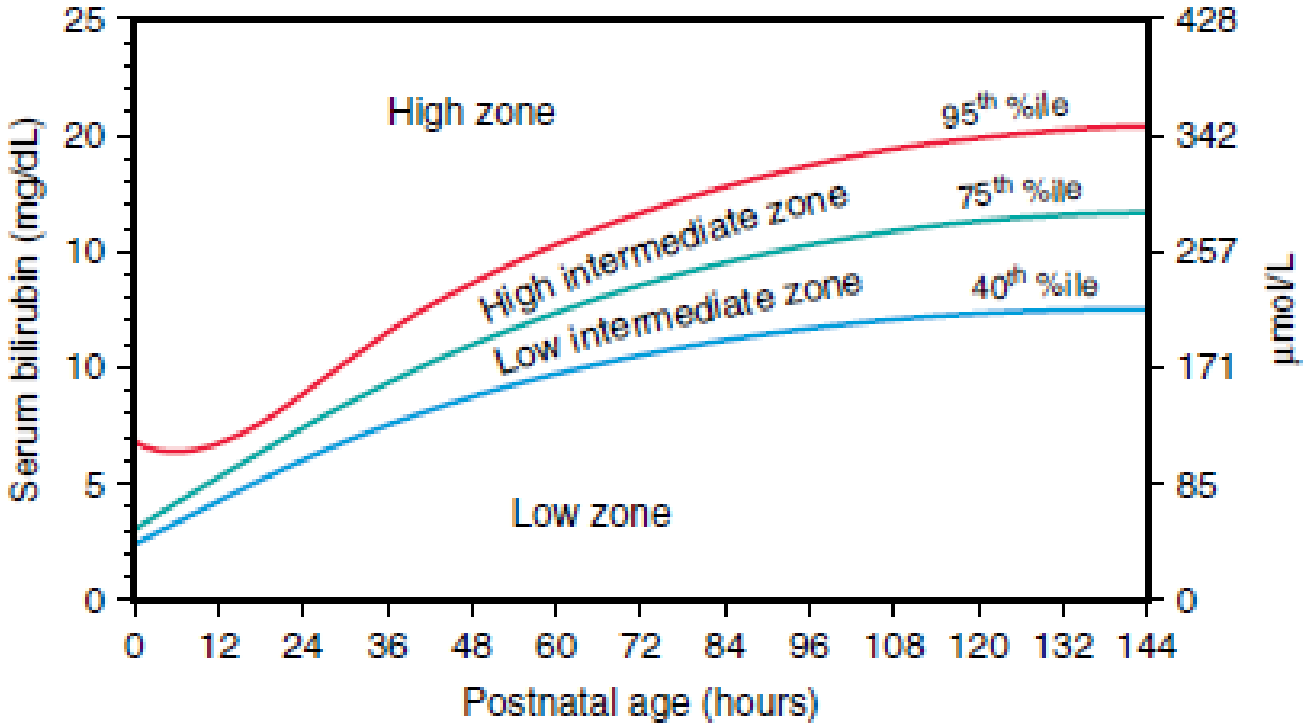


Fig. 137.3 Neonatal bilirubin nomogram. Percentile designation of well newborns ≥35 weeks' gestational age based on their hour-specific serum bilirubin values. The high zone is subdivided by the 95th percentile track. The intermediate zone is subdivided into upper and lower zones by the 75th percentile track. The low zone has been electively and statistically defined by the 40th percentile track. *(Modified from Bahr TM, Henry E, Christensen RD, et al. A new hour-specific serum bilirubin nomogram for neonates ≥35 weeks of gestation. J Pediatr. 2021;236:28–33. Fig. 2.)*

