

Approach to the management of Hyperbilirubinemia in Term Newborn Infant

Mohammad Bagher Hosseini MD

Neonatologist

Assosiated professor of Tabriz University of Medical science

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Case1



- You are called by the ER to see an infant whose bili is 22.
- Must you admit?
- What information do you need to answer this question?

Outline

- Review of physiology
- Kernicterus
- Risk factors
- Assessing the risk
- Therapies



Neonatal Hyperbilirubinemia

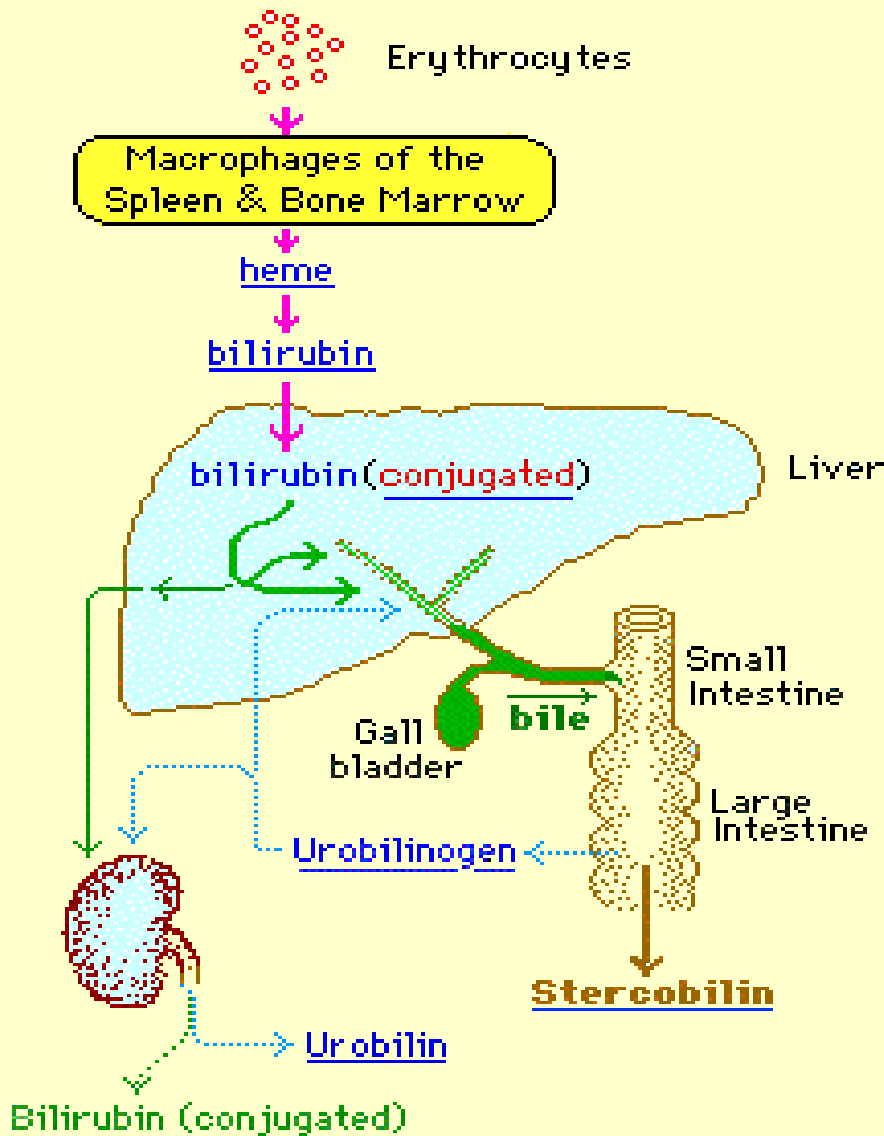


- Definition =
- Clinical ;
- Lab : (TSB) > 5 mg/dL
- Significance:
 - Present in up to 60% of term newborns
 - Severe complications possible
 - Deafness, CP (Kirnicterus)
 - Increase Kirnicterus 1990's (related to early hospital discharge)

Recent concern



- JACHO alert due to several case reports of kernicterus in healthy newborns
- Term 35-38 weeks, dehydrated breastfeeding, and with extremely high bilirubin levels



Bilirubin Production & Metabolism



Classification



- Benign
 - Physiologic
 - Breast Milk
 - Breastfeeding
- Pathologic
 - Many causes

