
بسم الله الرحمن الرحيم

NEONATAL DISORDERS

Bilirubin metabolism

Bilirubin is the main breakdown product of haem. Unconjugated bilirubin is lipid soluble, transported in the blood bound to albumin

and actively transported into hepatocytes where it is conjugated with glucuronic acid by the enzyme uridine diphosphoglucuronosyl transferase (UDPGT).

The water soluble conjugated bilirubin is excreted as a component of bile. A fraction of this bilirubin is hydrolysed and reabsorbed via the enterohepatic circulation

I- Physiologic Jaundice

Physiological jaundice

After birth bilirubin levels rise to a peak between day 3–4, fall quite rapidly for 2–3 days and then decline over 1–2 weeks.

This 'physiological jaundice' is a result of rapid breakdown of haemoglobin and immaturity of liver enzymes. Physiological jaundice is not clinically apparent in the first 24 h of life and is exacerbated in preterm or breast-fed infants who exhibit a delayed but higher peak in bilirubin levels with a more gradual decline. Physiological jaundice is exacerbated by polycythaemia, bruising, dehydration, and low caloric intake which is more common in breast-fed infants

Pathological jaundice: early onset Aetiology

The causes are best classified according to age of onset. *<24 h* Rapidly developing jaundice on the first day is usually caused by haemolysis due to:

Isoimmunisation:

rhesus disease: now uncommon because of prophylaxis. It is usually identified on antenatal screening tests and if severe can cause anaemia and fetal hydrops.

ABO incompatibility: now the most common cause of haemolytic jaundice. Although ~20% of pregnancies are 'ABO' incompatible only about 1% result in haemolysis. The most common combination is an Orh + ve mother with an ARh + ve or BRh + ve baby. Maternal IgG anti-haemolysin crosses the placenta and causes haemolysis in the infant.

The direct antibody test (DAT, Coombs test) is positive.

Red cell defects:

G6PD defi ciency: X-linked recessive disorder so mostly affects males; severe neonatal jaundice can occur with certain variants

hereditary spherocytosis (HS): autosomal dominant inheritance with a positive family history in 75%

Congenital infection: an uncommon cause of early onset haemolytic jaundice.

24 h to 2 weeks

Infection: urinary tract infection

Haemolysis: presenting late, especially G6PD deficiency

Extravasated blood: bruising, cephalhaematoma

Polycythaemia: delayed cord clamping

Increased enterohepatic circulation: bowel obstruction

Metabolic disorders: galactosaemia, tyrosinaemia

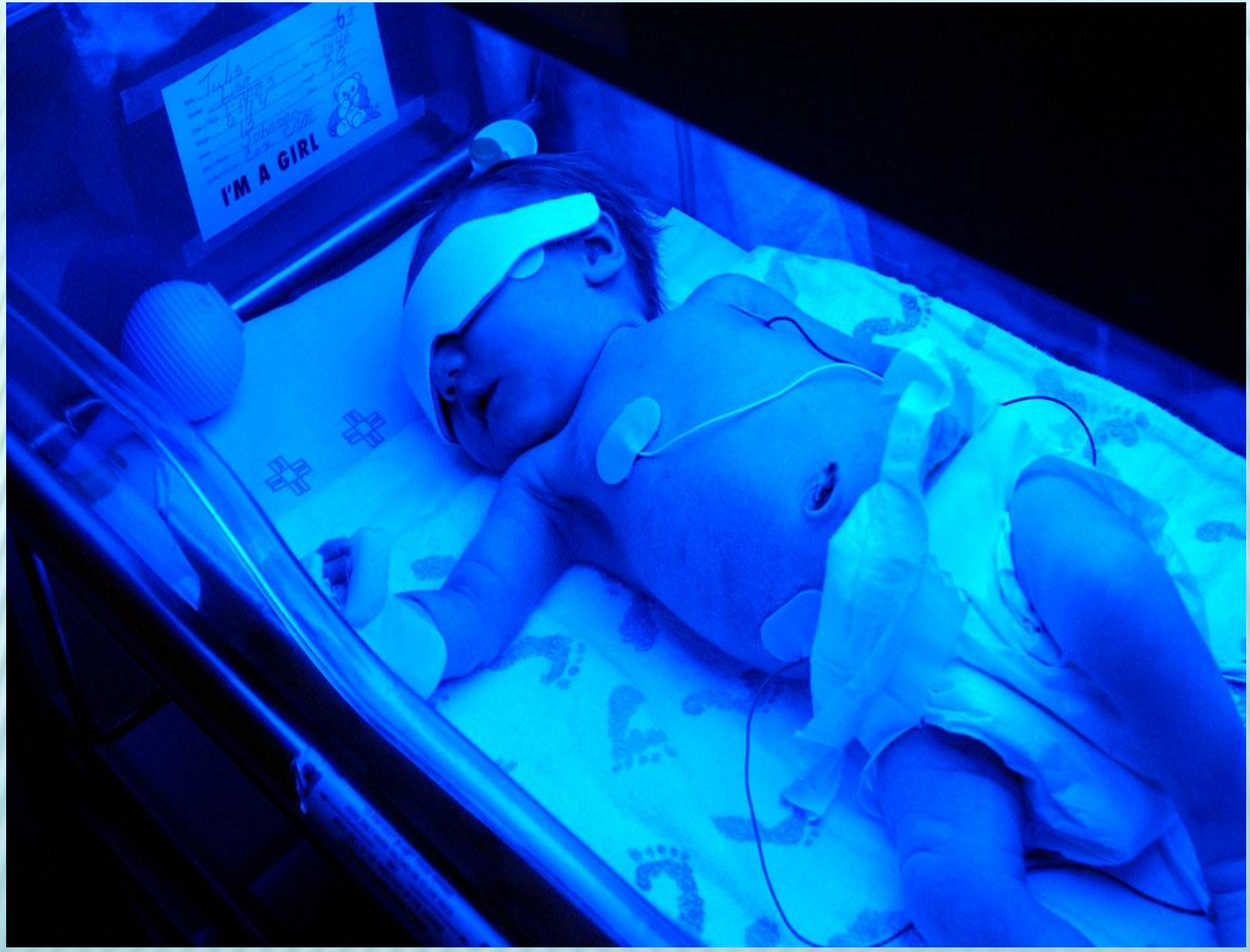
Hepatic enzyme defects: Crigler–Najjar, Gilbert syndrome.

