



Neonatal Hyperbilirubinemia

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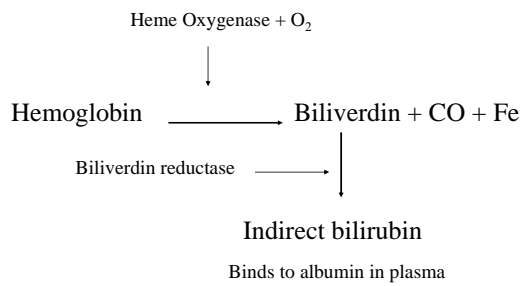
Neonatal Hyperbilirubinemia

- Visible jaundice:
 - Adults: Total serum bilirubin > 1.3-1.5 mg/dL
 - Newborns: > 5 mg/dL
- Situation where serum bilirubin is elevated to cause visible yellowing of skin / ocular sclerae
- Up to 50% of all newborns may develop jaundice in the first week of life

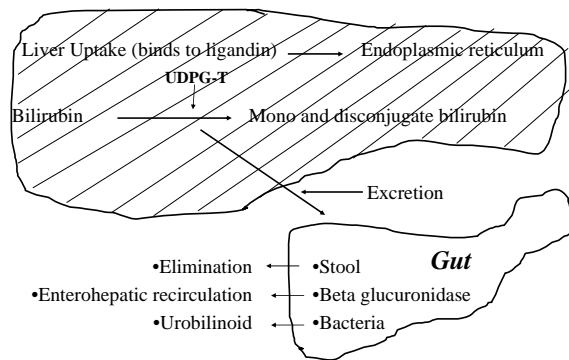
Source of Bilirubin

- Metabolism of heme. 6-10 mg/kg/day. (adults 3-4mg/kg/day)
 - 75%: from hemoglobin of old RBCs released from RES. 1 Gram produces 34 mg of bilirubin.
 - 25%: from ineffective erythropoiesis, myoglobin, cytochromes, catalase, peroxidase.

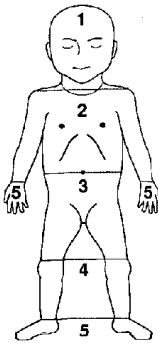
Metabolism



Conjugation



Dermal Zones of Jaundice



Dermal Zone	Bilirubin range (mg%)
1	4-6.4
2	5.3-12
3	8-17.5
4	15-20
5	> 15

Jaundice: Laboratory

- Total serum bilirubin
- Blood type, Rh, Coombs infant and mother
- Smear (morphology and reticulocytes)
- Hematocrit

Jaundice: Laboratory

- Antibody identification
- Direct bilirubin:
 - When more than 2 weeks old or signs of cholestasis
- If prolonged:
 - LFT, TORCH, sepsis work-up, metabolic, thyroid
- G6PD

Physiologic Jaundice

- Healthy infants
- up to 12mg/dL in 3rd day; in premature, 5th day.
- No hemolysis or bleedings
- No underlying metabolic disease

Mechanism

- ↑Production:
 - ↑ Volemia,
 - ↓ RBC span (90 days)
 - ↑ Ineffective erythropoiesis
 - ↑ Turnover of non Hb heme proteins

Mechanism

- ↑ Enterohepatic recirculation:
 - ↑ Glucuronidase
 - ↑ Bilirubin monoglucuronide
 - ↓ Intestinal bacteria
 - ↓ Intestinal motility and stooling

Mechanism

- ↓ Bilirubin Uptake : ↓ ligandin
- ↓ Conjugation : ↓ UDPG-T activity
- ↓ Hepatic excretion of bilirubin

Non Physiologic Jaundice

- May be difficult to distinguish from previous
- General features for recognition:
 - Onset at < 24 hrs
 - Bilirubin ↑ over levels for phototherapy
 - Bilirubin rise > 0.5 mg/dL/hr
 - Signs of underlying illness
 - vomiting, lethargy, poor feeding, ↓ ↓ weight
 - Age > 8 days in term or 15 days in premature

Non Physiologic Jaundice

•History:

- Familial:
 - G6PD, spherocytosis, metabolic, enzymes.
- Siblings:
 - Immune, breast milk.
- Pregnancy:
 - Infections, drugs, diabetes.
- Delivery:
 - Trauma, cord clumping, asphyxia.

Bilirubin toxicity:

Cerebral Penetration:

As free indirect bilirubin or bound when disrupted BBB

- Disrupted BB barrier
 - Hyperosmolarity
 - Anoxia
 - Hypercarbia
 - Prematurity



Bilirubin toxicity:

- ↑ Unbound indirect bilirubin
 - ↓ Albumin concentration
 - 1 Gram albumin binds 8.5 mg bilirubin
 - Displacement from albumin site
 - FFA
 - Drugs:
 - Sulfonamides
 - Acidosis



Bilirubin toxicity: Kernicterus

Neuronal injury + yellow staining of brain
↑ incidence in hemolytic disease especially Rh

Localization

- Basal ganglia
- Cranial nerve and cerebral nuclei
- Hippocampus
- Anterior horn of spinal cord

Bilirubin toxicity: Acute encephalopathy

- I) Hypotonia, lethargy, high pitched cry, poor suck
- II) Hypertonia of extensor muscles
 - opisthotonus, rigidity, oculogyric crises, retrocollis
- III) Return of hypotonia after 1 week

Bilirubin toxicity: Chronic complications

- Athetosis
- Sensorial deafness
- Limited upward gaze
- Intellectual deficits
- Dental dysplasia