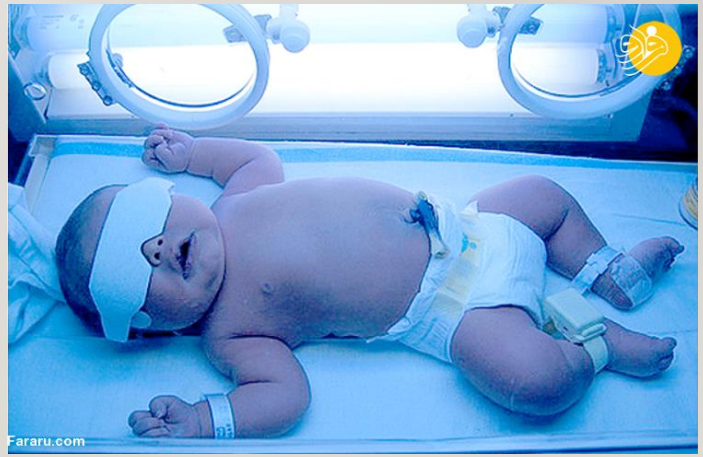
ADMINISTRATION TECHNIQUE

- Historically, the term "intensive phototherapy" was used for phototherapy applied with an irradiance of at least 30 microW/cm /nm, whereas the terms "standard" or "conventional" phototherapy were used for phototherapy applied at a lower irradiance.

- However, intensive phototherapy is now the standard of care and we no longer make a distinction between "intensive" versus "standard" phototherapy.

ADMINISTRATION TECHNIQUE

- **Positioning the newborn** – When initiating phototherapy, the newborn should be placed **supine**, with body exposed and the area covered by the diaper minimized (for hygiene only), and eyes shielded with an opaque orbital shield.
- Care should be taken to prevent the shield from covering the nose or sliding off the orbits.



ADMINISTRATION TECHNIQUE

- **Deliver phototherapy from above and below** – Light should be delivered to as much of an infant's skin as possible with a combination of light sources both above and below the newborn

ADMINISTRATION TECHNIQUE

- **Minimize interruptions** – Interruptions to phototherapy should be minimized.

- For newborns with TSB <20 mg/dL, phototherapy can be interrupted intermittently for feeding and/or parent/caregiver holding.

- For newborns with TSB ≥20 mg/dL, phototherapy should be administered continuously, without interruptions for parent/caregiver holding or during feeding (ie, newborns should be fed with a bottle while under phototherapy)until the TSB falls below this level.

ADMINISTRATION TECHNIQUE

- **Irradiance** – Effective phototherapy requires an irradiance of at least 30 microW/cm/nm with light at a blue to blue-green wavelength (460 to 490 nm; optimal at 478 nm).

- This is ideally provided with a narrow-spectrum blue light-emitting diode (LED) light

ADVERSE EFFECTS

ADVERSE EFFECTS

- **Short-term effects:** Modern-day phototherapy devices using blue LED lights generate minimal heat and do not emit UV light. They are generally safe and well tolerated. They are less likely to cause short-term adverse effects (eg, rashes, hyperthermia, fluid losses) compared with older phototherapy devices that used fluorescent or halogen lights

1. **Interruption of breastfeeding**
2. **Bronze baby syndrome**

ADVERSE EFFECTS

- **Potential long-term effects** — It remains uncertain whether neonatal phototherapy is associated with any long-term sequelae when used appropriately.

1. Seizures – Phototherapy in newborns appears to be associated with a small increased risk of neonatal and childhood seizures, particularly in boys
2. Childhood cancer
3. Skin manifestations
4. Unproven retinal effects
5. No effect on childhood asthma and allergic diseases
6. No effect on food allergies

RESPONSE TO TREATMENT

- Measurements using transcutaneous bilirubin (TcB) devices are **not** reliable in patients undergoing phototherapy and should not be used in this setting

- **Expected response** — Effective phototherapy results in a decline of TSB of at least 2 to 3 mg/dLwithin 4 to 6 hours. A decrease in TSB can be detected as early as 2 hours after initiating treatment. 24 hours of phototherapy can effectively reduce TSB levels by 25 to 40 percent

DISCONTINUING PHOTOTHERAPY

- The timing of phototherapy discontinuation depends on the newborn's TSB level and risk of developing rebound hyperbilirubinemia

- For newborns without rebound risk factors, we generally discontinue phototherapy when the TSB is ≥2 mg/dL below the phototherapy threshold at the time of phototherapy initiation.
- For newborns with risk factors for rebound, a longer period of phototherapy may be warranted. In these newborns, we typically discontinue phototherapy when TSB is<12 mg/dL.

