Neonatal jaundice

What is neonatal jaundice?

Bilirubin levels are higher in neonates than in adults because newborn babies have a higher concentration of red blood cells, which also have a shorter lifespan. Red blood cell breakdown creates unconjugated bilirubin which circulates mostly bound to albumin. Unconjugated bilirubin is metabolised by the liver to produce conjugated bilirubin which is excreted in the stool.[1]

Neonatal jaundice causes (aetiology)[1] [2]

Physiological jaundice

- This results from increased erythrocyte breakdown and immature liver function.
- It presents at 2 or 3 days of age, begins to disappear towards the end of the first week and has resolved by day 10.
- The bilirubin level does not usually rise above 200 µmol/L and the baby remains well.
- However, the bilirubin level may go much higher if the baby is premature or if there is increased red cell breakdown - eg, extensive bruising, cephalohaematoma.

Early neonatal jaundice
Onset less than 24 hours:

- Haemolytic disease: eg, haemolytic disease of the newborn (rhesus), ABO incompatibility, glucose-6-phosphate dehydrogenase deficiency, spherocytosis.
- Infection: congenital (eg, toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex, syphilis) or postnatal infection.

- Increased haemolysis due to haematoma.
- Maternal autoimmune haemolytic anaemia: eg, systemic lupus erythematosus.
- Crigler-Najjar syndrome or Dubin-Johnson syndrome.
- Gilbert's syndrome.

Prolonged jaundice
Jaundice lasting for longer than 14 days in term infants and 21 days in preterm infants:

- Infection - eg, urinary tract infection.[3]
- Hypothyroidism, hypopituitarism.
- Galactosaemia.
- Breast milk jaundice: the baby is well and the jaundice usually resolves by six weeks but occasionally continues for up to four months.
- Gastrointestinal (GI): biliary atresia, choledochal cyst, neonatal hepatitis.

Conjugated hyperbilirubinaemia

- Infection.
- Parenteral nutrition.
- Cystic fibrosis.
- Metabolic: alpha-1-antitrypsin deficiency, galactosaemia, aminoacidurias, organoacidaemias.
- GI: biliary atresia[4] , choledochal cyst, neonatal hepatitis.
- Endocrine: hypothyroidism, hypopituitarism.

How common is neonatal jaundice? (Epidemiology)

Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life; about 10% of breastfed babies are still jaundiced at 1 month of age.[5]

Risk factors

The risk of developing significant **neonatal jaundice** is increased in:[2] [6]

- Low birth weight: premature and small for dates.
- Breast-fed babies.
- A previous sibling with neonatal jaundice requiring phototherapy.
- Visible jaundice in the first 24 hours.
- Infants of mothers who have diabetes.
- Male infants.
- East Asians.
- Populations living at high altitudes.

Neonatal jaundice symptoms

Parents, carers and healthcare professionals should all look for jaundice. Check the naked baby in bright and preferably natural light. Examination should include the sclerae, gums and blanched skin. You should not rely on visual inspection alone to estimate the bilirubin level in a baby with jaundice.[7]

- Neonatal jaundice first becomes visible in the face and forehead. Blanching reveals the underlying colour. Jaundice then gradually becomes visible on the trunk and extremities.
- In most infants, yellow colour is the only finding on physical examination. More intense jaundice may be associated with drowsiness.
- Neurological signs - eg, changes in muscle tone, seizures, or altered crying - require immediate attention to avoid kernicterus.

- Hepatosplenomegaly, petechiae and microcephaly are associated with haemolytic anaemia, sepsis and congenital infections.
- Hepatitis (eg, congenital rubella, CMV, toxoplasmosis) and biliary atresia cause a raised conjugated bilirubin and have a marked jaundice and pale stools and dark urine, usually presenting in the third week of life.

Investigations

Do not rely on visual inspection alone to estimate the bilirubin level in a baby with suspected jaundice. Usually, a total serum bilirubin level is the only testing required in a moderately jaundiced infant who presents on the second or third day of life and is otherwise well. Further investigation is essential for any baby who is also unwell, presents in the first 24 hours or has prolonged (after 10 days) jaundice.[8]

- Bilirubin level:[7]
    - Use a transcutaneous bilirubinometer in babies with a gestational age of 35 weeks or more and postnatal age of more than 24 hours.
    - If a transcutaneous bilirubinometer is not available, measure the serum bilirubin.
    - If a transcutaneous bilirubinometer measurement indicates a bilirubin level greater than 250 µmol/L check the result by measuring the serum bilirubin.
    - Always use serum bilirubin measurement to determine the bilirubin level in babies:
        - With jaundice in the first 24 hours of life.
        - Less than 35 weeks of gestational age.
    - Always use serum bilirubin measurement for babies at or above the relevant treatment thresholds for their postnatal age and for all subsequent measurements.
    - Do not use an icterometer.
    - Do not measure bilirubin levels routinely in babies who are not visibly jaundiced.
    - Measurement of conjugated bilirubin is particularly important for babies with hepatosplenomegaly, petechiae or thrombocytopenia (or any other indication of liver or biliary disease, metabolic disorder or congenital infection) and for babies with prolonged jaundice.
- LFTs: hepatitis, cholestatic disease.
- Infection screen (must be excluded in any baby who is unwell or presents in the first 24 hours or after day 3): TORCH syndrome (**t**oxoplasmosis, **o**ther, **r**ubella, **C**MV and **h**erpes simplex) congenital infection screen, surface swabs including umbilicus, throat swabs, urine culture, blood culture, lumbar puncture, CXR.