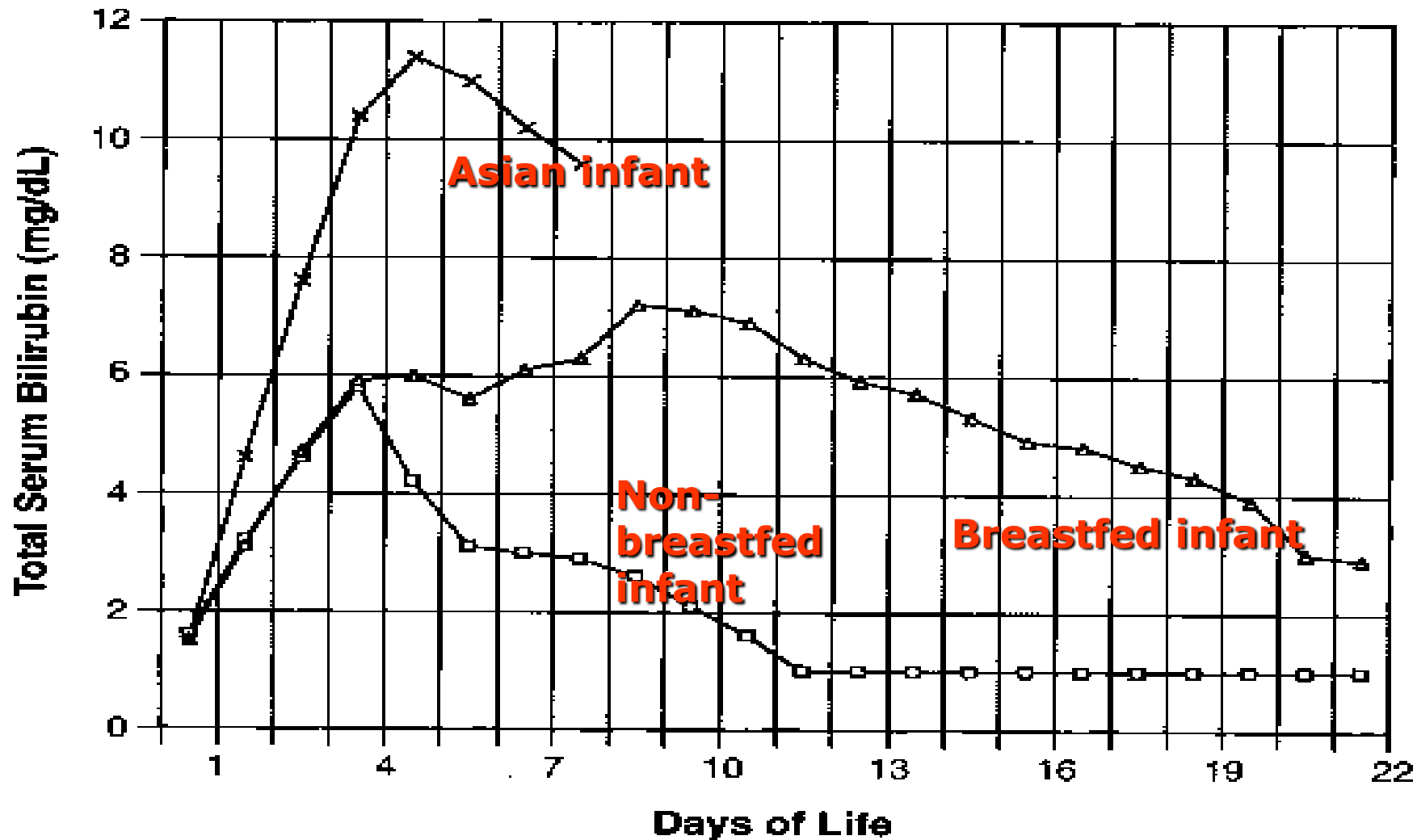
Physiologic Jaundice



- **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)

Physiologic Jaundice



Ethnic differences



- Exaggerated Hyperbilirubinemia ($>12.8\text{mg/dl}$)
 - 4% African-Americans
 - 6-10% Caucasian
 - 25% Asian ($>20\text{mg}\%$ in 2%)

Effect of Type of Feeding



- 2/3 of breastfeeding infants (BF) will have chemical **jaundice** for 2-3 weeks
- TSB > 12mg% in 12% (BF) vs. 4% Formula Fed infants (FF)
- TSB > 15mg% in 2% BF vs. 0.3% FF