SUBSEQUENT MANAGEMENT

- If TSB levels have effectively declined, subsequent TSB measurements can be obtained every 8 to 12 hours. Feeding and holding by the parents/caregivers can be reinstated if they had been stopped.
- If TSB levels have declined less than expected, phototherapy administration should be verified and adjusted accordingly.
- If TSB levels are close to (ie, <2 mg/dL below) or at the exchange transfusion threshold, care should be escalated

DE-ESCALATING THERAPY

- Rebound hyperbilirubinemia is defined as a total serum or plasmabilirubin (TSB) level that reaches the phototherapy threshold within 72 to 96 hours of stopping phototherapy.

DE-ESCALATING THERAPY

Risk factors for rebound hyperbilirubinemia include:

- Gestational age (GA) <38 weeks.
- Early need for phototherapy (within 48 hours after birth).
- Hemolytic diseases (eg, alloimmune hemolytic disease, glucose-6-phosphatedehydrogenase [G6PD] deficiency). Infants with alloimmune hemolytic disease may have prolonged hemolysis
- TSB level close to the phototherapy threshold at the time of discontinuation.

FOLLOW-UP TESTING

- Measurements performed within 24 hours of stopping phototherapy should be performed with TSB and **not** transcutaneous bilirubin (TcB) since TcB is not reliable in newborns recently exposed to phototherapy.
- After 24 hours, either method is acceptable

FOLLOW-UP TESTING

- For newborns with risk factors for rebound, TSB should be checked within 6 to12 hours of discontinuing phototherapy. Discharge should not occur until the TSB result is obtained.

- A subsequent bilirubin level (either measured by TSB or TcB) should be obtained **one day after stopping phototherapy**; this can be performed in the hospital or outpatient setting.

- For all other newborns, a follow-up bilirubin level should be obtained the day after stopping phototherapy.

Home phototherapy

HOME PHOTOTHERAPY

- Home phototherapy is less disruptive to the family and is an optionfor discharged newborns with TSB levels near the **TSB** threshold for phototherapy (ie, <2 mg/dL below to ≤1 mg/dL above the threshold)
- We use home phototherapy only if **all** of the following conditions are met:

HOME PHOTOTHERAPY

- Gestational age ≥38 weeks
- ≥48 hours postnatal age
- Clinically well with adequate feeding
- No known hyperbilirubinemia neurotoxicity risk factors
- No previous phototherapy
- TSB ≤1 mg/dL above the phototherapy treatment threshold
- An LED-based phototherapy device can be available in the home immediately
- TSB can be measured daily

HOME PHOTOTHERAPY

- Newborns receiving home phototherapy should have TSB levels checked daily. If the TSB increases or is >1mg/dL above phototherapy threshold, the infant should be admitted for inpatient phototherapy.
- Home phototherapy should **not** be used in newborns with any clinical risk factors for severe or progressive hyperbilirubinemia, especially hemolytic disease. Its efficacy and safety in this setting remain unproven

ESCALATING THERAPY

- **Newborns with any of the following require escalation of care :**

➢Signs of acute bilirubin encephalopathy (ie, lethargy, hyper- or hypotonia, poor suck, high-pitched cry, recurrent apnea, opisthotonos, retrocollis, seizures).

➢Rapidly rising total serum or plasma bilirubin (TSB) levels (ie, increasing by ≥0.3 mg/dL per hour in the first 24 hours or ≥0.2 mg/dL per hour there after) despite intensive phototherapy.

➢TSB levels that are within 2 mg/dL of the exchange transfusion threshold

IVIG

- Intravenous immune globulin (IVIG; 0.5 to 1 g/kg) over 2 hours may be provided to infants with isoimmune hemolytic disease (ie, positive DAT) whose TSB reaches or exceeds escalation of care threshold. The dose can be repeated in 12 hours.

BILIRUBIN TO ALBUMIN RATIO

The bilirubin to albumin ratio can be used in conjunction with the TSB level in determining the need for exchange transfusion.