- Haemolysis:
    - Blood type and Rh determination in mother and infant.
    - Reticulocyte count.
    - Direct Coombs' testing in the infant.
    - Haemoglobin and haematocrit values.
    - Peripheral blood film for erythrocyte morphology.
    - Red cell enzyme assays: G6PD activity (G6PD deficiency), pyruvate kinase deficiency.
- Reducing substance in urine: screening test for galactosaemia (provided the infant has received sufficient quantities of milk).
- TFTs.
- Ultrasound, hepatobiliary iminodiacetic acid (HIDA) radionuclide scan, liver biopsy and laparotomy may be required for cholestatic jaundice in the differentiation between hepatitis and biliary atresia.

Neonatal jaundice treatment and management

- Monitor the bilirubin level.
- Referral for urgent hospital assessment if jaundice presents in the first 24 hours of life, the baby is jaundiced and unwell, or for prolonged jaundice (see below).
- Treatment of the underlying cause.
- Increase fluid intake - usually oral but may require intravenous fluids depending on the cause and the well-being of the baby.

- Phototherapy:
    - The indications and use of phototherapy vary between units and are dependent not only on the level of the serum bilirubin but also on the gestation of the baby, rate of rise of bilirubin, likely underlying cause and well-being of the baby.
    - Phototherapy should be started immediately if a rapidly rising bilirubin is expected (eg, haemolytic disease) and with jaundice at less than 24 hours.[9]
    - The more premature the infant, the lower the levels of bilirubin that are tolerated. Prophylactic phototherapy to prevent jaundice in preterm or low-birth-weight infants helps to maintain a lower serum bilirubin concentration and may have an effect on the rate of exchange transfusion and the risk of neurodevelopmental impairment.[10]
    - Essential care of a baby receiving phototherapy includes ensuring maximum skin exposure, providing eye protection and eye care, carefully monitoring thermoregulation, maintaining adequate hydration and supporting parent-infant interaction.[11]
    - Light-emitting diode (LED) light source phototherapy is effective in bringing down levels of serum total bilirubin at rates that are similar to phototherapy with conventional (compact fluorescent lamp (CFL) or halogen) light sources.[12]
    - The main complications of phototherapy are separation from the mother, dehydration (fluid intake must be increased) and loose stools. Home phototherapy has been trialled in the UK with encouraging results.[13]
    - Phototherapy is not normally carried out for conjugated hyperbilirubinaemia, because this does not cause kernicterus.

- Exchange transfusion via an umbilical artery or vein; indications depend on the clinical well-being (unwell babies are transfused earlier), cause, rate of increase in bilirubin and the gestational age of the baby. The National Institute for Health and Care Excellence (NICE) recommends:[7]
    - Use a double-volume exchange transfusion (double the estimated total blood volume is removed and replaced) to treat babies:
        - With clinical features and signs of acute bilirubin encephalopathy, whose serum bilirubin level indicates its necessity (threshold tables and treatment threshold graphs are included in the NICE guideline). For example, the threshold total serum bilirubin for exchange transfusion for a baby with gestational age of 38 weeks or more is 100 µmol/L at birth and then increases to 450 µmol/L at and after about 42 hours of age. Any level of total serum bilirubin at or above the threshold level indicates the need for exchange transfusion.
- - During exchange transfusion do not:
        - Stop continuous multiple phototherapy.
        - Perform a single-volume exchange.
        - Use albumin priming.
        - Routinely administer intravenous calcium.
    - Following exchange transfusion:
        - Maintain continuous multiple phototherapy.
        - Measure serum bilirubin level within two hours and manage according to threshold table and treatment threshold graphs.
    - Double-LED phototherapy may be an alternative treatment strategy to exchange transfusion.[14]

Jaundice presenting in the first 24 hours of life

Jaundice presenting in the first 24 hours of life is more likely to have a serious underlying cause such as infection, haemolytic disease or metabolic disorder. Any baby presenting with jaundice in the first 24 hours of life should therefore be seen urgently for assessment in hospital.

Prolonged jaundice [7]

In babies with a gestational age of 37 weeks or more with jaundice lasting for more than 14 days and in babies with a gestational age of less than 37 weeks with jaundice lasting for more than 21 days:

- Look for pale chalky stools and/or dark urine that stains the nappy.
- Measure the conjugated bilirubin.
- Carry out an FBC.
- Carry out a blood group determination (mother and baby) and direct antiglobulin test (DAT, or Coombs' test). Interpret the result taking account of the strength of reaction and whether the mother received prophylactic anti-D immunoglobulin during pregnancy.
- Carry out a urine culture.
- Ensure that routine metabolic screening (including screening for congenital hypothyroidism) has been performed.
- Follow expert advice about care for babies with a conjugated bilirubin level greater than 25 µmol/L because this may indicate serious liver disease.

Complications

- Kernicterus. Studies in the USA and Europe suggest that kernicterus still occurs in about 0.5-1.0 per 100,000 infants born after 35 weeks of gestation. [15]

Prognosis

- This is dependent on the underlying cause but otherwise excellent with prompt diagnosis and treatment.

- Biliary atresia requires surgery within the first two months of life for a better prognosis.[8]

Further reading

- Neonatal jaundice, NICE Quality Standards, Mar 2014
- Siu SL, Chan LW, Kwong AN; Clinical and biochemical characteristics of infants with prolonged neonatal jaundice. Hong Kong Med J. 2018 Jun;24(3):270-276. doi: 10.12809/hkmj176990. Epub 2018 May 25.
- Althnian A, Almanea N, Aloboud N; Neonatal Jaundice Diagnosis Using a Smartphone Camera Based on Eye, Skin, and Fused Features with Transfer Learning. Sensors (Basel). 2021 Oct 23;21(21). pii: s21217038. doi: 10.3390/s21217038.

Authored by:	Peer Reviewed by: Dr Toni Hazell	
Originally Published: 20/11/2023	Next review date: 30/06/2022	Document ID: doc_2502