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Neonatal Jaundice case presentation

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Objectives:

- Management in birth hospital(Screening)
- Management of outpatient(mild to moderate, prolong jaundice)
- Intervention in hospitalized patients(severe & extreme hyperbilirubinemia)
  - Intensive phototherapy
  - Exchange transfusion

Definition

- **Benign neonatal hyperbilirubinemia:** transient and normal increase in bilirubin levels, referred to "physiologic jaundice.“

- **Significant neonatal hyperbilirubinemia:** in infants ≥35 weeks gestational age (GA) is defined as TB >95 percentile on the hour-specific Bhutani nomogram.

- **Severe neonatal hyperbilirubinemia:** TB >25 mg/dl. Increased risk for developing BIND.

- **Extreme neonatal hyperbilirubinemia:** TB >30 mg/dl. Associated with a significant increased risk of BIND and likelihood of kernicterus.

What we must notice for management of jaundice in birth hospital?

Case I

- It’s Thursday morning, and you are examining a 25-h-old neonate whose parents are anxious to go home.

- The baby is a male, 3kg,GA: 36 2/7weeks. The mother is 36 years old, G2P1A1, B+, and with gestational diabetes.

- The baby has been doing well. he is taking breast milk. The exam is unremarkable except for a caput and ecchymosis on the scalp. The abdomen is soft, and there is no palpable liver or spleen.
- The baby has mild yellowish discoloration of face and sclera.

At this time you

- 1. Order a transcutaneous bilirubin(TcB).
- 2. Order a total serum bilirubin(TSB).
- 3. Discharge the patient with follow-up 48 hour later.
- 4. Place the baby under phototherapy.

Answer: 1 or 2

Transcutaneous bilirubinometry (TcB)

TcB devices use multi wavelength spectral reflectance from the skin surface and can be used to measure or estimate TSB , thus, avoid blood sampling

Limitations of TcB:

- High(TB ≥ 15 mg/dl),TcB underestimated TB level.
- Prior exposure to phototherapy or sunlight.
- Light skin (underestimate) & dark skin(overestimate)

When to confirm with TSB?

A confirmatory TSB should be measured in the following settings:

- When TcB exceeds the 75th percentile on the TSB nomogram .
- When the TcB exceeds the 95th percentile on the TcB nomogram.
- If the TcB is >12.5 mg/dl.
- When therapeutic intervention is being considered. Therapy should be initiated while awaiting confirmatory results.
- TcB is within 3 mg/dL of the phototherapy threshold levels

In this case a TcB was done and was reported as 8.5 mg/dL. You order a serum bilirubin, and results return an hour later. The bilirubin is 7.5 mg/dL.