BILIRUBIN TO ALBUMIN RATIO

- In addition to the criteria described above, an exchange transfusion may be considered if the bilirubin to albumin ratio is:

➢ >=8.0 if the gestational age is >=38 weeks' gestation and there are no hyperbilirubinemia neurotoxicity risk factors, or

➢ >=7.2 if the gestational age is >=38 weeks' gestation and there is at least 1 hyperbilirubinemia neurotoxicity risk factor, or

➢ >=7.2 if the gestational age is 35 through 37 weeks' gestation with no hyperbilirubinemia neurotoxicity risk factor, or

➢ >=6.8 if the gestational age is 35 through 37 weeks' gestation and at least 1 hyperbilirubinemia neurotoxicity risk factor.

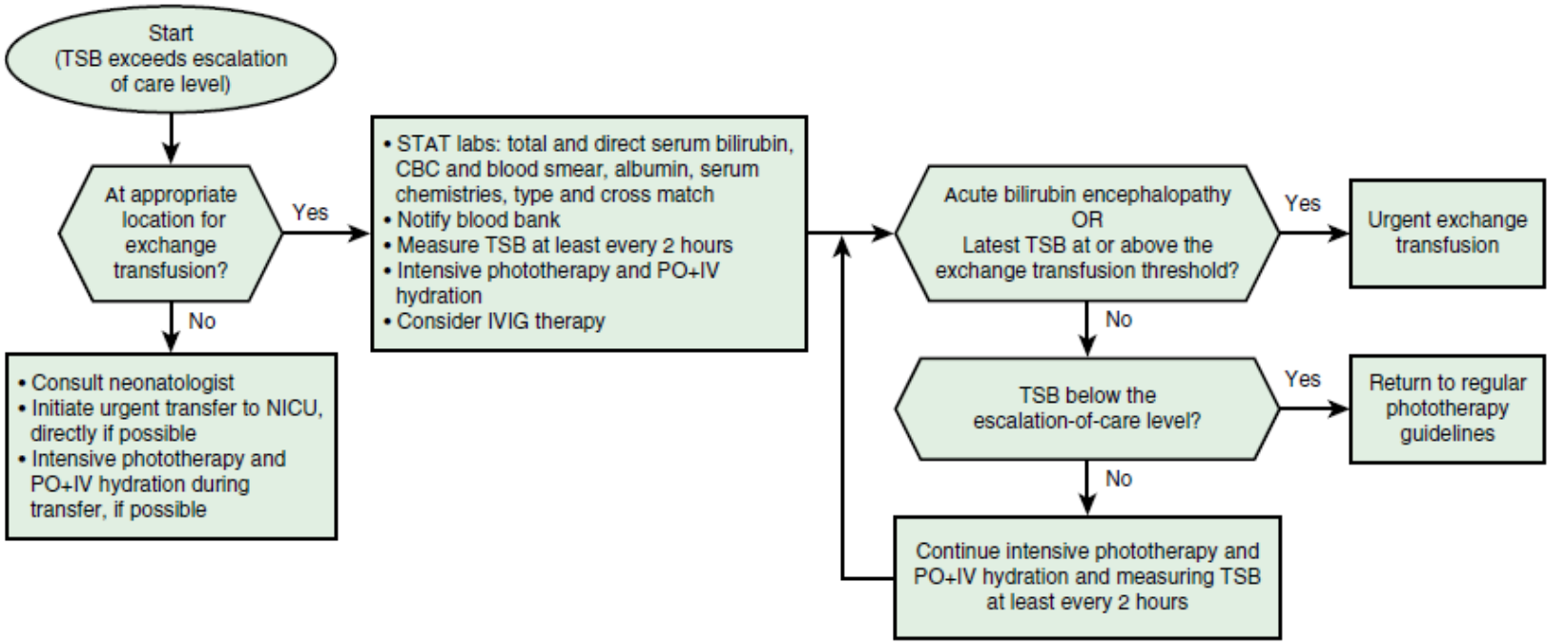


Fig. 137.8 Approach to escalation of care. The escalation-of-care threshold is 2 mg/dL below the exchange transfusion threshold. IVIG, Intravenous immunoglobulin; NICU, neonatal intensive care unit; PO, orally; TSB, total serum bilirubin. *(Modified from Kemper AR, Newman TB, Slaughter JL, et al. Clinical practice guideline revision: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2022;150[3]:e2022058859. Fig. 4.)*