Mechanism of Physiologic Jaundice

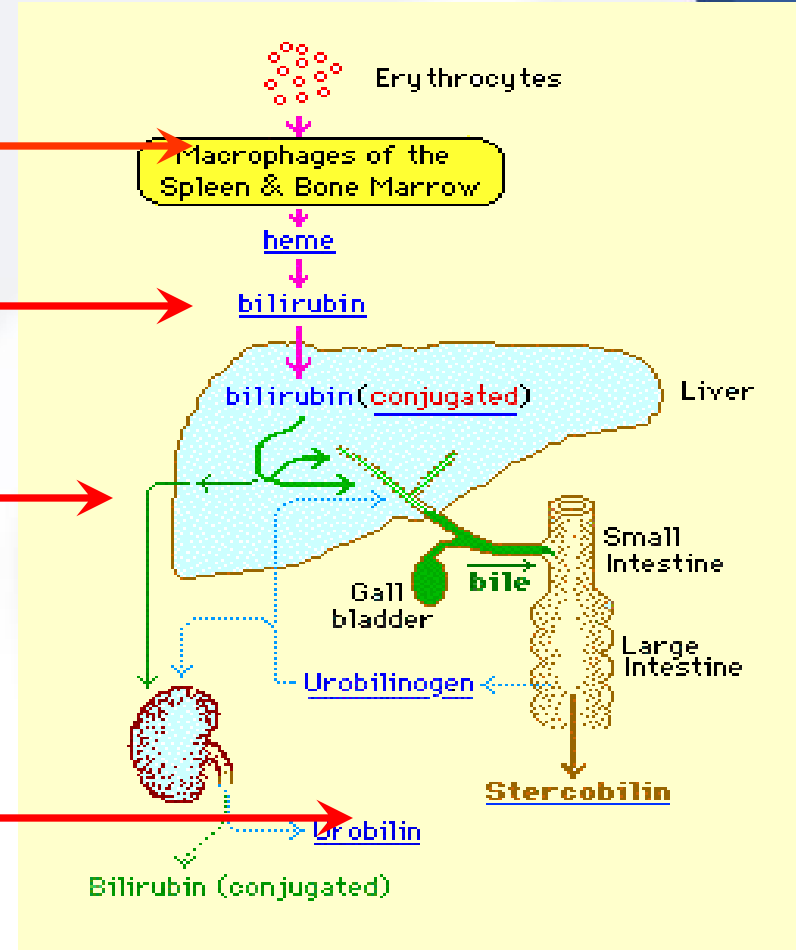


Increased rbc's

Shortened rbc lifespan

Immature hepatic uptake & conjugation

Increased enterohepatic Circulation



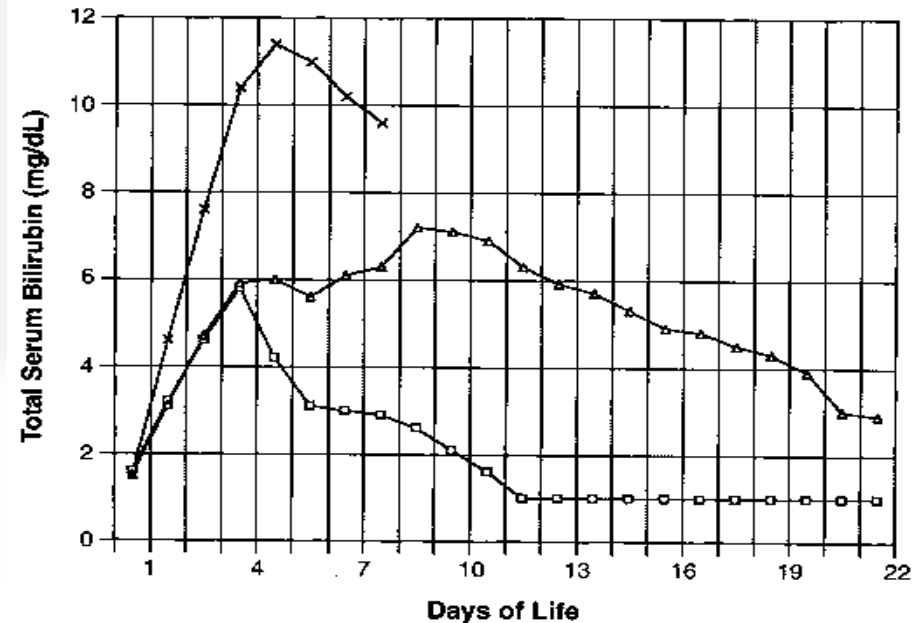
Breast feeding Jaundice



- Elevated unconjugated bilirubin
- Benign or pathologic
 - Elevated bilirubin in the 1st week of life tends to worsen breast milk jaundice during later weeks
- Equivalent to starvation jaundice in adults
- Mandates improved/increased breastfeeding
 - No water or dextrose supplementation
 - Formula OK(Sometime , No bottle)

Breast Milk Jaundice

- Elevated unconjugated bilirubin
- Prolongation of physiologic jaundice
 - Slower decrease to adult levels of bilirubin
 - 66% of breastfed babies jaundiced into 3rd week of life
 - May persist up to 3 months
 - May have second peak @ day 10
- Average max TSB = 10-12 mg/dL
- TSB may reach 22-24 mg/dL
- ?Milk factor



BREASTMILK/BREASTFEEDING JAUNDICE



- Breastfeeding jaundice occurs early
- It is due to the lack of breast milk
- It is often associated with poor passage of meconium.
- Treatment should be aimed at supporting breastfeeding while supplementing as needed to avoid extreme weight loss, dehydration, and worsening jaundice.

