A child with jaundice

Is this one for the family physician?

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

EDWARD O'LOUGHLIN
MD, FRACP

Dr O'Loughlin is Staff Specialist, Department of Gastroenterology, The Children's Hospital at Westmead, Westmead, NSW.

Series Editor
CHRISTOPHER S. POKORNY
MB BS, FRACP

Dr Pokorny is Honorary Secretary, Board of Continuing Education, Royal Australasian College of Physicians, and a gastroenterologist in private practice, Sydney, NSW.

Jaundice in childhood can be classified into two main groups depending on the age of presentation: neonatal jaundice and jaundice in the older child or adolescent. The approach to neonatal jaundice is clinically more challenging than jaundice in the older child. A discussion of this subject is beyond the limits of this article and thus my comments will be restricted to jaundice in the older child.

An important principle in childhood liver disease is that some disorders are curable if diagnosed and treated early but can lead to end-stage liver disease if missed. Examples include Wilson's disease, choledochal cyst and hereditary fructose intolerance. A simple clinical approach to the investigation of the child with jaundice will be provided in this article. I will focus on hepatobiliary disorders rather than attempt to be all encompassing. Because of the nature of the possible underlying disorders, children with conjugated hyperbilirubinaemia that is not due to infectious hepatitis should be referred to a tertiary centre for investigation and management.

Clinical assessment

The history and physical examination are important. In some disorders, aspects of the history or specific physical signs may be diagnostic.

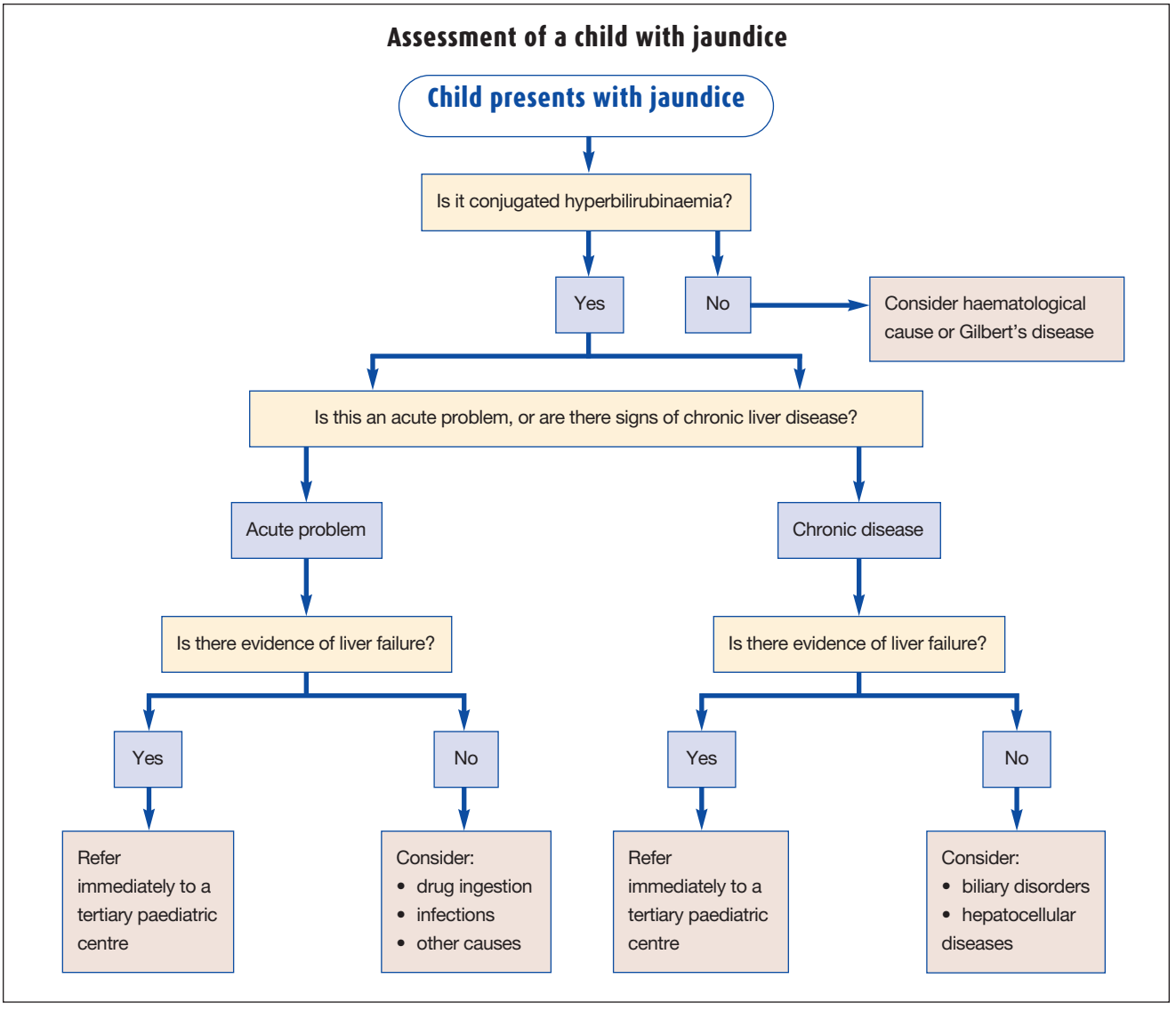
Is the jaundice unconjugated or conjugated?