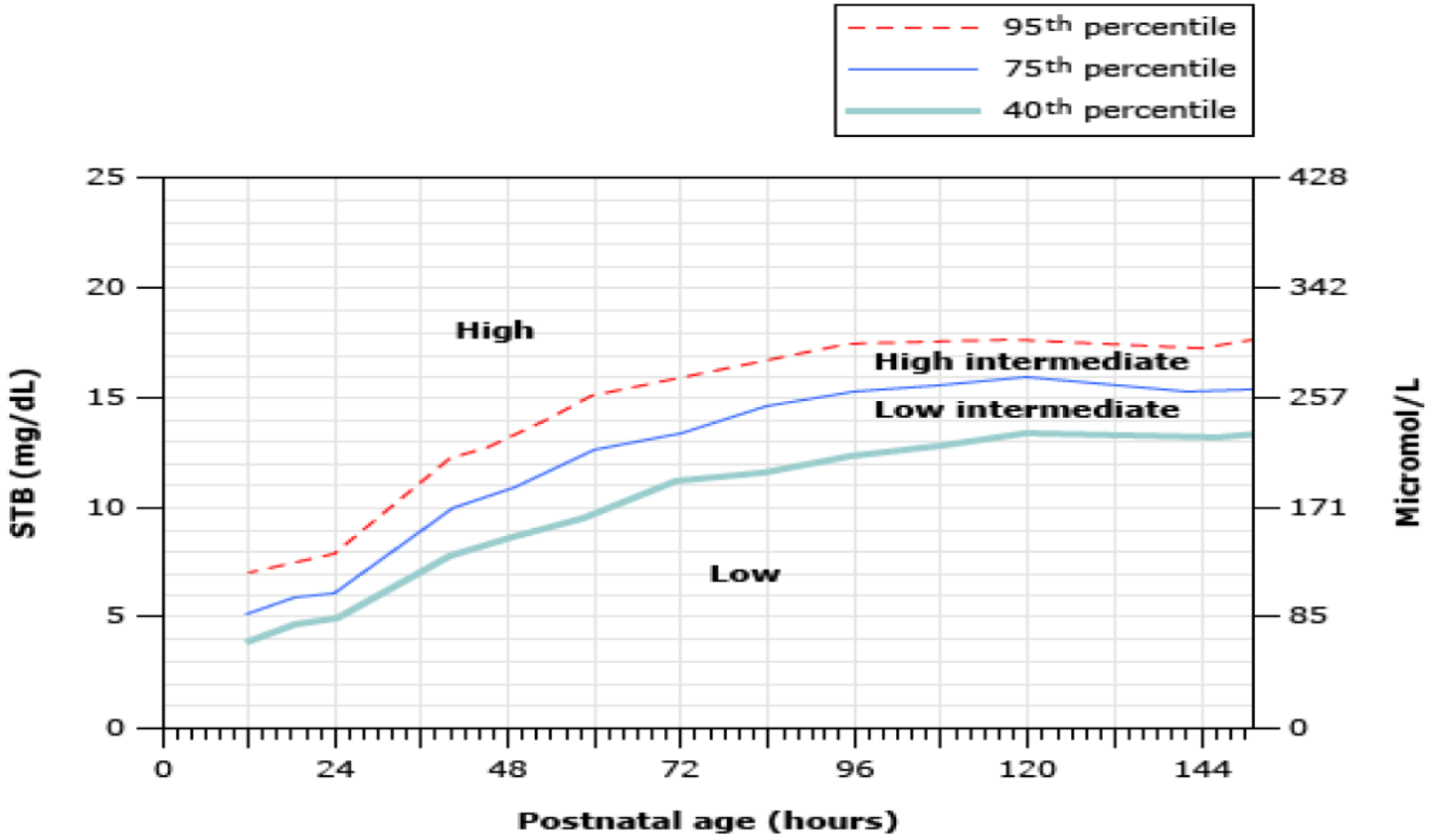
How would you manage this patient?

- 1. Discharge with a follow-up on Saturday(3^{th} postnatal days).
- 2. Discharge and follow up on monday (5^{th} days of life).
- 3. Follow in hospital with further serum bilirubin testing.
- 4. Place under phototherapy.

There are a number of tools available to help make your decision. The first is the Bhutani nomogram for the designation of risk for future hyperbilirubinemia.

The Bhutani nomogram is an indicator of risk and does not determine what treatment a baby should receive. 60% who originally plot out in the high-risk zone will fall below the 95th percentile on future bilirubin measurements.

Universal predischarge screening (Bhutani nomogram)



TSB before discharge	Newborns who developed TSB> 95th percentile (%)
High-risk zone (>95 percentile)	40
High intermediate-risk zone (>75 to < 95 per)	13
Low intermediate-risk zone (≥ 40 to ≤ 75 per)	2.1
Low-risk zone (<40 per)	0

Using the Bhutani nomogram, this baby with a bilirubin of 7.5mg/dL plots out in the top of the high intermediate zone.

