Jaundice

Essential History

Ask about:

- Age of onset
- Any viral prodrome
- Abdominal pain or distension
- Acholic (pale) stools
- Dark urine
- Pruritus
- Prenatal and birth history in neonatal jaundice
- Patient's age at onset of jaundice
- Exposure to hepatotoxic agents
- Detailed family history of jaundice, liver disease, metabolic disease, and haemolysis
- Travel history

Keywords / also known as: hyperbilirubinaemia, yellowing of the skin

'Red Flag' Symptoms and Signs

Ask about:

- Onset of jaundice in the first 24 hours of life. See Jaundice in newborn babies under 28 days [NICE clinical guidance CG98]
- Rapid progression of jaundice in newborns
- Persistence beyond 2 weeks of life in term babies and beyond 3 weeks in preterm babies
- Urine and stool colour in infants
- Neurological symptoms
  - Drowsiness
  - Seizures
  - Decreased level of consciousness

Look for:

- Conjugated bilirubin levels > 25 µmol/L in newborns
- Bruising or bleeding (see Petechiae and Purpura)
- Neurological signs
- Hepatomegaly

- Splenomegaly
- Ascites

Differential Diagnosis / Conditions

Jaundice in newborns and young infants

- Unconjugated hyperbilirubinaemia
  - A pathological cause is suggested by:
    - Early onset (in the first 24 hours of life)
    - Rapid progression
    - Persistence beyond 2 weeks of life in term babies and beyond 3 weeks in preterm babies
- Increased production of bilirubin
  - Haemolysis (ABO or Rh incompatibility, erythrocyte defects, erythrocyte enzyme defects, or Disseminated Intravascular Coagulation (DIC))
  - Haemoglobinopathies
    - α-Thalassaemia
    - Erythrocyte enzyme defects
  - Cephalohaematoma resorption
  - Polycythaemia
- Decreased hepatocellular uptake or conjugation
  - Prematurity
  - Physiological jaundice of the newborn
  - Congenital hypothyroidism
  - Breast milk jaundice
  - Drug toxicity
    - Ibuprofen, rifampicin, cephalosporins, and sulfonamides can all impair bilirubin transport by altering bilirubin-albumin binding
  - Gilbert and Crigler-Najjar syndromes
    - Familial unconjugated hyperbilirubinaemias caused by mutations in gene encoding for BUGT
  - Conjugated hyperbilirubinaemia
    - Conditions associated with conjugated hyperbilirubinaemia in newborns or infants include:
      - Primary hepatobiliary disorders (biliary atresia should be excluded in all cases)
      - Genetic or metabolic diseases
      - Systemic infections

- Liver diseases
  - Acute liver damage (ischaemia, hypoxia, or acidosis)
  - Infection
    - Sepsis
    - TORCH (ie, toxoplasmosis, rubella, cytomegalovirus, herpes simplex)
    - Urinary tract infections
  - Obstruction of the biliary system
    - Biliary atresia
    - Choledochal cyst
    - Cholelithiasis
  - Viral or other hepatitis
  - Liver disease associated with parenteral nutrition
  - Metabolic liver diseases
    - α_1-Antitrypsin deficiency
    - Galactosaemia
    - Neonatal haemochromatosis
    - Tyrosinaemia type 1 (hepatorenal tyrosinaemia)
    - Primary mitochondrial hepatopathies
    - Alagille's syndrome, also known as arteriohepatic dysplasia, which is inherited as an autosomal-dominant condition with variable penetrance
- Defects of bilirubin or bile acid metabolism or transport
  - Progressive familial intrahepatic cholestasis (PFIC)
  - Dubin-Johnson syndrome, and Rotor's syndrome

Jaundice in older infants and children

- Unconjugated hyperbilirubinaemia
  - Unconjugated hyperbilirubinaemia is seen in older infants and children in association with:
    - Haemolysis (erythrocyte defects, erythrocyte enzyme defects, DIC)
    - Gilbert's syndrome and Crigler-Najjar syndrome
- Conjugated hyperbilirubinaemia
  - Liver disease
    - Viral hepatitis (hepatitis A, B, C, or E) (see PHE Green Book Chapter 17 and Chapter 18)
    - Autoimmune hepatitis (AIH), which is a progressive inflammatory condition of the liver of unknown aetiology
    - Toxins and drugs
      - Ethanol
      - Paracetamol
      - Isoniazid

    - Phenytoin
  - Other liver diseases with conjugated hyperbilirubinaemia include:
    - Wilson's disease
    - Acute liver damage (ischaemia, hypoxia, acidosis)
    - Infiltrative cancers, which may occur rarely and can cause jaundice at any age
  - Conjugated hyperbilirubinaemia may also be associated with liver disease related to:
    - Total parenteral nutrition
    - Pregnancy
      - Acute fatty liver of pregnancy
      - Pre-eclampsia
- Obstruction of the biliary system
  - Choledochal cyst
  - Cholelithiasis or choledocholithiasis
  - Cholecystitis
  - Diseases of the bile ducts
    - Primary sclerosing cholangitis
    - Cholangiopathy in acquired immunodeficiency syndrome
- Bilirubin or bile acid metabolism or transport defects
  - Progressive familial intrahepatic cholestasis
  - Dubin-Johnson syndrome
  - Rotor's syndrome

Investigations

To be undertaken by non-specialist practitioners (eg, General Practitioner (GP) Team):

Please check discharge information (letters) in neonates. For older children a discussion with the on-call paediatrician should be considered.