Start
(TSB exceeds escalation of care level)

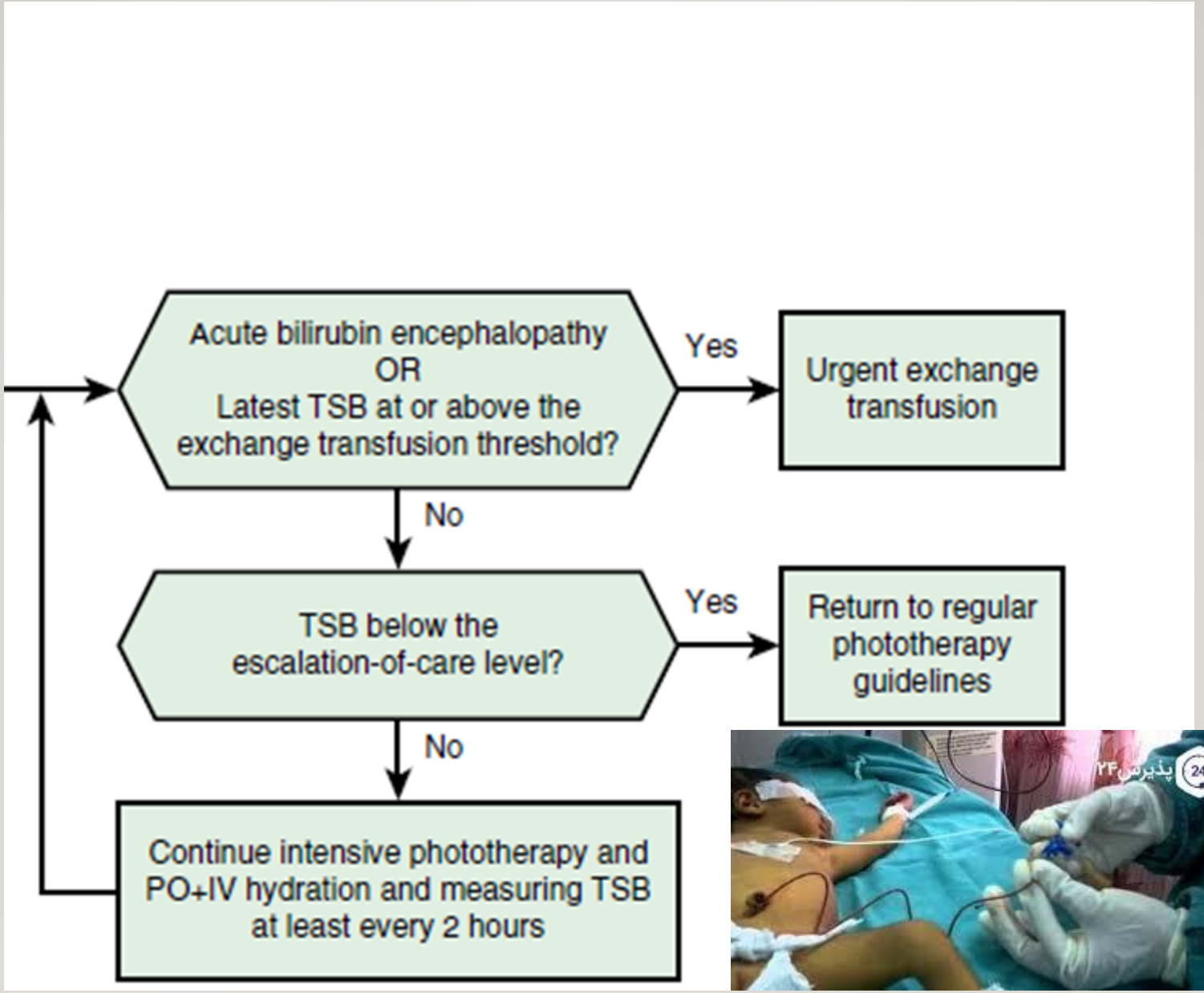
At appropriate location for exchange transfusion?