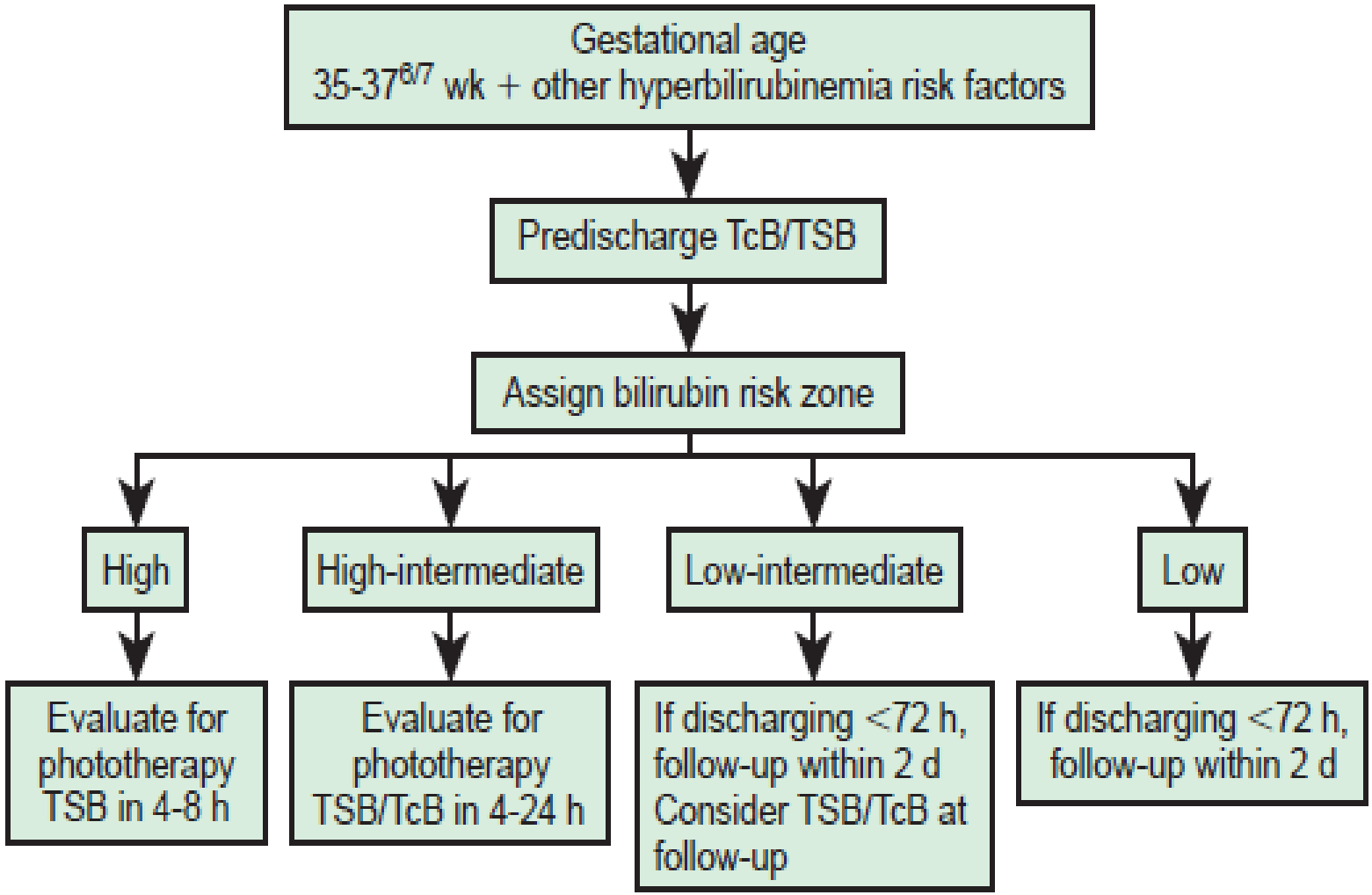
As emphasized in Dr. Bhutani's original paper, the provider must not only determine the risk zone but also determine what risk factors are present.

Table 6.1 Risk factors for development of severe hyperbilirubinemia in infants of 35 or more weeks of gestation

Major risk factors
Pre-discharge TSB or TcB level in the high-risk zone
Jaundice observed in the first 24 h
Blood group incompatibility with positive direct antiglobulin test, other known hemolytic disease (e.g., G6PD deficiency)
Gestational age of 35–36 weeks
Previous sibling received phototherapy
Cephalohematoma or significant bruising
Exclusive breastfeeding
East Asian race
Minor risk factors
Pre-discharge TSB or TcB level in the high-intermediate-risk zone
Early discharge
Gestational age of 37–38 weeks
Jaundice observed before discharge
Previous sibling with jaundice
Macrosomic infant of a diabetic mother
Maternal age ≥25 years
Male gender

Adapted from Ref. [13]
Risk factors for the development of significant hyperbilirubinemia (≥95th percentile)

It should also be remembered that these are risk factors for developing hyperbilirubinemia and are different than those used when determining whether phototherapy and/or exchange transfusion are necessary


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

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If appropriate follow-up cannot be ensured in the presence of elevated risk for developing hyperbilirubinemia, it may be necessary to delay discharge either until appropriate follow-up can be ensured or the period of greatest risk has passed (72–96 h)

The patient had a 7.5 bilirubin at 25th hours of life.