Clinical evaluation

Jaundice is detectable clinically when serum bilirubin exceeds 5 mg/dl. Unconjugated hyperbilirubinaemia imparts a light yellow discoloration whereas conjugated hyperbilirubinaemia has a darker, greener hue.

The history should include enquiry about the pregnancy, family history of haemolytic or genetic disease, drug history, associated symptoms, and whether breast or formula fed.

Examination may reveal: pallor due to haemolysis and anaemia, fever or weight loss from infection or dehydration, dysmorphic features, or signs of congenital infection


I'M A GIRL

Management

Investigations

Bilirubin: measurement of serum bilirubin is indicated if there is jaundice in the first 24 h or signifi cant clinical jaundice.

Blood group and direct antibody test

Full blood count: reticulocytes, red cell morphology

Haemolysis with negative DAT: tests for HS, G6PD

Urine: microscopy and culture, reducing substances

Treatment

Treatment options are designed to prevent bilirubin encephalopathy and include phototherapy and exchange transfusion. There is no universal agreement with regard to the precise level of serum bilirubin at which treatment should commence. Tables of guideline thresholds are available which incorporate relevant additional factors including gestational age and weight, postnatal age, well or sick, and bilirubin/albumin ratios.

Phototherapy

Phototherapy is commenced in an infant <24 h with a bilirubin level >6-10 mg/dl and in well term infants with level >17-19 mg/dl at 72h. Lower thresholds apply to preterm and sick infants.

Blue light of wavelength 425—475 nm converts unconjugated bilirubin to harmless, water-soluble products. After 4 h, 20% of total bilirubin is in the form of non-toxic isomers. Intensive phototherapy combines overhead lights with a fibreoptic blanket and can reduce bilirubin levels by 40% or more in 24 h in a non-haemolysing infant.

Disadvantages of phototherapy include parental anxiety and separation, loose stools due to decreased gut transit time, rashes, risk of hypothermia/hyperthermia, and increased fluid loss via skin and gut

- Phototherapy should ideally be continuous.
- infants can ‘come out of the lights’ for feeds.
- A rebound is usual after stopping a course of phototherapy and this must be monitored.
- When phototherapy is used in an infant with an increased conjugated bilirubin component a transient bronze pigmentation of the skin may occur.

Exchange transfusion

This technique not only provides rapid correction of hyperbilirubinaemia but also corrects anaemia and removes haemolytic antibody in haemolytic jaundice due to isoimmunisation.

It is now rarely required, but indications include:

- Severe haemolytic disease: bilirubin rising at >0.5 mg/dl per hour despite phototherapy
- Symptomatic bilirubin encephalopathy.
- The infant's blood is removed in aliquots up to a total of twice the blood volume (2 × 80 mL/kg) and replaced with transfused blood.