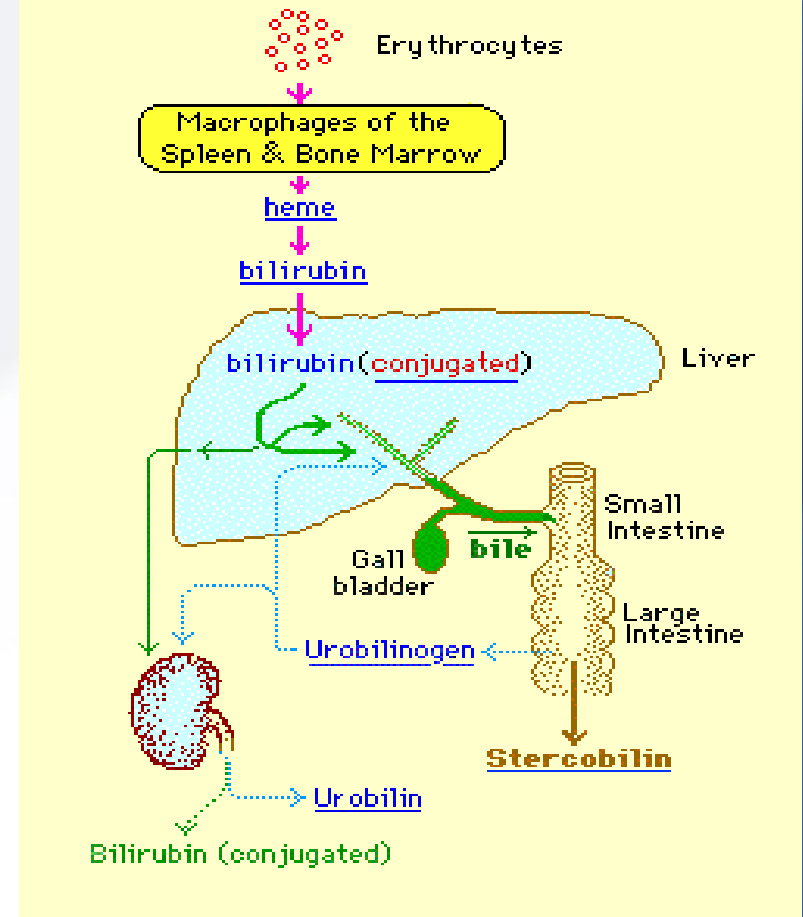
BREASTMILK/BREASTFEEDING JAUNDICE



- Breast milk jaundice is a different, more benign entity, which tends to occur late in the first week or afterwards.
- It is actually due to something in the breast milk which tends to prolong jaundice.
- Usually weight gain is good, and the baby is otherwise well.
- Jaundice might persist as late as 3-4 weeks, but usually will peak by 2 weeks.
- Textbook treatment is to interrupt breastfeeding (I usually do not do this).

Pathologic Jaundice

- Features
 - Jaundice in 1st 24 hrs
 - Rapidly rising TSB (> 5 mg/dL per day)
 - TSB > 17 mg/dL
- Categories
 - Increased bilirubin load
 - Decreased conjugation
 - Impaired bilirubin excretion



Increased Bilirubin Load



Hemolytic Disease

- Features: elevated reticulocytes, decreased Hgb
- Coomb's + Rh incompatibility, ABO incompatibility, minor antigens
- Coomb's - G6PD, spherocytosis, pyruvate kinase deficiency

Pathologic Jaundice



- **Non-hemolytic Disease**
 - normal reticulocytes
 - Extravascular sources – I.e. cephalohematoma
 - Polycythemia
 - Exaggerated enterohepatic circulation – I.e. CF, GI obstruction

G6PD Deficiency



- A cause of kernicterus in up to 35% of cases
- Always suspect if severe hyperbili or poor response to phototherapy
- Ethnic origin
 - 11-13% of African Americans
 - Mediterranean, Middle East, Arabian peninsula, SE Asia, Africa
- Requires intervention at lower TSB levels
- Testing
 - Levels may be normal or elevated early
 - Especially in presence of hemolysis
 - Repeat level at 3 months

Decreased Bilirubin Conjugation



- Elevated unconjugated bilirubin
- Genetic Disorders
 - Crigler-Najjar
 - 2 types
 - Severe hyperbilirubinemia
 - Gilbert Syndrome
 - Mild hyperbilirubinemia
- Hypothyroidism

Impaired Bilirubin Excretion



- Elevated unconjugated and conjugated bilirubin ($> 2 \text{ mg/dL}$ or $> 20\%$ of TSB)
- Biliary Obstruction
 - Structural defects – I.e. biliary atresia
 - Genetic defects – Rotor's & Dubin-Johnson syndromes
- Infection – sepsis, TORCH
- Metabolic Disorders – I.e. α_1 antitrypsin deficiency
- Chromosomal Abnormalities – Turner's syndrome
- Drugs – I.e. ASA, sulfa, erythromycin

Diagnosis & Evaluation

- Physical Exam
 - Bilirubin > 5 mg/dL
 - Milder jaundice - face & upper thorax
 - Caudal progression generally signifies higher bilirubine levels
 - Should not rely on this system
 - Liberally check bilirubin values
- Laboratory
 - Blood
 - Transcutaneous
 - Generally within 2mg/dL of serum test
 - Most useful if serum bili < 15



Physical Exam



- Poor correlation inter-observer and with serum bilirubin
- Best cut appears to be **jaundice** to nipples for bili > 12.0 mg/dl
- 97% sensitive
- 19% specific

Arch Pediatr Adolesc Med. 2000; 154:391-4

- Zone 1 head - clavicle 5
- Zone 2 clavicle-umbilicus 6-8
- Zone 3 umbilicus-knee 9-12
- Zone 4 knees-ankles 13-15
- Zone 5 palms + soles 15
- ***Clinical Exam: Unreliable***
- ***Clinical Exam: Unreliable***