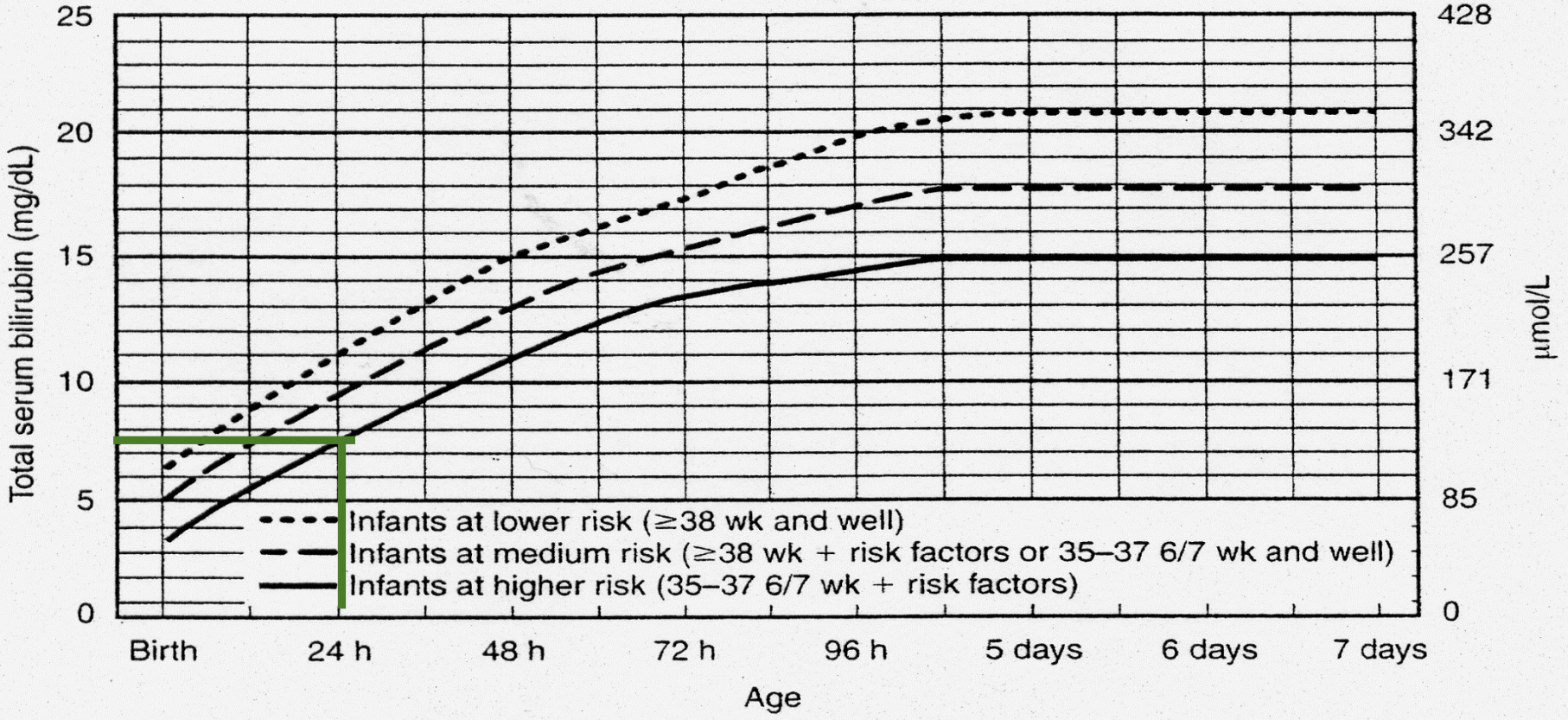
Is he a candidate for phototherapy?

- 1. Yes
- 2. No

Although this baby was only in the high-intermediate zone for risk, he is 36 weeks. Whether or not to start phototherapy is not based on the risk zones from the Bhutani nomogram but from the criteria for the initiation of phototherapy published in the AAP guideline for hyperbilirubinemia

Guidelines for Phototherapy in Hospitalized infants ≥ 35 Weeks

Note: These guidelines are based on limited evidence and the levels shown are approximations. The guidelines refer to the use of intensive phototherapy which should be used when the TSB exceeds the line indicated for each category.



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease. G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0 g/dL (if measured)
- For well infants 35-37 $^{6}/_{7}$ wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wk and at higher TSB levels for those closer to 37 $^{6}/_{7}$ wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50 µmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

As mentioned previously, the risk factors that are considered in the decision to start phototherapy differ from those for the risk of hyperbilirubinemia.

Risk factors for phototherapy

Isoimmune hemolytic disease

G6PD deficiency

Asphyxia, significant lethargy

Temp instability, sepsis, acidosis

Albumin < 3.0 g/dl (if measured)

The patient had a 7.5 bilirubin at 25 h of life. Is he a candidate for intensive phototherapy?

- 1. Yes
- 2. No

Answer 2

Home Phototherapy

Can be effective and safe

Advantages: 1. reduced cost
2. avoidance of parent-infant separation
3. parental satisfaction
4. less likely to stop breast feeding

Disadvantage: complications of inadequate nursing supervision include corneal abrasion, eye patch misuse, excessive weight loss, temperature derangement and ineffective bilirubin reduction.