Hazards include thrombosis and embolism, infection, NEC, metabolic abnormalities including • hypocalcaemia andhyperkalaemia, and coagulation abnormalities

Bilirubin toxicity

Unconjugated bilirubin is lipid soluble and able to cross the blood–brain barrier to enter the brain where it exerts a toxic effect in the brain stem, basal ganglia, hippocampus, cerebellum, and acoustic nerve.

Bilirubin entry is increased by hypoxia, acidosis, infection, or displacement from albumin.

Bilirubin encephalopathy and kernicterus

Kernicterus describes the yellow staining of basal ganglia seen in infants who have died of acute bilirubin toxicity.

Bilirubin encephalopathy is the clinical state caused by hyperbilirubinaemia

and characterized by initial hypotonia and lethargy followed by hypertonicity, opisthotonus, seizures, coma, and death.

The sequelae of bilirubin encephalopathy include athetoid cerebral palsy, high-frequency sensorineural hearing loss, paralysis of upward gaze, and learning

difficulties. The relationship between serum bilirubin, bilirubin encephalopathy, and permanent CNS damage is complex, rendering it difficult to establish guidelines for jaundice treatment based on serum bilirubin levels.

The risk of toxicity is increased by:

Pre-term birth: short gestation Rapidly rising serum bilirubin and prolonged peak

Hypoalbuminaemia Coexisting hypoxia, acidaemia, hypoglycaemia, sepsis.

Prolonged jaundice

Prolonged jaundice is defined as visibly detectable hyperbilirubinaemia beyond 2 weeks in a term infant and 3 weeks in a preterm infant. It can be a sign of serious underlying liver disease but the most common cause in term infants is benign, breast-milk related jaundice.

Unconjugated hyperbilirubinaemia

Breast milk jaundice is the most common cause. Jaundice persists beyond 14 days in up to 40% of breastfed babies and 9% of breastfed infants are still jaundiced at 28 days of age.

Acute neonatal causes such as haemolysis or low-grade infection may persist beyond 2 weeks.

Less common causes include increased enterohepatic circulation from intestinal obstruction in pyloric stenosis, hepatic enzyme defects, and hypothyroidism or cystic fibrosis

Conjugated hyperbilirubinaemia

Obstruction:

extrahepatic: biliary atresia, choledocal cyst, inspissated bile/bile plug

intrahepatic: Alagille syndrome

Neonatal hepatitis syndrome

Metabolic or endocrine: ⟨1-antitrypsin defi ciency, galactosaemia, fructosaemia, tyrosinosis, hypermethioninaemia, glycogen storage diseases, cystic fibrosis, peroxisomal disorders, hypopituitarism, hypoadrenalism

- *Chromosomal disorders:* Turner syndrome, trisomy 13, 18, or 21

Infections: UTI, congenital infections, viral infections.

Miscellaneous: drugs erythromycin, rifampicin, prolonged TPN.

Total and conjugated bilirubin: split bilirubin

Haematocrit/PCV

Urine dipstick, microscopy, and culture LFT TFT

Conjugated hyperbilirubinaemia >25 micromol/L is always pathological and requires full investigation

One important aim is to distinguish biliary obstruction requiring surgical intervention from intrahepatic causes

gamma GT levels

Coagulation screen, viral serology ⟨1-antitrypsin levels, urine for reducing substances

Plasma and urine organic and amino acids

Abdominal ultrasound scan.

IM vitamin K should be given prior to transfer for investigation to prevent late-onset haemorrhagic disease.

Neonatal seizures

The causes of seizures in the newborn may be:

Cerebral:

hypoxic-ischaemic encephalopathy

cerebral infarction

intracrania haemorrhage

Metabolic:

hypoglycaemia, hypocalcaemia,

hypo- or hypernatraemia.

inborn errors of metabolism

Infection: meningitis or encephalitis

Drug withdrawal: neonatal abstinence syndrome.

Rare causes include brain malformations, pyridoxine defi ciency, and benign familial neonatal seizures.

10% are of unknown cause.

Seizures in the newborn may be subtle and manifest as episodes of apnoea and oxygen desaturation, transient eye deviation, altered consciousness, and floppiness as well as generalized or focal clonic or tonic movements.

Investigations to consider include:

Blood glucose, U&E, calcium, magnesium levels, coagulation screen

Blood gases, ammonia, lactate, amino acids

Septic screen: FBC, blood cultures, lumbar puncture

EEG and cerebral function monitoring (CFM)

Neuroimaging: cranial ultrasound, CT or MRI.

Treatment of the underlying cause is combined with control of the fits if they are prolonged or frequent with anticonvulsants:

phenobarbital, phenytoin or midazolam. Assisted ventilation may be necessary.

Thank you