# Neonatal Jaundice

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# Neonatal hyperbilirubinemia

- **Jaundice** - yellow discoloration of the skin and sclerae caused by increased concentration of bilirubin in the intracellular and extracellular space
  - becomes visible around 80 μmol/l

- **Hyperbilirubinemia** - elevation of the bilirubin in blood serum > 17 μmol/l

# Incidence

- Term infants 60%
- Preterm infants 80%

- The most common condition that requires medical attention in newborns

# Metabolism of Bilirubin

- **source:** heme molecule
  - 80% haemoglobin
  - 20% nonhaemoglobin molecules (myoglobin, cytochromes..)
- **daily production**
  - adult: 3-4 mg/kg/day
  - neonate 6-10 mg/kg/day

# Types of Bilirubin

- **Unconjugated Bilirubin**
  - non-direct
  - soluble in fat
  - bind to albumin
  - toxic
  - can cross haemato-encephalic barrier
- **Conjugated Bilirubin**
  - direct
  - soluble in water
  - conjugated to glucuronic acid
  - non toxic
  - excreted in urine and stool

# Physiological Differences in Newborns

- **Increased production of bilirubin**
  - higher hematocrit
  - shorter life of erythrocytes (90 days)
  - higher entero-hepatic circulation

- **Decreased elimination of bilirubin**
  - decreased liver uptake of bilirubin (ligandin Y)
  - lower conjunctional function (glucuronic acid)
  - decreased elimination through GIT (higher β glucuronidase activity)

# Pathological Differences in Newborns

- **Increased production of bilirubin**
  - Hemolytic disease
  - Congenital defects of erythrocytes
  - Polycythemia
  - Haemathomas, cephalhaematoma
- **Decreased elimination of bilirubin**
  - Prematurity
  - Defects of conjugation
  - GIT obstruction (congenital disease)
- **Complex diseases**
  - Hypoxia, infections, sepsis...

# Bilirubin Toxicity

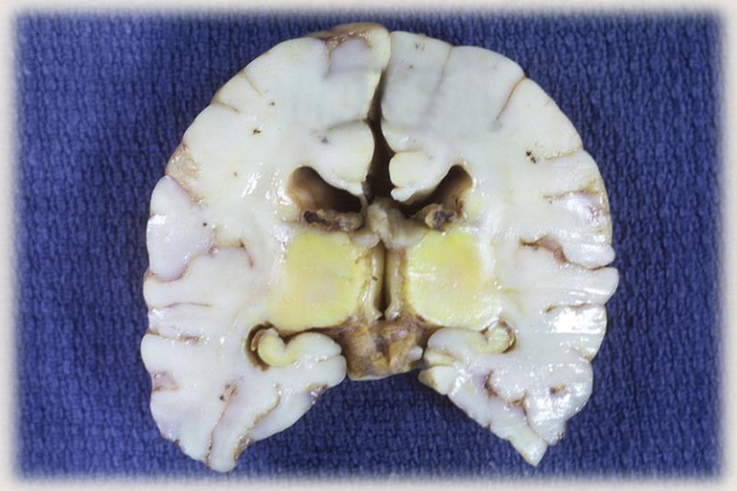
- unconjugated bilirubin can cross blood-brain barrier
- **cytotoxicity** - disfunction of cell membranes, efflux of ions from cells, inhibition of enzymes of mitochondria and neurotransmitters, oxidative phosphorylation and DNA synthesis
- factors: level of bilirubin, albumin levels, blood brain barrier function, pH, prematurity, hypoxia, sepsis,

# Neurotoxicity - Kernicterus

**Acute bilirubin encephalopathy**

- 1.phase: hypotony, lethargy, high pitched cry, fever
- 2.phase: opisthotonus, seizures, exitus

**Chronic bilirubin encephalopathy**



- 1.phase: spasticity
- 2.phase: spasticity,  athetoid cerebral palsy, dystonia, auditory dysfunction, PMR,

# Diagnosis

**Hyperbilirubinemia**

Unconjugated

Conjugated

Physiological

Pathological

Pathological

# Physiological Jaundice

- appears after 24 hours
- increases slowly
- maximal increase - 5th day
- decrease after one week
- usually lower than 300 μmol/l
- otherwise healthy appearing baby
- usually intervention is not needed

# Pathologic Jaundice

- appears in first 24 hours of life
- increases rapidly
- prolonged duration after 10 days
- unhealthy looking baby
- high risk of neurotoxicity if levels > 420-500 μmol/l
- need for treatment

# Pathological Jaundice

- Unconjugated hyperbilirubinemia
- **Haemolytic**
  - Rh incompatibility
  - ABO incompatibility
  - Haematomas, cephalhaematoma, polycythemia
  - Sepsis, DIC
  - Spherocytosis, eliptocythosis….
- **Non-haemolytic**
  - Breast milk jaundice
  - Crigler-Najjar syndrome
  - Gilbert syndrome
  - Hypothyreosis, mothers DM, medications