Indication: Can be considered for healthy infants without hemolysis or other risk factors who have TSB levels 2 to 3 mg/dl below the recommended treatment levels, are feeding well, and can be closely followed.

Follow up

Infant discharged	Should be seen by age
< 24 h	72 h
24 - 47.9 h	96 h
48 – 72 h	120 h

Jaundice in the outpatient setting (mild or prolong jaundice)

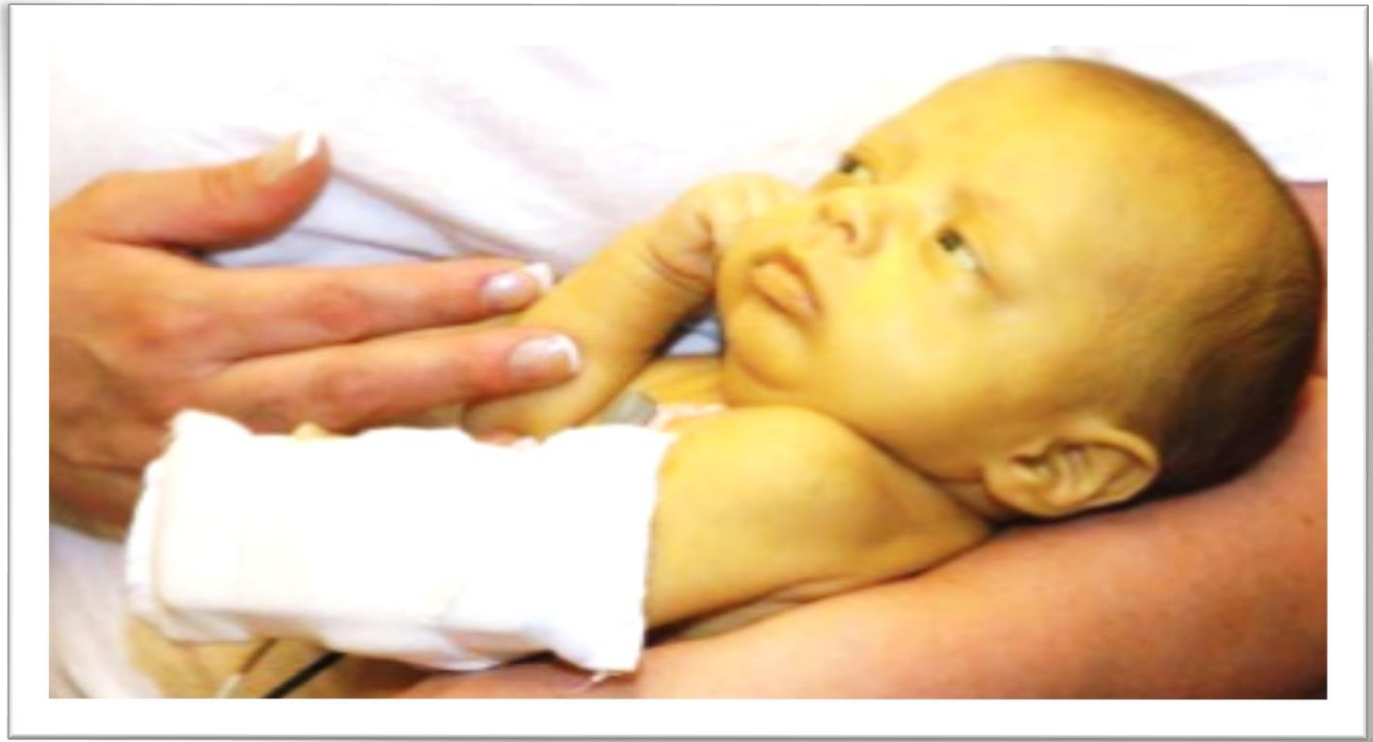
Case II

A 28 d/o neonate with gestational age: 32 weeks and birth weight: 1700 gr refer due to jaundice in clinic.

In P/E, the neonate appear healthy and other than jaundice, no other abnormal findings are noted. Current weight is 2500gr.

What's your recommendation for jaundice?

