JOURNAL CLUB

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Hyperbilirubinemia

Introduction

- Hyperbilirubinemia is defined as a total bilirubin >95th percentile on the hour specific Bhutani nomogram.
- **Physiological jaundice :**

  . This is attributable to physiological immaturity of the neonate to handle increased bilirubin production.

Physiological jaundice

Appears between 24 – 72hrs of age.

F**ull term infants**:

- **peak peak of 6 – 8 mg/dl by 3 days** of age.
  - **Max: 12 mg/dl**

Premature infants

- peak **10 – 12mg/dl on the fifth day** of life, rising
  - **Max: 15 mg/dl**

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- **Pathological jaundice :**

  . TSB concentrations are defined as non physiologic if it exceeds 5mg/dl on day 1 of life in a term neonate, 10mg/dl on day 2 of life or 12 – 13 mg/dl thereafter.

  (acc. to AIIMS PROTOCALS).

. Appearance of jaundice within 24hrs,
. TSB levels above the normal expected range,
. Presence of clinical jaundice beyond 3 weeks and conjugated bilirubin would be categorized as pathological jaundice.

Causes :

- 1. Increased bilirubin production.
- 2. Decreased bilirubin clearance.
- 3. Increased enterohepatic circulation.

RISK FACTORS

Major Risk Factors For Significant Hyperbilirubinemia Infants:

1. Clinical jaundice observed in first 24 hours of birth.
2. Previous sibling received phototherapy.
3. Cephalhematoma, subgaleal bleed or significant brusing.
4. Non optimal sucking/nursing.
5. Gestational age 35 – 36 weeks.
6. Blood group incompatilbility with +ve DCT, incidentally known hemolytic disease.

NEUROTOXICITY RISK FACTORS

1. Isoimmune hemolytic disease
2. G6PD deficiency
3. Asphyxia
4. Sepsis
5. Acidosis
6. Albumin < 3.0 mg/dl

Evaluation of infant with Hyperbilirubinemia

- HISTORY
- PHYSICAL EXAMINATION
- LAB INVESTIGATIONS

HISTORY	RELAVENCE
• Previous sibling with neonatal jaundice or family H/O anemia or splenectomy.	• Blood group incompatability (Rh or ABO), G6PD deficiency, spherocytosis, crigler-najjar, UGT varients.
• Maternal illness with fever and rash during pregnancy.	• Intra uterine infections
• Labour and delivery events.	• Asphyxia, trauma, use of oxytocin, .delayed cord clamping
• Maternal drugs (sulfonamides, nitrofurantoin, antimalarials)	• Hemolysis in a G6PD deficient infant.
• Liver disease in the family	• Glactosemia, alpha-1 antitrypsin deficiency

PHYSICAL EXAMINATION:

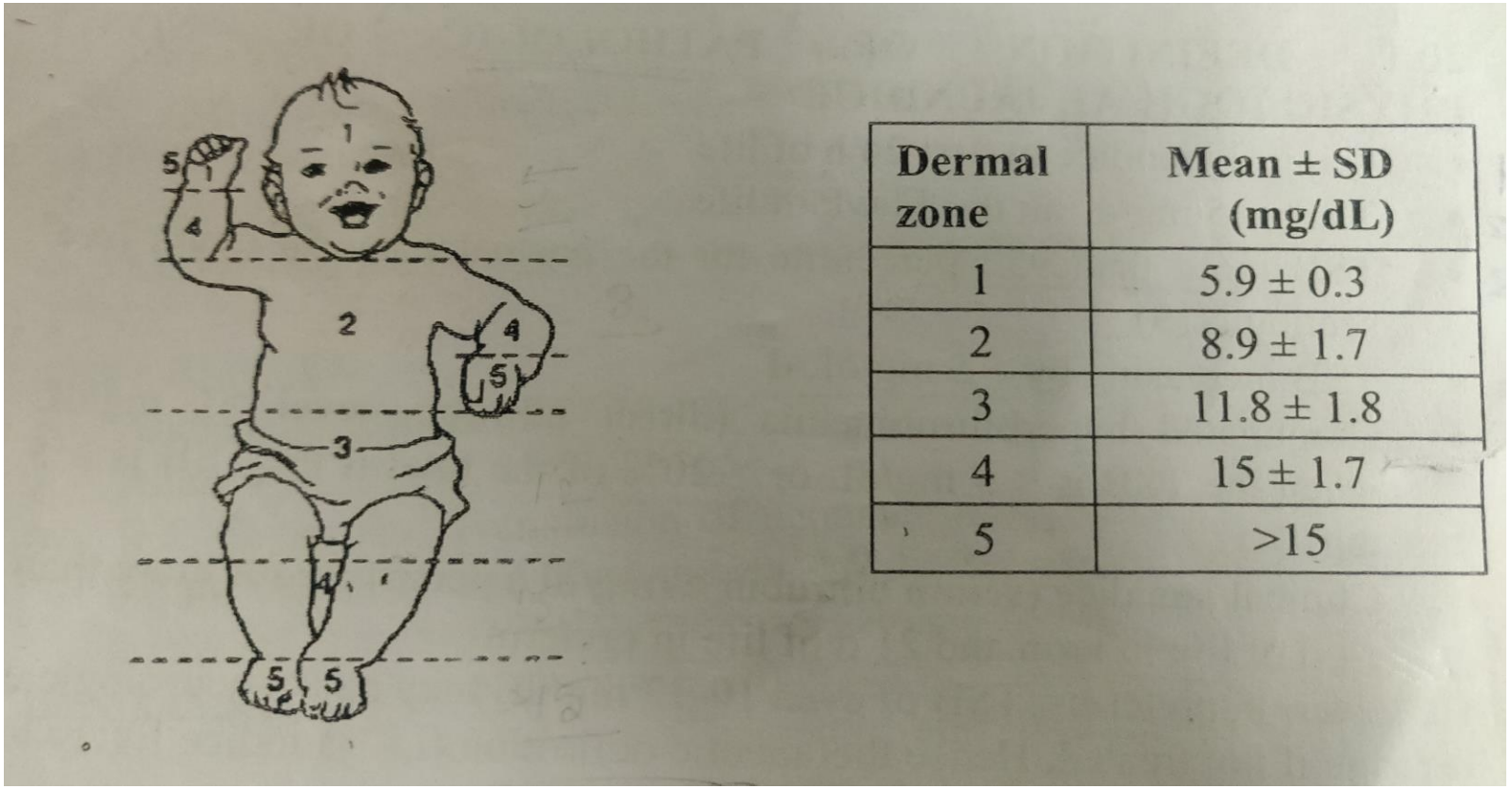
. Jaundice results from deposition of bilirubin in the skin and subcutaneous tissue.

.Blanching the skin with finger pressure makes it easier to observer jaundice.

. Jaundice typically progresses in a "cephalocaudal" direction, starting from face.

.The highest bilirubin levels are typically associated with jaundice below knees and in the hands.

- Correlation between icteric dermal zones(KRAMER) and serum bilirubin values.



Dermal zone	Mean ± SD (mg/dL)
1	5.9 ± 0.3
2	8.9 ± 1.7
3	11.8 ± 1.8
4	15 ± 1.7
5	>15

Jaundice infants should have a bilirubin measurement and to be examined for the following factors:

PHYSICAL EXAMINATION	RELAVENCE
• Small for gestational age	• Polycythemia, intra uterine infections
• Microcephaly	• Intra uterine infections
• Pallor	• Hemolytic anemia, extravasation of blood
• Bruises, cephalhematoma	• Increased bilirubin formation

Jaundice infants should have a bilirubin measurement and to be examined for the following factors:

PHYSICAL EXAMINATION	RELAVENCE
• Petichae	• Intra uterine infections, sepsis, erythroblastosis
• Hepatosplenomegaly	• Hemolytic anemia, intra uterine infectons, liver disease
• Chorioretinitis	• Intra uterine infections
• Urine staining diapers and clay coloured stools	• Cholestatsis

LAB INVESTIGATION:

1. **Blood grouping and Direct coombs test(DCT):** This should be done only if mother's group is O or Rh negative or if a minor blood group incompatibility is strongly suspected.