2004 AAP Guidelines

Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation

Subcommittee on Hyperbilirubinemia
Pediatrics 2004; 114;297-316

Prevention

- **Breastfeeding**

- Should be encouraged for most women
 - Separate AAP guidelines
- 8-12 times/day for 1st several days
- Assistance and education
- Avoid supplements in non-dehydrated infants
 - Do not decrease level & severity of hyperbili



Prevention



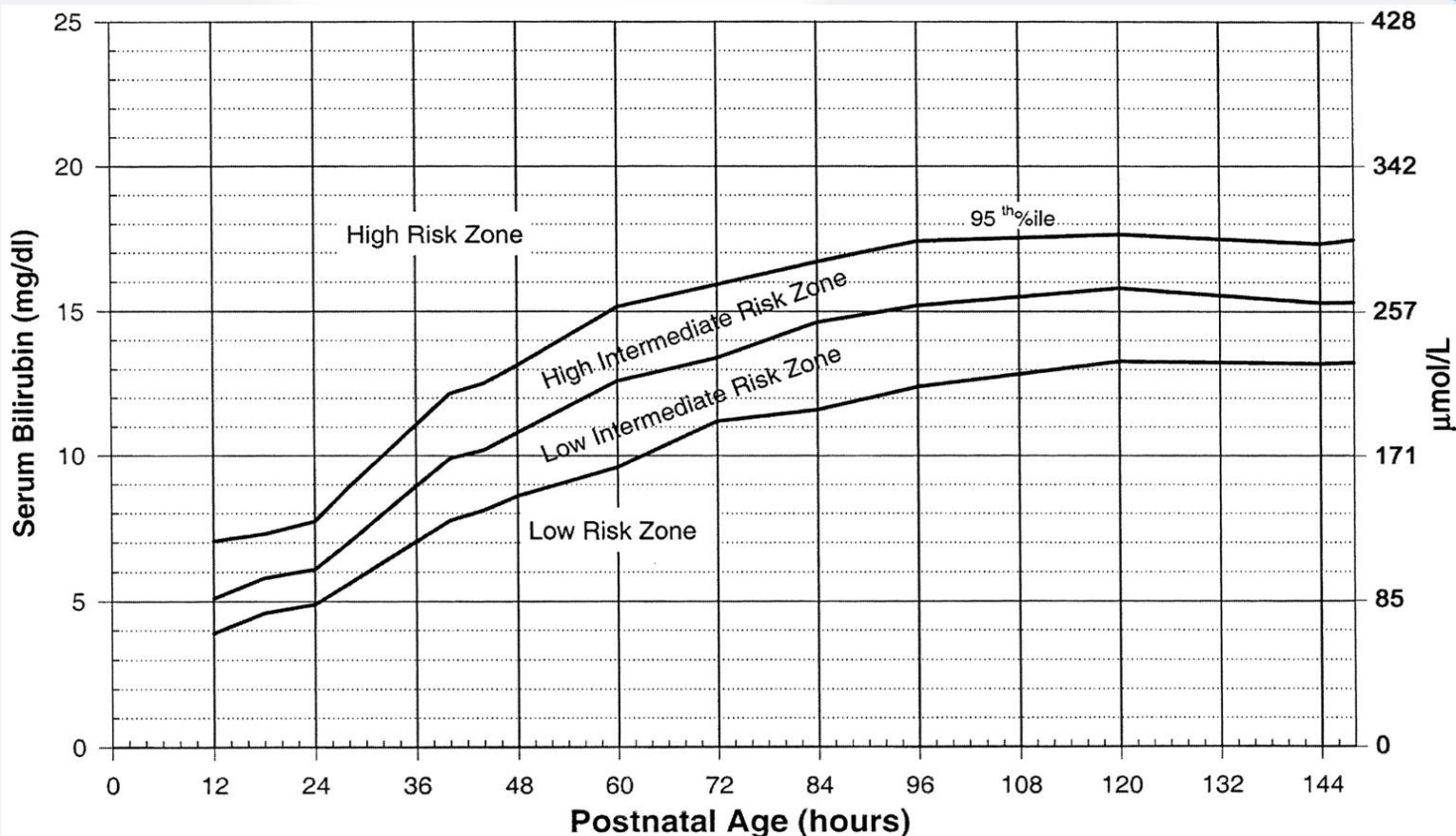
- Ongoing assessments for risk of developing severe hyperbilirubinemia
 - Monitor at least every 8-12 hours
 - **Don't rely on clinical exam**
 - Blood testing
 - Prenatal (Mom): ABO & Rh type, antibody
 - Infant cord blood
 - Mom not tested, Rh (-): Coomb's, ABO, Rh
 - Mom O or Rh (+): optional to test cord blood

Laboratory investigation



- **Indicated (if bilirubin concentrations reach phototherapy levels)**
 - **Serum total or unconjugated bilirubin concentration**
 - **Serum conjugated bilirubin concentration**
 - **Blood group with direct antibody test (Coombs' test)**
 - **Hemoglobin and hematocrit determinations**
- **Optional (in specific clinical circumstances)**
 - **Complete blood count including manual differential white cell count**
 - **Blood smear for red cell morphology**
 - **Reticulocyte count**
 - **Glucose-6-phosphate dehydrogenase screen**
- **Serum electrolytes and albumin or protein concentrations**