Prolong jaundice



Definition:

- Jaundice persisting beyond day 14 in term neonates

- Jaundice persisting beyond day 21 in preterm infants

Importance of prolonged jaundice

- Underlying disease(R/O cholestasis)
- The level of bilirubin (bilirubin encephalopathy)
- Parental worrisome
- One of the criteria of pathologic jaundice

History

- History of blood group incompatibility
- Family history of prolong jaundice
- Method of feeding and weight gain (birth weight and current weight)
- Lethargy
- Urine color
- Color of stool
- Bleeding/bruising /hematoma

Examination

- Jaundice
- Pallor
- Hydration status
- Dysmorphic features
- Cataracts
- Hepatosplenomegaly
- Hypotonia and encephalopathy
- Petechia/purpura
- Look in the nappy – color of stool and urine

Investigations

- Total and conjugated bilirubin(don't rely to previous results)
- CBC, retic
- U/A,U/C
- Check result of routine metabolic (heel prick) screening (including screening for congenital hypothyroidism and galactosemia)

Results of lab data

- Hb=9 mg/dl retic = 1%
- Bilirubin (Total=8 mg/dl , Direct=0.5)
- U/A, U/C: Normal
- Result of screening test for TFT and galactosemia and G6PD: Normal

What's your diagnosis and recommendation?

Prolong Unconjugated Hyperbilirubinemia

- **Breast milk jaundice**
- **Hemolysis**
- **Increased enterohepatic circulation**
  - Pyloric stenosis
  - Intestinal obstruction
- **Decreased conjugation**
  -Crigler-Najjar syndrome
  - Gilbert's disease
  - Hypothyroidism
  -Prematurity

Treatment of prolonged jaundice

- No treatment (reassurance to family, wait and watch)
- Phototherapy (based on the level of bilirubin)
- Treatment of hemolysis (folic acid and f/u)
- Phenobarbital
- Avoid of breast milk
- Others(Hypothyroid , HPS,….)

Jaundice in the hospital (readmission)

Case III

- A 6 days old male neonate with GA=36weeks and BW=2500 gr refer due to jaundice and poor feeding.
- Jaundice begins 36 hours after birth, he received herbal medication.
- The baby developed poor feeding and irritability since one day ago.

P/E:

- The patient is febrile and irritable.
- Has severe jaundice which covers palms and soles
- Has backward arching of the neck and trunk.
- All neurologic reflex are fair to poor

What's your impression?

Answer : Acute bilirubin encephalopathy

Complication

Bilirubin is a potential neurotoxin.

Free bilirubin can enter the brain and cause cell death by apoptosis and/or necrosis.

The regions most often affected include basal ganglia and the brain stem nuclei for oculomotor and auditory function.

- Term infants are at risk for bilirubin toxicity when TSB exceed 25 to 30 mg/dl.

- The relationship between TSB and bilirubin toxicity is variable and influenced by other factors such as levels of free bilirubin and blood brain barrier

- Although measurement of free bilirubin is useful, clinical testing is not available; the ratio of bilirubin to albumin can be used as an approximate surrogate for free bilirubin.

- Bilirubin toxicity can occur in healthy term infants

Acute bilirubin encephalopathy

Typically progresses through three phases:

- Early phase occurs in the first few days and consists of lethargy(sleepy), hypotonia, and poor sucking, with a slightly high-pitched cry.
- Intermediate phase evolves later in the first week. The infant becomes irritable with a high-pitched cry, and develops hypertonia, often with backward arching of the neck (retrocollis) and trunk (opisthotonos) with stimulation and fever.
- Advanced phase typically starts after the first week. Characterized by apnea, poor feeding, fever, seizures, stupor that progresses to coma, hypertonia with marked retrocollis and opisthotonos with twitching of the hands and feet. The cry is inconsolable, or may be weak or absent. Death is due to respiratory failure or intractable seizures.

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Acute bilirubin encephalopathy

Clinical signs can be divided into three domains :

- Mental status
- Tone
- Cry pattern

Auditory brainstem -evoked responses(ABER) can be used to detect the acute neurologic effects and confirm the presence of BIND.

Increased TB correlated with prolonged brainstem conduction time. These abnormalities resolve as TB values decline.

