

## Intensive Care Nursery House Staff Manual

### Neonatal Jaundice

#### **PHYSIOLOGIC JAUNDICE (non-pathologic unconjugated hyperbilirubinemia):**

##### **1. Term Infants:**

- 50-60 % of all newborns are jaundiced in the first week of life.
- Total serum bilirubin peaks at age 3–5 d (later in Asian infants).
- Mean peak total serum bilirubin is 6 mg/dL (higher in Asian infants).

##### **2. Preterm Infants:**

- Incidence of visible jaundice is much higher than in term infants.
- Peak is later (5-7d).
- Because of ↑ risk of bilirubin encephalopathy (see below), “physiologic” jaundice is more difficult to define and jaundice should be followed closely.

#### **DEFINITION of NON-PHYSIOLOGIC JAUNDICE:**

- Jaundice in the first 24 hours
- Bilirubin rising faster than 5 mg/dL in 24 hours
- Clinical jaundice >1 week
- Direct bilirubin >2 mg/dL
- In healthy term infants** total serum bilirubin concentration >15 mg/dL
- Lower levels in **preterm infants, “sick” infants, and hemolytic disease**  
(See section on Hemolytic Disease of the Newborn, P. 121)

**BILIRUBIN METABOLISM:** As red blood cells are lysed, they release hemoglobin. Heme molecules (from hemoglobin) are converted to bilirubin. Bilirubin (unconjugated or indirect) is bound to serum albumin and transferred to the liver where it is conjugated to glucuronate by glucuronyl transferase. Conjugated (direct) bilirubin is excreted into bile. A fraction of bilirubin from the stool is reabsorbed into the blood via the portal circulation (enterohepatic circulation).

**BILIRUBIN ENCEPHALOPATHY:** The mildest form of bilirubin encephalopathy is **sensorineural hearing loss** due to damage to the cochlear nuclei. Severe encephalopathy causes **kernicterus**. Factors predisposing to neurotoxicity of **unconjugated** hyperbilirubinemia include:

- When bilirubin concentration **exceeds the binding capacity of serum albumin**
- Displacement of bilirubin from albumin by **acidosis** or certain drugs (*e.g.*, sulfonamides, ceftriaxone)
- Sepsis**
- Preterm infants** due to ↑ risk due lower serum albumin concentrations and ↑ risk for acidosis and sepsis.

#### **CAUSES of UNCONJUGATED (INDIRECT) HYPERBILIRUBINEMIA:**

##### **1. Increased lysis of RBCs (*i.e.*, increased hemoglobin release)**

- Isoimmunization (blood group incompatibility: Rh, ABO and minor blood groups)
- RBC enzyme defects (*e.g.*, G6PD deficiency, pyruvate kinase deficiency)
- RBC structural abnormalities (hereditary spherocytosis, elliptocytosis)
- Infection (sepsis, urinary tract infections)
- Sequestered blood (*e.g.*, cephalohematoma, bruising, intracranial hemorrhage)

- Polycythemia
  - Shortened life span of fetal RBCs (80 vs. 120 d)
- 2. Decreased hepatic uptake and conjugation of bilirubin**
    - Immature glucuronyl transferase activity in all newborns: term infants have 1% of adult activity, preterm infants have 0.1%.
    - Gilbert Syndrome
    - Crigler Najjar Syndrome (Non-hemolytic Unconjugated Hyperbilirubinemia): inherited conjugation defect (very rare)
    - Pyloric stenosis (mechanism is unknown)
    - Hypothyroidism
    - Infants of Diabetic Mothers (polycythemia is also common)
    - Breastmilk Jaundice (pregnanediol inhibits glucuronyl transferase activity)
  - 3. Increased enterohepatic reabsorption**
    - Breast feeding jaundice (due to dehydration from inadequate milk supply)
    - Bowel obstruction
    - No enteric feedings

### **EVALUATION of JAUNDICE (UNCONJUGATED)**

- 1. Initial evaluation:**
  - Total and direct bilirubin
  - Hematocrit
  - Blood type and Rh (infant & mother)
  - Direct Antiglobulin (Coombs) Test on infant
- 2. Later evaluation (as indicated):**
  - RBC smear, reticulocyte count (if evidence or suspicion of hemolytic disease)
  - Blood culture, urinalysis, urine culture
  - Thyroid function tests, G6PD assay, Hgb electrophoresis

### **MANAGEMENT of UNCONJUGATED HYPERBILIRUBINEMIA:**

#### **1. Healthy Term Newborn**

Age (h)	Bilirubin (mg/dL)	Treatment	
		Phototherapy	Exchange Transfusion
≤ 24	Visible Jaundice	Consult attending physician	
25-48	≥ 15	X	
	≥ 20	X	X
49-72	≥ 18	X	
	≥ 25*	X	X
> 72	≥ 20	X	
	≥ 25*	X	X

Recent data suggest that even healthy term infants may suffer mild neurologic damage with bilirubin concentrations >20 mg/dL.

- 2. Sick Term Newborns:** Start above therapies at lower total serum bilirubin levels. Consult attending physician for specific values.

- 3. Preterm Infants:** Because of ↑ risk of bilirubin encephalopathy, therapy should be started at lower bilirubin concentrations. In general, bilirubin should not be allowed to exceed the infant's weight in kg x 10 (*e.g.*, for 1.0 kg infant, keep bilirubin <10 mg/dL).

**CONJUGATED (DIRECT) HYPERBILIRUBINEMIA (CHOLESTASIS):**

Clinically, jaundice is green compared to jaundice due to unconjugated hyperbilirubinemia (yellow).

**1. Hepatocellular diseases:**

- A. Hepatitis:
  - Neonatal idiopathic hepatitis
  - Viral (Hepatitis B, C, TORCH infections)
  - Bacterial (*E. coli*, urinary tract infections)
- B. Total parenteral nutrition
- C. Hepatic ischemia (post-ischemic damage)
- D. Erythroblastosis fetalis (late, "Inspissated Bile Syndrome")
- E. Metabolic disorders (partial list):
  - Alpha-1 antitrypsin deficiency
  - Galactosemia, tyrosinemia, fructosemia
  - Glycogen storage disorders
  - Cerebrohepatorenal disease (Zellweger)
  - Cystic fibrosis
  - Hypopituitarism

**2. Biliary tree abnormalities:**

- A. Extrahepatic biliary atresia: In first 2 weeks, unconjugated bilirubin predominates; elevated conjugated bilirubin is late.
- B. Paucity of bile ducts (Alagille's vs. non-syndromic)
- C. Choledochal cyst
- D. Bile plug syndrome

**EVALUATION and MANAGEMENT of CHOLESTASIS:**

**1. Initial evaluation:**

- Total and direct bilirubin
- AST, ALT, GGT, urine reducing substances
- Hepatic ultrasound

**2. Later evaluation (as indicated):**

- Hepatitis B and C serology
- Very long chain fatty acids
- HIDA scan
- α1-antitrypsin deficiency studies
- Brain sonogram
- Cholangiogram

**3. Management:**

- Conjugated bilirubin is not toxic.
- Management is treatment of cause.
- Phototherapy will cause "bronzing" with conjugated hyperbilirubinemia.