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

ASSESSING THE RISK OF JAUNDICE BY THE NUMBERS



- www.bilitool.org

- Palm downloadable! 😊

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option one

Date and time of birth to closest hour:

2011 May | 26 12 am - midnight

Date and time of blood sampling to closest hour:

2011 May | 27 12 am - midnight

Total Bilirubin*: mg/dl (US)

option two

Age (hours): (18-168 hours)

Total Bilirubin*: mg/dl (US)

*Note: The default *unit of measure* for total bilirubin is **mg/dl**. Please select $\mu\text{mol/L}$ if your bilirubin values are captured in the global standard SI metric units. Bilirubin conversion from US to SI units is 17.1.

Results are based on the [Hour-Specific Nomogram for Risk Stratification](#) published in "Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation" (2004) by the AAP journal.

Use

BiliTool is designed to help clinicians assess the risks toward the development of hyperbilirubinemia or "jaundice" in newborns over 35 weeks gestational age.

Required values include the age of the child in hours (between 18-168 hours) and the total bilirubin in either US (mg/dl) or SI ($\mu\text{mol/L}$) units.

Two entry options are available.

Search for more information about neonatal jaundice:

Risk Factors for Severe Hyperbilirubinemia



- **Major risk factors**

- Predischarge bili in high-risk zone
- Jaundice in 1st 24 hrs
- Blood group incomp with + direct antiglobulin test, other known hemolytic disease (eg, G6PD deficiency)
- Gestational age 35–36 wk
- Previous sibling received phototherapy
- Cephalohematoma or significant bruising
- Exclusive breastfeeding
- East Asian race

- **Minor risk factors**

- Bili in high intermed-risk zone
- Gestational age 37–38 wk
- Jaundice before discharge
- Previous sibling with jaundice
- Macrosomia infant with diabetic mother
- Maternal age ≥ 25
- Male

- **Decreased Risk**

- Bili in low-risk zone
- ≥ 41 wks gestation
- Exclusive bottle feed
- Black race
- D/c from hospital > 72 hrs

Discharge



- Assess risk
 - Predischarge bili
 - Use nomogram to determine risk zone
 - And/or Assessment of risk factors

TSB Zone	Newborns (%)	% with TSB >95 th %
High risk	6	39.5
High intermed	12.5	12.9
Low intermed	19.6	2.26
Low	61.8	0