BIND score
for term & late preterm infants

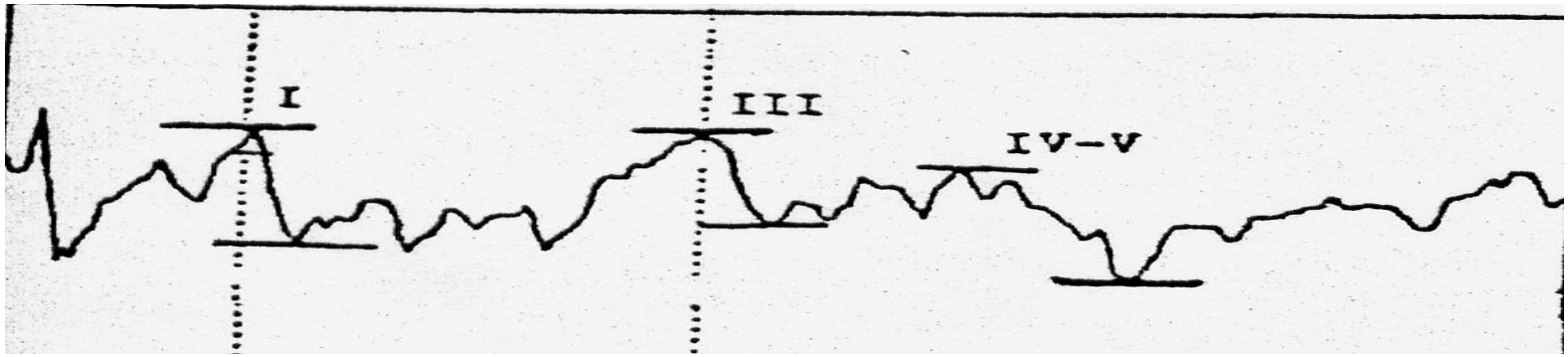
Clinical signs	Score
Mental status	
Normal	0
Sleepy but arousable, decreased feeding	1
Lethargic, poor suck, irritable, and/or jittery	2
Semicomatose to comatose, unable to feed, seizures	3
Muscle tone	
Normal	0
Persistent mild to moderate hypotonia	1
Mild to moderate hypertonia alternating with hypotonia	2
Persistent retrocollis and opisthotonos	3
Cry pattern	
Normal	0
High pitched when aroused	1
Shrill, difficult to console	2
Inconsolable crying or weak/absent cry	3
Total BIND score	

BIND score

- Scores between >7: Advanced ABE, requiring emergency intervention (exchange transfusion) to prevent further brain injury and potentially reverse acute brain damage.
- Scores between 4 and 6: Moderate ABE, requiring urgent intervention (intensive phototherapy and potentially exchange transfusion) to possibly (based on timing of intervention) prevent and reverse brain injury.
- Scores between 1 and 3: Consistent with subtle signs of ABE, requiring intervention (phototherapy) depending on total bilirubin. In these patients, auditory brainstem response testing is helpful, as an abnormal result would confirm the presence of moderate ABE.

Abnormal ABER

Auditory brainstem evoked responses (ABER) are affected by hyperbilirubinemia.



Increased TSB correlated with prolonged brain stem conduction time. These abnormalities may resolve as TSB valve decline.

Change in ABER associated with elevated free bilirubin levels.

No evidence for a risk of hearing loss related to hyperbili in full term infant, deficits in central hearing, speech and language can occur in the absence of pure tone hearing loss and these may be manifestations of auditory neuropathy (abnormal ABER and normal OAE) .

Chronic bilirubin encephalopathy (Kernicterus)

The chronic and permanent sequelae of bilirubin toxicity develops during the first year after birth.

The three major features are:

Choreoathetoid CP(chorea, tremor, and dystonia)

Gaze abnormalities esp. limitation of upward gaze

Sensorineural hearing loss due to auditory neuropathy (abnormal ABER with normal OAE)

Some patient have dental enamel hypoplasia

Cognitive function is relatively spared

What's your recommendation?

1. Intensive phototherapy.
2. Immediate exchange transfusion
3. sepsis w/u and antibiotics
4. Additional laboratory evaluation.

Intensive phototherapy

For intensive(aggressive) phototherapy, high levels of irradiance in the 430-490 nm band (usually ≥ 30 μw/cm^2/nm) are delivered to as much of the surface area as possible

With a bank of special blue lights placed at a distance of 10 to 12 cm from the infants body and a fiberoptic pad or special blue fluorescent tubes below the infant. The area covered by diaper should be minimized.