Isoimmune hemolytic disease of the newborn

- Etiology: Rh , A, B, or minor blood types (Kell, Duffy, E, C, c)
- 15% of people are Rh-
- Coombs +
- Maternal sensitization due to previous pregnancy, transfusion, amniocentesis, abortion

IHDN: Newborn Management

- Check immediately after birth
 - Hematocrit
 - Bilirubin
 - Blood type
- 50% will only need phototherapy
- 24% will be anemic and cord bilirubin > 4/dL
 _____ exchange transfusion

ABO hemolytic disease of the newborn

- 15% of pregnancies mother O infant A or B
- 20% will develop significant jaundice
- 10% will need phototherapy.
- Presentation:
 - Early jaundice (< 24hs of life)
 - Many times Combs -, but there are antibodies
 - Blood smear: spherocytes

Treatment: Phototherapy

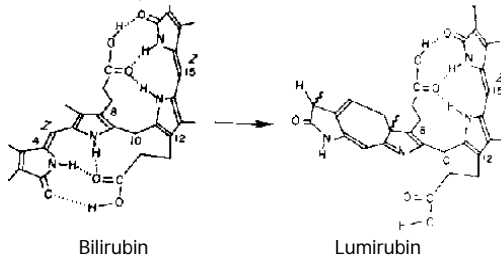
- Bilirubin best absorbs light at 450 nm.
- The best is to provide it with blue light.
- White range: 380-700 nm also adequate.
- Irradiation generates photochemical reaction in the extravascular space of the skin
- A higher illuminated area increases effectiveness

Treatment: Phototherapy mechanism

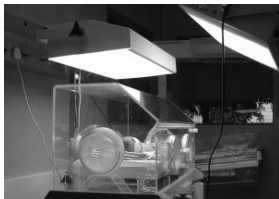
- Photoisomerization:
 - Natural Isomer 4Z,15Z \rightleftharpoons 4Z15E polar, hydrosoluble \rightarrow blood \rightarrow biliar secretion (unconjugated)
 - Slow excretion and fast reisomerization, reabsorbed.
- Structural isomerization:
 - Cyclization to lumirubin (irreversible) \rightarrow bile and urine
 - Fast excretion not reabsorption.
 - Related to dose of phototherapy (intensity of light)
- Photooxidation: Small polar products. very slow

Treatment: Phototherapy mechanism

Main Pathway



Treatment: Phototherapy



PHOTOTHERAPY
UNIT



BILIBED

Phototherapy: Technique

- Fluorescents ,spots or bili blankets
- More than $5\mu\text{w}/\text{cm}^2$ at 425-475nm
- Naked , covering eyes
- Increase fluids 10-20%
- Check bilirubin every 12-24hs
- Stop at $13\pm 1\text{mg}\%$ in term and $10\pm 1\text{mg}\%$ in preterm
- Check 12-24hs later for rebound

Phototherapy: Side effects

- Increased water loss
- Diarrhea
- Retinal damage
- Bronze baby, tanning
- Mutations in DNA? → shield scrotum
- Disturb of mother-infant interaction.

Exchange transfusion:

- Oldest & most effective treatment for hyperbili
- Mortality 0.3-1.2% in term infants, up to 10-25% in sicker preterm infants
- Morbidity includes: anemia, apnea, bradycardia, hypothermia, sepsis, NEC, thromboembolic phenomena, thrombocytopenia, metabolic disturbances, GVHD/transfusion reaction

Indications for Early Exchange

- Hydrops in a known sensitized infant
- In hemolytic disease:
 - Cord bilirubin > 4.5 mg/dL and Hb <11 mg/dL
 - Serum bilirubin rising > 1 mg/dL/hr on Phototherapy
 - Hb 11-13 mg/dl, and bili rising >0.5 mg/dl on Phototherapy

Exchange Transfusion

- NPO
- Place UAC / UVC preferably
- Generally use type specific PRBC, Rh- in Rh sensitized and O type in ABO sensitized with Hct 50-60
- Double volume exchange: $\text{wt (kg)} \times 80 \text{ cc/kg} \times 2$
- Exchange in 5-20 cc increments depending on baby size (< 5% of blood volume)

Exchange transfusion: Complications

- Bleeding
 - Thrombocytopenia, loss of factors.
- Infections
- Hemolysis
- GVHD
- Other
 - Fever, hypothermia, NEC?



Neonatal Jaundice: Other treatments

- Phenobarbital: ↑ conjugation
- Oral agar: ↓ enterohepatic circulation
- Metalloporphyrins: inhibit bilirubin production.
 - competitors of heme oxygenase
- IVIG: inhibits hemolysis.
 - (binds to FC receptor of reticuloendothelial cells)

Management of Hyperbilirubinemia in the Healthy Term Newborn*

Age, hours	TSB Level, mg/dL (µmol/L)			
	Consider Phototherapy	Phototherapy	Exchange Transfusion if Intensive Phototherapy Fails	Exchange Transfusion and Intensive Phototherapy
<= 24§
25-48	≥12 (170)	≥15 (260)	≥20 (340)	≥25 (430)
49-72	≥15 (260)	≥18 (310)	≥25 (430)	≥30 (510)
> 72	≥17 (290)	≥20 (340)	≥25 (430)	≥30 (510)

* TSB indicates total serum bilirubin.

§ Term infants who are clinically jaundiced at <=24 hours old are not considered healthy and require further evaluation.

Diagnostic approach to neonatal jaundice