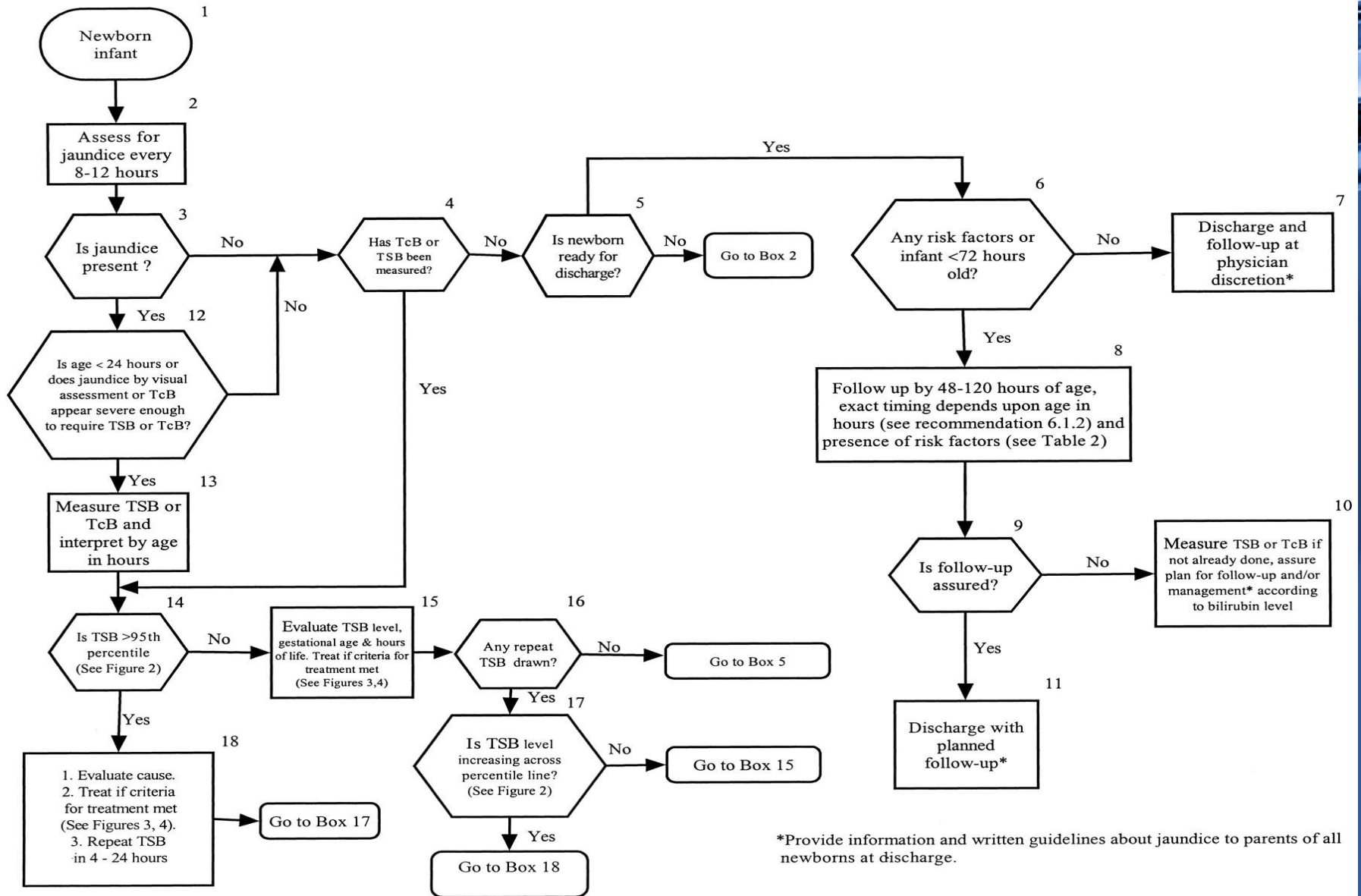
Discharge



- 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

Algorithm for the management of jaundice in the newborn nursery



*Provide information and written guidelines about jaundice to parents of all newborns at discharge.

Phototherapy



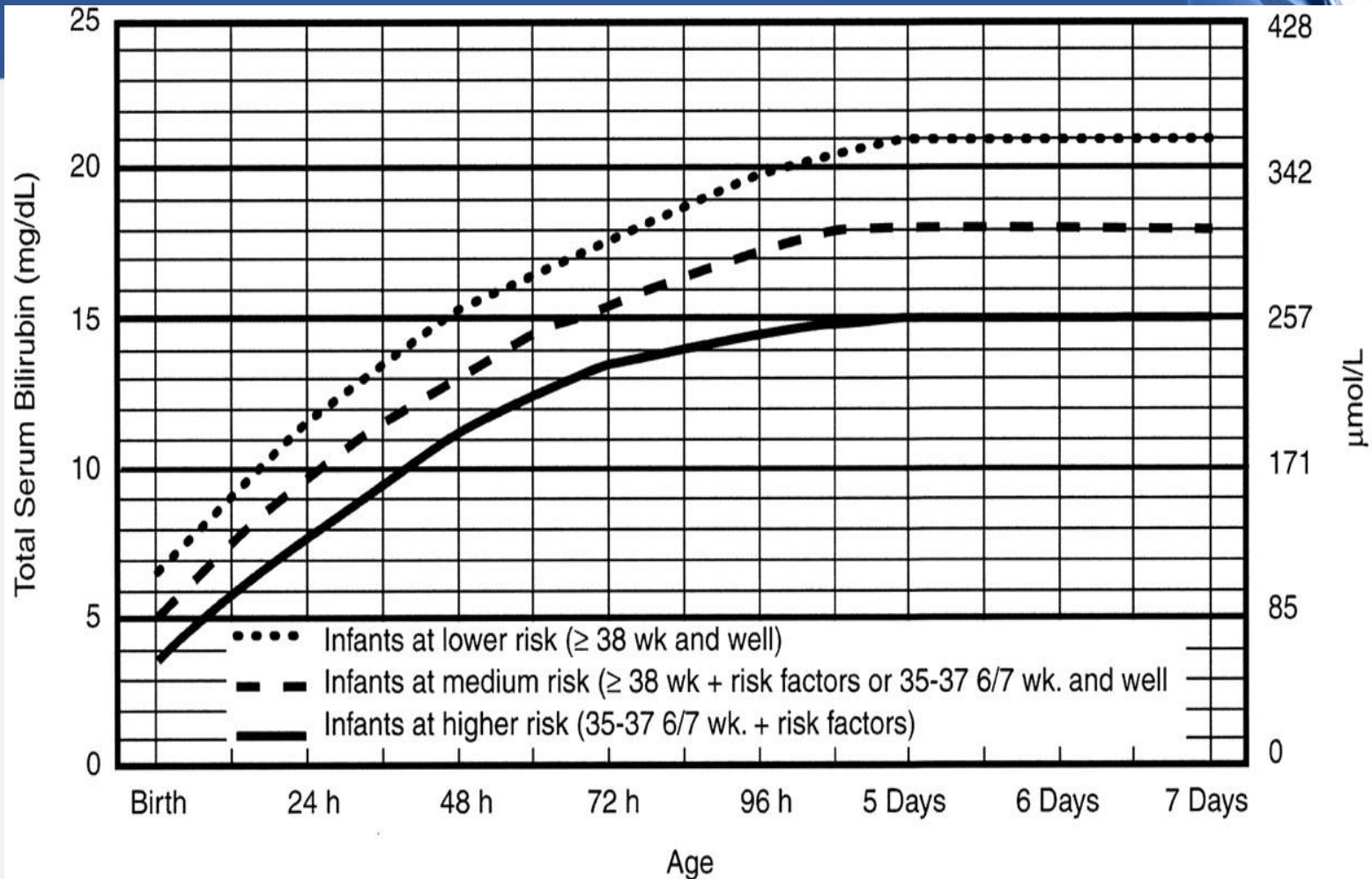
- Mechanism: converts bilirubin to water soluble form that is easily excreted
- Forms
 - Fluorescent lighting
 - Fiberoptic blankets
- Goal is to decrease TSB by 4-5 mg/dL or < 15 mg/dL total
- Breastfed infants are slower to recover