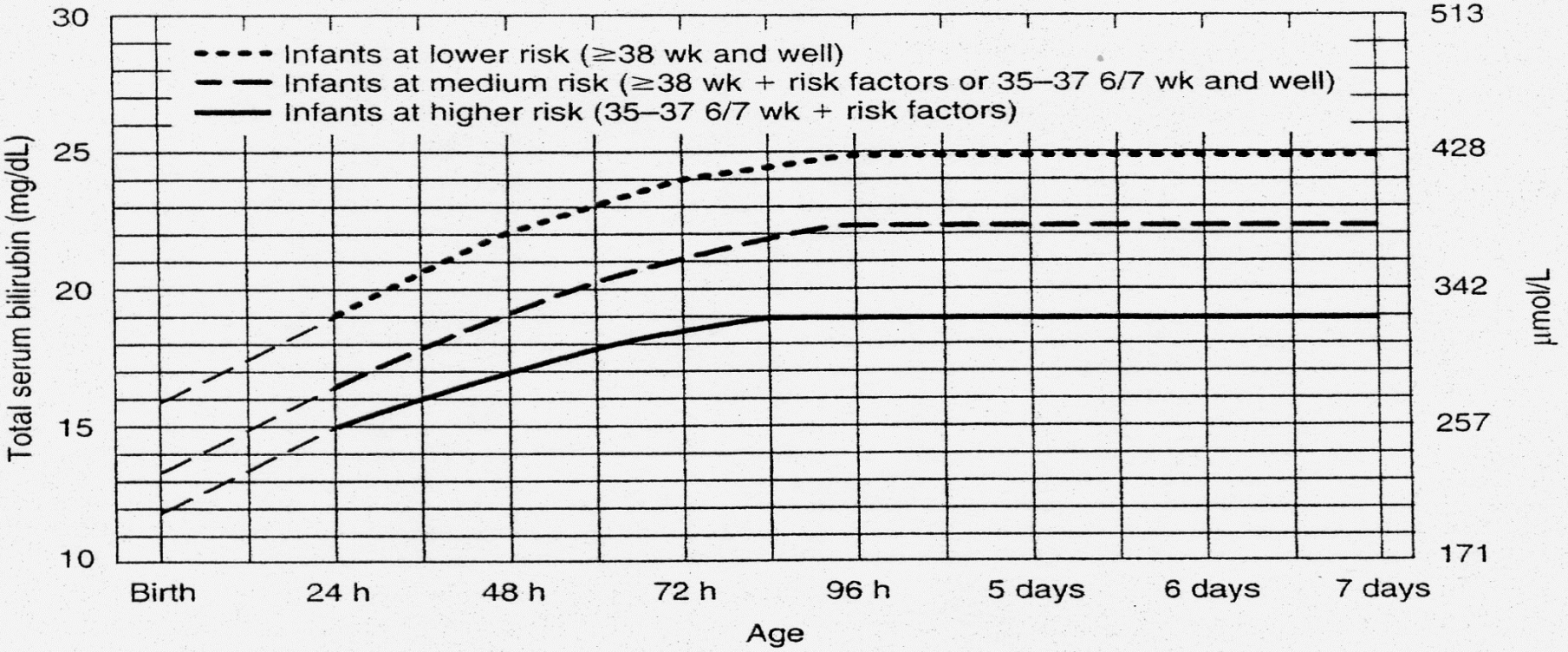
There isn’t a saturation point and overdose for phototherapy.

- Phototherapy should be continuous, with interruptions only for feeding (less than 1 hour).

- If the TSB is at a near toxic level, blanket exposure can continue during feeding.

Guidelines for Exchange Transfusion in Infants ≥ 35 Weeks

Note: These guidelines are based on limited evidence and the levels shown are approximations. During birth hospitalization, exchange transfusion is recommended if TSB rises to these levels despite intensive phototherapy. For readmitted infants, if TSB is above exchange level, repeat TSB every 2-3 hr and consider exchange if TSB remains above levels indicated after intensive phototherapy for 6 hours.



- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is 25mg/dL, (85µmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend).
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

Indications of immediate exchange

IF TSB ≥ 25 and with early sign of bilirubin neurotoxicity (eg. lethargy, hypotonia, high pitch crying)

If TSB is ≥ 5 mg/dl above the threshold value for exchange

With any TSB and signs of kernicterus. (Phase 2,3 bilirubin encephalopathy)

Additional laboratory evaluation

- Mother’s and neonate’s blood type
- Direct coombs test
- CBC & Reticulocyte count
- Peripheral smear
- G6PD
- Direct bilirubin

Results of lab data:

- Hb: 16 g/dl
- WBC: 8000 with normal diff
- Retic : 1%
- Direct coombs test :negative
- MBG:O+ BBG:A+
- G6PD:deficient
- peripheral smear : NL
- Bilirubin total :26 mg/dl, Direct Bili:0.3
- CRP: negative

What is the cause of severe hyperbilirubinemia ?

1. Sepsis
2. G6PD deficiency
3. ABO incompatibility
4. prematurity

Answer : 2 & 4

Pharmacologic agents

- Intravenous immune globulin (IVIG)
- Phenobarbital
- Ursodeoxycholic acid (UDCA)
- Metalloporphyrins
- Clofibrate
- Agar (bilinuster)


Thanks for your attention