Yes

- STAT labs: total and direct serum bilirubin, CBC and blood smear, albumin, serum chemistries, type and cross match
- Notify blood bank
- Measure TSB at least every 2 hours
- Intensive phototherapy and PO+IV hydration
- Consider IVIG therapy

No

- Consult neonatologist
- Initiate urgent transfer to NICU, directly if possible
- Intensive phototherapy and PO+IV hydration during transfer, if possible


Acute bilirubin encephalopathy
OR
Latest TSB at or above the exchange transfusion threshold?
Yes
Urgent exchange transfusion
No
TSB below the escalation-of-care level?
Yes
Return to regular phototherapy guidelines
No
Continue intensive phototherapy and PO+IV hydration and measuring TSB at least every 2 hours

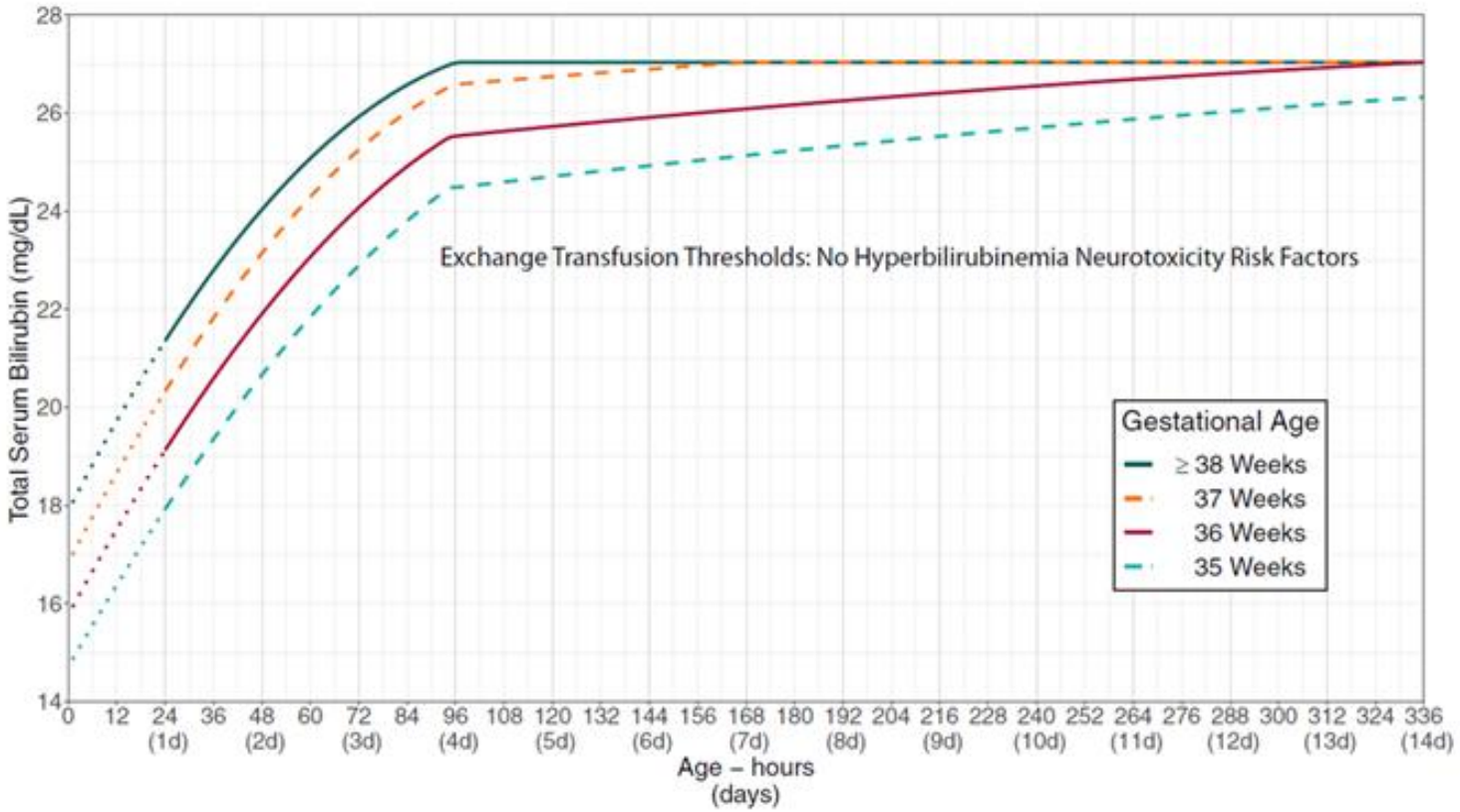


FIGURE 5

Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. See Fig 4, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 4.