Phototherapy



- Severe rebound hyperbilirubinemia is rare
 - Average increase is 1 mg/dL
- Intensive
 - Special blue tube with light in blue-green spectrum
 - Close to infant
 - Expose maximum surface area

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



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

PEDIATRICS[®]

Exchange Transfusion



- Mechanism: removes bilirubin and antibodies from circulation and correct anemia
- Most beneficial to infants with hemolysis
- **Generally never** used until after intensive phototherapy attempted

Complications

- Toxicity to Basal Ganglia and brainstem nuclei
- 2 terms
 - Acute bilirubin encephalopathy
 - Kernicterus
- Multiple phases

Effects of Bilirubin Toxicity in Newborns

Early

Lethargy

Poor feeding

High-pitched cry

Hypotonia

Late

Irritability

Opisthotonos

Seizures

Apnea

Oculogyric crisis

Hypertonia

Fever

Chronic

Athetoid cerebral palsy

High-frequency hearing loss

Paralysis of upward gaze

Dental dysplasia

Mild mental retardation



Risk of Kernicterus

- TSB level > 25-30 mg/dl
- Acidosis
- Increased free bilirubin
- low albumin, drug displacement
- Blood-brain barrier disruption
- prematurity, sepsis, ischemia



Kernicterus cases

potentially correctable causes

- Early discharge (<48hrs) without f/u within 48 hrs
- Failure to check bilirubin level if onset in first 24 hours
- Failure to note risk factors
- Visual assessment underestimate of severity
- Delay in testing jaundiced newborns or treating elevated levels
- Lack of concern for presence of **jaundice** or parental concern
- Pediatrics 2001; 108:763-765



Common Clinical Risk Factors for Severe Hyper-bilirubinemia

A blue stethoscope is positioned in the top right corner of the slide, partially overlapping the title area.

- **Jaundice** in the first 24 hours
- Visible **jaundice** at discharge
- Previous jaundiced sibling
- Near term gestation 35-38 weeks
- Exclusive breastfeeding
- East Asian (4), Mediterranean (1), African origin (12) (G6PD deficiency), 19/61 kernicterus cases = G6PD
- Bruising, cephalohematoma, birth trauma
- Hemolysis risk, O + maternal blood type, sepsis

Medications increasing bilirubin toxicity



- Sulfisoxazole (displacement or G6PD hemolysis)
- Ceftriaxone (displacement from albumin)

Trans cutaneous bilirubin



- Older devices affected by skin pigmentation
- Newer multi-wavelength spectral reflectance correlate 0.88 with the serum value,
- example SpectRx, ± 3 mg/dl
- ? Confirm values $> 40\%$ per age
- Carbon monoxide exhaled

Direct Coombs Testing



Strongly positive:

- Rh
 - Kell
 - Kidd
 - Duffy
- Negative or “weakly positive:
 - Anti-A

Hemolysis consider present



- Hct < 45%
- Abnormal blood smear with 3-4+ spherocytes
- Reticulocyte count is 4.5% in the first 72 hrs, or
- Reticulocyte count is >1-2% in the first 1-2 wks

Review of Case 2



- How old is the patient?
- What is the fractionation?
- Breast or bottle fed?
- Other risk factors?
 - 10 days
 - 22 total / 0.8 direct
 - Breast fed
 - None



QUESTIONS?

References

- American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114:297-316
- Johnson LH, Bhutani VK, Brown AK. System-based approach to management of neonatal jaundice and prevention of kernicterus. *J Pediatr*. 2002;140:396-403
- American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. Classification of recommendations for clinical practice guidelines. *Pediatrics*. 2004;114:874-877
- Gartner LM, Herschel M. Jaundice and breastfeeding. *Pediatr Clin North Am*. 2001;48:389-399
- Moyer VA, Ahn C, Sneed S. Accuracy of clinical judgment in neonatal jaundice. *Arch Pediatr Adolesc Med*. 2000;154:391-394
- Ip S, Glicken S, Kulig J, O'Brien R, Sege R, Lau J. *Management of Neonatal Hyperbilirubinemia*. Rockville, MD: US Department of Health and Human Services, Agency for Healthcare Research and Quality; 2003. AHRQ Publication 03-E011
- Bhutani VK, Johnson LH, Sivieri EH. Predictive ability of a predischarge hour-specific serum bilirubin for subsequent hyperbilirubinemia in healthy term and near-term newborns. *Pediatrics*. 1999;103:6-14.
- American Academy of Pediatrics, Subcommittee on Neonatal Hyperbilirubinemia. Neonatal jaundice and kernicterus. *Pediatrics*. 2001;108:763-765