1. **G6PD enzyme deficiency**

3 . **Complete blood picture** – for evidence of hemolysis (increased reticulocyte count, fall in PCV, peripheral smear for spherocyte, elevated nucleated RBC count, anisopoikilocytosis and polychromasia.)

4. **Conjugated bilirubin fraction**: It must be assyaed at least once if jaundice persists beyond 5 days and/or when cholestasis is suspected.

5. If history and/ or presentation suggest sepsis, investigate for sepsis.

management

- **1. Phototherapy**

  . Initial intervention used to treat and prevent severe hyperbilirubinemia in

  - asymptomatic infants
  - infants with signs of Acute bilirubin encephalopathy.

. The rate of decline in TSB is determined by

- increased irradiance
- more exposed surface area
- a higher initial TB value.

2. Pharmacotherapy :

. **Intravenous IVIG** has been used in infants with hemolytic disease caused by Rh or ABO incompatability, when TB continues to raise even after intensive phototherapy.

. **0.5 to 1 gm/kg IVIG over 2 hrs and repeat the dose in 12 hrs if needed.**

No evidence of benefit with the above intervention.

Phenobarbitone :

- Improves **hepatic uptake, conjugation and excretion of bilirubin** thus helping in lowering of bilirubin.
- When used prophylactically **5mg/kg for 3 – 5 days** after birth, has shown to be effective in infants with hemolytic disease, extravasated blood and in preterms with out any side effects.

3. Exchange transfusion *:*

. Used when intensive phototherapy fails to prevent a rise in bilirubin.

. Effective method for rapid removal of biliruibin.

. In case of isoimmune hemolytic disease, ET also removes antibody and sensitized RBC's which replaced with donor RBCs lacking the sensitizing antigen.

. O Rh negative irradiated packed RBC that are resuspended in AB plasma and cross matched against maternal plasma and cells is used for the procedure.
. The volume required is to be 2 times the infants estimated blood volume, (2 times 80 – 90 ml/kg plus additional volume to account for tubing loses i.e, ~30 ml)

. Exchange transfusion is usually performed through an umbilical venous catheter using pull - push method in which alliquots of infants blood are removed and replaced with donor blood.
. Induvidual alliquot should be about 10% or less than the infants blood volume with a maximum volume of 10 ml for a term baby with weight > 3kg.

. Blood can be steadily withdrawn from umblical artery catheter at a rate of 2 to 4 ml/kg/min while an equivalent volume is slowly infused at the same rate through a venous catheter.

(**a isovolumetric procedure**.)

. **Albumin infused 1 to 2 hrs prior to the exchange transfusion promotes removal of more bilirubin because more extravascular bilirubin is drawn into circulation..**

. Immediately after double volume exchange transfusion, **TB level returns to approximately two – thirds of preexchange level.**

. This procedure replaces about 85% of the circulating RBC.
. Intensive phototherapy is to be stopped and TB should be monitored at 2, 4, 6 hrs of transfusion and then every 12 or 24 hrly.
. Increasing TB or recurrent neurologic signs are followed to asses need for exchange transfusion.

. Infants should be monitored for **complications**

- thrombocytopenia
- coagulation abnormalities
- hypoglycemia, hyperkalemia, hypocalcemia
- acid base abnormalities.

. **Less common complications:**

- NEC, portal vein thrombosis, cardiac arrythimias and infection.