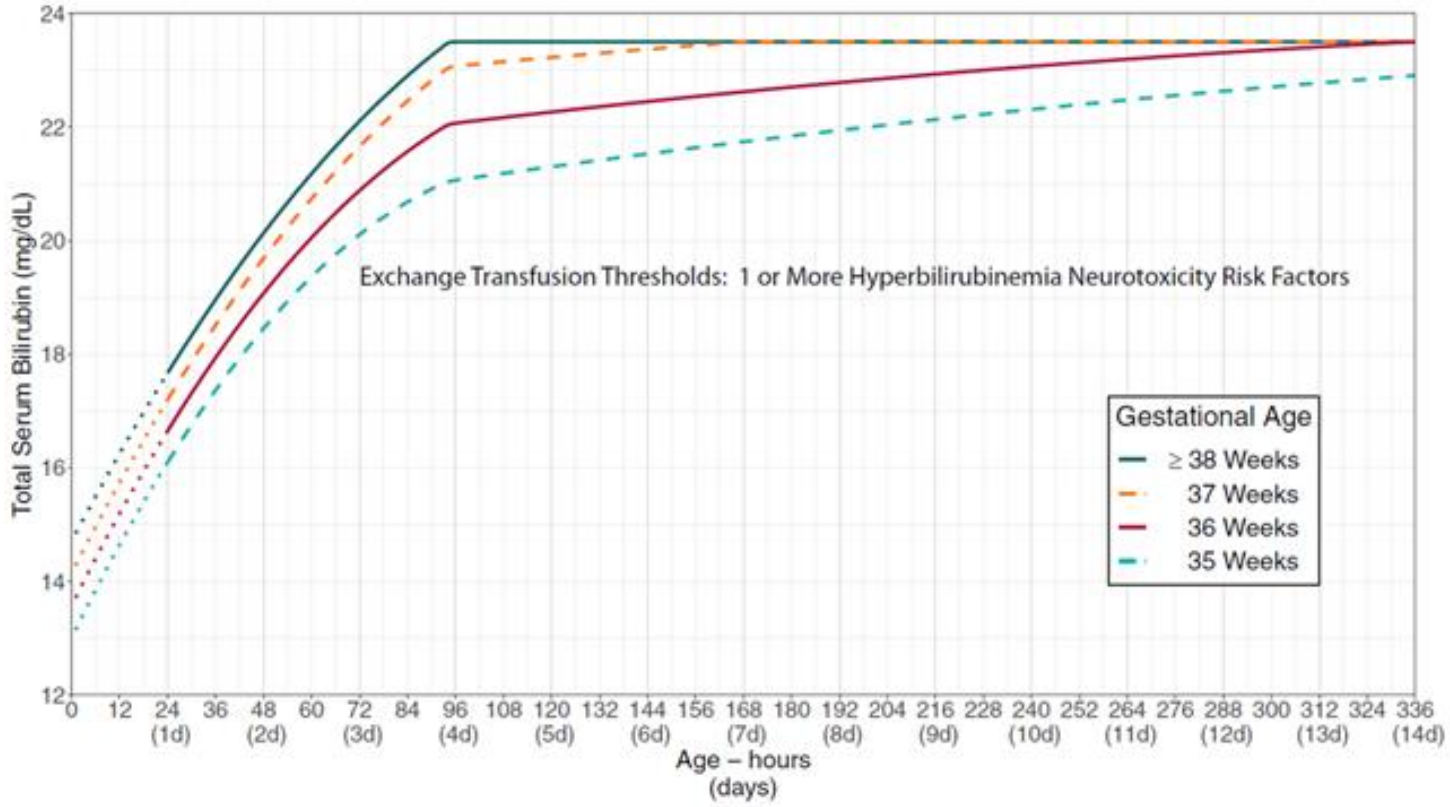


FIGURE 6

Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. See Fig 4, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 5.

Thanks for your attention