# Pathological Jaundice

- Conjugated hyperbilibinemia
- **Hepatic**
  - Infections - sepsis, TORCH
  - Idiopatic neonatal hepatitis
  - Inborn errors of metabolism (tyrosinemia, galactosemia..)
- **Post-hepatic**
  - Biliary atresia
  - Allagile syndrome

# Rh Incompatibility

- Rh negative mothers
- Rh positive baby
- in first pregnancy mother forms antibodies against baby's erythrocytes
- in second pregnancy Rh antibodies passes the placenta and may destroy erythrocytes of fetus (hemolysis)
  - anemia, ascites, hydrops faetalis (erythroblastosis faetalis)
  - icterus - anemia
- prevention: Rhega

# ABO Incompatibility

- Mothers with blood type 0
- Baby with other blood type
- mother forms antibodies against antigens of baby’s erythrocytes
- may appear in first pregnancy
  - icterus - anemia

# Breast Milk Jaundice

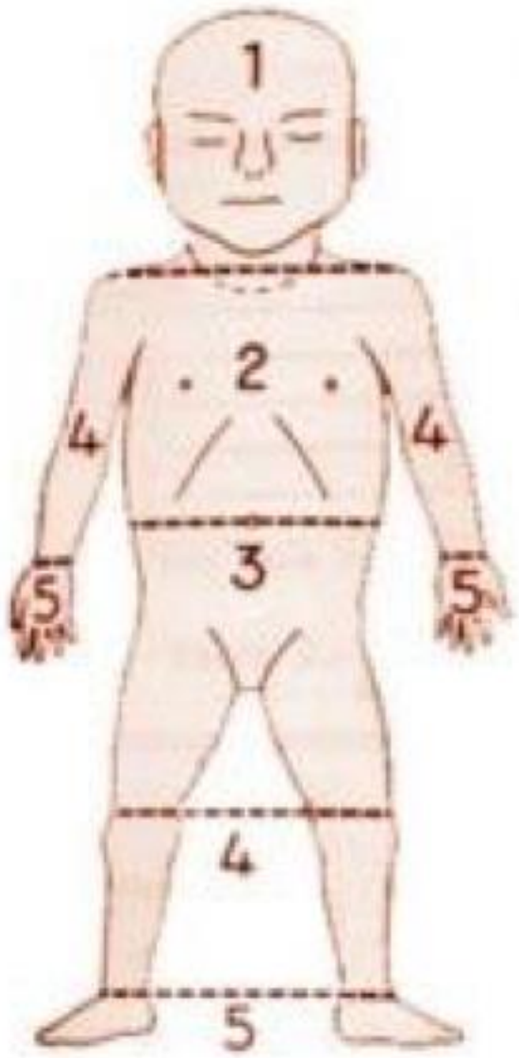
- jaundice of neonates that are breastfed
- prolonged duration due to increased entero-hepatic circulation
- increased activity of beta-glucuronidase (present in breas milk)
- decreases if breastfeeding is interrupted
- the most common cause of prolonged jaundice in term infants

# Gilbert Syndrome

- Unconjugated hyperbilirubinemia
- autosomal recessive
- 8% of population
- more frequent in males
- appears without signs of hemolysis or liver disease
- mild, chronic, intermittent episodes of jaundice
- worsened by stress, illness, fasting, sport, alcohol or nicotine abuse

# Clinical Assessment of Jaundice

Schema for grading extent of jaundice




| Grade | Extent of Jaundice |
|---|---|
| 0 | None |
| 1 | Face and neck only |
| 2 | Chest and back |
| 3 | Abdomen below umbilicus to knees |
| 4 | Arms and legs below knees |
| 5 | Hands and Feet |

- Gestational age
- Birthweight
- Risk factors
- Healthy newborn - unhealthy newborn
- Clinical assessment of hyperbilirubinemia
- Poor feeding, lethargy
- Signs of kernicterus
- Laboratory tests

# Laboratory tests

- Blood count , reticulocytes, peripheral smear (anemia, polycythemia)
- Blood group, Coomb's ‘test (incompatibility)
- Bilirubin (conjugated, total)
- CRP (sepsic screening)
- Hepathal enzymes
- TORCH
- Lactate
- Amonium, thyroid function,

# Threatment

- Phototherapy
- Imunoglobulins
- Exchange transfusion
- Drugs

# Phototherapy

**Bilirubin**

water insoluble

↓

**Photo isomere of bilirubin**

(photodegradation of Bi)

water soluble

↓

urine

# Adverse Effects of Phototherapy

- increased insensible water loss, dehydratation
- hyperthermia
- skin rash
- loose stools
- retinal damage
- hypocalcemia
- interference with mother - child bonding
- bronze baby syndrome (if conjugated hyper bilirubinemia)

# Immunoglobulins

- IVIG
- indication: Rh, AB0, other blood group incompatibility
- significantly decreases the need for exchange transfusion
- Dose: 1g/kg/day

# Exchange Transfusion

- procedure performed to remove bilirubin and antibodies associated with red blood cell haemolysis
- aim:
  - lower bilirubin levels (avoid neurotoxicity)
  - remove affected red blood cells and circulating antibodies
  - correct anemia
- very risky procedure