- Full blood count
- Liver function tests including a 'split' bilirubin
- Coagulation profile
- Urine culture

To be undertaken by specialist practitioners (eg, Emergency Department / General Paediatric / Paediatric Hepatology Team(s)) if not already done:

- Blood culture
- Viral serological studies
- Toxin and drug screen
- Autoimmune markers

- α_1-Antitrypsin phenotype
- Ceruloplasmin
- Urine succinyl acetone
- Urinary bile acid profile in unexplained cases
- TORCH titres
  - In jaundiced newborns or young infants with abnormal liver function tests
- Ultrasonography
- Computed tomography (in selected cases)
  - May be preferred for assessing the general anatomy of the hepatobiliary system and possible non-cystic hepatic lesions
- Endoscopic retrograde cholangiopancreatography (ERCP)
  - Allows possible therapeutic intervention, such as:
    - Sphincterectomy
    - Biliary stone extraction
    - Stent placement
  - Diagnosis of extrahepatic biliary atresia is confirmed by ERCP with cholangiography or intraoperative cholangiography
- Liver biopsy provides information on the histology and architecture of the liver

Treatment Approach

To be undertaken by specialist practitioners (eg, Emergency Department / General Paediatric / Paediatric Hepatology Team(s)):

- Unconjugated (indirect) hyperbilirubinaemia
  - For treatment of newborns see Jaundice in newborn babies under 28 days [NICE clinical guideline CG98, Section 1.3–1.4].
- Conjugated (direct) hyperbilirubinaemia
  - Management should focus on correcting the underlying cause, optimising nutrition, and controlling pruritus.
  - Supplementation of fat-soluble vitamins A, D (see vitamins A, B Group, C and D for Dalivit© and Abidec©), E (alpha tocopheryl acetate), and K (phytomenadione) is essential.
- Cholestasis-associated pruritus
  - Several different therapeutic agents have been used with little success.
    - Ursodeoxycholic acid and colestyramine are usually first choice.
    - In general, single drugs should be tried serially and discontinued if ineffective.

When to Refer

Refer to a paediatric specialist if:

- The patient has:
  - Onset of jaundice in the first 24 hours of life
  - Rapidly progressing jaundice in a neonate
  - Unexplained jaundice
  - Direct hyperbilirubinaemia at any age
  - Persistently abnormal liver tests
  - Jaundice with hepatomegaly or splenomegaly or pale stools
  - Liver failure (coagulopathy not responding to parenteral vitamin K)
- Jaundice occurs in an ill patient
- There is feeding intolerance and dehydration
- Inpatient management of underlying conditions is required

'Safety Netting' Advice

- The parents of neonates and infants should be advised to see a medical practitioner if they develop pale stools.

Patient / Carer Information

Please note: whilst these resources have been developed to a high standard they may not be specific to children.

- Jaundice (Web page), the NHS website
- Jaundice in newborn babies under 28 days: Information for the public (Web page), NICE clinical guideline CG98, National Institute of Health and Care Excellence
- Newborn jaundice (Web page), the NHS website
- Baby jaundice (Web page), Children's Liver Disease Foundation

Resources

National Clinical Guidance

Jaundicein newborn babies under 28 days (Web page), NICE clinical guideline CG98, National Institute of Health and Care Excellence

Hepatitis B (chronic): diagnosis and management (Web page), NICE clinical guideline CG165, National Institute of Health and Care Excellence

Hepatitis B and C testing: people at risk of infection (Web page), NICE clinical guideline PH43, National Institute of Health and Care Excellence

Investigation of Neonatal Conjugated Hyperbilirubinaemia (Web page), British Society of Paediatric Gastroenterology, Hepatology and Nutrition guideline

Medical Decision Support

Hepatitis A (Web page), Public Health England's Green Book

Hepatitis B (Web page), Public Health England's Green Book

Jaundice and Kernicterus (Web page), Centers for Disease Control and Prevention.

Suggested Resources

Please note: these resources include links to external websites. These resources may not have national accreditation and therefore PCO UK cannot guarantee the accuracy of the content.

Vitamin D Deficiency (eLearning - requires log-in), RCPCH Compass

Multivitamin preparations for vitamin deficiency (Web page), Medicines for Children

Dalton HR, Bendall R, Ijaz S, et al. Hepatitis E: an emerging infection in developed countries. Lancet Infect Dis 2008;8(11):698–709 [Pubmed]

Maddrey WC. Drug-induced hepatotoxicity: 2005. J Clin Gastroenterol 2005;39(4 Suppl 2):S83–S89 [Pubmed]

Oettinger R, Brunnberg A, Gerner P, et al. Clinical features and biochemical data of Caucasian children at diagnosis of autoimmune hepatitis.J Autoimmun 2005;24(1):79–84 [Pubmed]

Pratt DS. Cholestasis and cholestatic syndromes. Curr Opin Gastroenterol 2005;21(3):270–274 [Pubmed]

Rand EB, Karpen SJ, Kelly S, et al. Treatment of neonatal hemochromatosis with exchange transfusion and intravenous immunoglobulin. J Pediatr 2009;155(4):566–571 [Pubmed]

Reiser DJ. Neonatal jaundice: physiologic variation or pathologic process. Crit Care Nurs Clin North Am 2004;16(2):257–269 [Pubmed]

Squires RH Jr. Autoimmune hepatitis in children. Curr Gastroenterol Rep 2004;6(3):225–230 [Pubmed]

Acknowledgements

Content Editor: Dr Srini Bandi

Clinical Expert Reviewer: Dr Patrick McKiernan

GP Reviewer: Dr Zoe Cameron

AAP Reviewer: Dr Kelly J Kelleher

Paediatric Trainee Reviewer: Dr Akhila Vasanth Hassan

Update reviewer: Dr Ruth Taylor (trainee paediatrician)

Paediatric Specialty Group: British Society for Paediatric Gastroenterology, Hepatology and Nutrition

Update information

Created: 2015

Date last updated: 2018

Next review due: 2021