The initial step is to ascertain whether the jaundice is unconjugated or conjugated (see the flowchart on page 81).

Unconjugated hyperbilirubinaemia results in jaundice without bilirubin in the urine. Gilbert's disease, a common disorder due to defective bilirubin conjugation, may present with fluctuating jaundice precipitated by intercurrent illness or fasting, such as for anaesthesia. Haemolytic disorders (for example, those due to glucose-6-phosphate dehydrogenase deficiency and hereditary spherocytosis) may present with jaundice and symptoms of anaemia such as shortness of breath, palpitations or pallor. Acute haemolysis can be precipitated by medications or acute intercurrent illness. Disorders causing conjugated hyperbilirubinaemia usually produce dark urine (due to

IN SUMMARY

- **The first step is to determine if the jaundice is due to haematological or hepatobiliary disorders, i.e. conjugated or unconjugated hyperbilirubinaemia.**
- **Childhood liver disease resulting in jaundice can be due to either acute liver injury or an acute exacerbation or decompensation of chronic hepatobiliary disease.**
- **Some hepatobiliary disorders presenting in childhood are potentially 'curable' if diagnosed early.**
- **Physical or biochemical evidence of liver synthetic failure or encephalopathy is a life-threatening scenario and requires urgent referral to a paediatric tertiary centre.**
- **Assessment of synthetic function is mandatory. Low serum albumin, or abnormal coagulation not responding to vitamin K, indicates liver synthetic failure.**



bilirubin in the urine) and, depending on the degree of cholestasis or biliary obstruction, acholic stools that appear grey–white. Urinalysis will detect bilirubin in the urine.

The next step is to determine if the patient is sick or well. The presence of conjugated hyperbilirubinaemia in a very unwell patient may indicate liver failure and/or sepsis, which requires urgent referral to a tertiary referral paediatric centre.

What are the possible causes: acute versus chronic liver disorders?

Conjugated hyperbilirubinaemia can be caused by an acute illness (such as viral hepatitis, biliary stones or a drug reaction) or can develop on a background of chronic liver disease (Table). A history of exposure to others with jaundice or overseas travel may implicate an infectious cause such as hepatitis A. A past history of transfusion with blood products or parental history of intravenous drug use may suggest hepatitis B or C.

Information regarding recent drug ingestion is important. Accidental paracetamol overdose is the commonest cause of fulminant liver failure in my hospital. Other drugs that cause liver reactions in children include: anticonvulsants, ranitidine, cytotoxic agents, and antibiotics such as sulfonamides, penicillin derivatives and erythromycin.

Table. Acute and chronic hepatobiliary disorders presenting with jaundice

Acute liver disease
Biliary
Stones
Hepatocellular
Drug-induced disease
Infection
Metabolic disorder
Chronic liver disease
Biliary
Choledochal cyst
Fibrosing pancreatitis
Cystic fibrosis
Sclerosing cholangitis
Caroli's disease
Hepatocellular
Infection (hepatitis B, C)
Wilson's disease
Autoimmune hepatitis
Systemic lupus erythematosus
Alpha-1-antitrypsin deficiency
Cryptogenic cirrhosis

A history of abdominal pain and/or fever could be indicative of a biliary disorder such as stones, choledochal cyst or pancreatic disease leading to biliary obstruction.

Sudden development of jaundice may occur with some metabolic diseases. For example, hereditary fructose intolerance is a disorder of fructose metabolism. Ingestion of sweet foods or syrupy medications (containing sucrose or fructose) can result in acute liver injury and jaundice, which may be accompanied by vomiting and symptoms of hypoglycaemia. The hallmark of this disorder in the older child or adult is a history of profound aversion to sweet foods – the avoidance of soft drink and lollies is very unusual in children! This symptom should be sought in any child presenting with sudden onset of jaundice.

Children with chronic liver disease and cirrhosis may exhibit lethargy, poor school performance and poor growth.

What does the physical examination find?

Thorough physical examination should be undertaken. Physical signs may establish a diagnosis and provide information about chronicity and degree of liver synthetic function. It is important to determine if the patient has chronic liver disease because this has a significant bearing on the differential diagnosis.

Measurement of height and weight and assessment of pubertal status should be undertaken because growth faltering and delayed pubertal development are common in decompensated cirrhosis.

Examination of the eyes is important. Scleral icterus indicates jaundice (Figure 1), but yellow skin with clear sclera is a sign of carotenaemia. Slit lamp examination may reveal Kayser–Fleischer rings, which are usually diagnostic of Wilson's disease in the paediatric age range. Examination of the skin and nails may reveal spider naevi (Figure 2), palmar erythema and liver nails (signs of chronic liver disease).

Peripheral oedema, bruising and ascites indicate liver synthetic failure (Figure 3). Changes in behaviour, sleep disturbances or changes in mentation may indicate encephalopathy.

It is important to assess liver consistency and size. Tender hepatomegaly is common in viral hepatitis, and it may occur in other forms of hepatitis such as autoimmune hepatitis, drug-induced hepatitis or Wilson's disease. In hereditary fructose intolerance, a soft large liver is usual because of fatty liver; if the liver is hard, it suggests fibrosis or cirrhosis.

The presence of splenomegaly and/or caput medusae indicates portal hypertension. A soft mass in the right upper quadrant may indicate gall bladder distension due to biliary obstruction or even a choledochal cyst.

Investigations

Patients presenting with overt signs of liver failure should be referred immediately because prompt investigation and intervention may be life saving.

The serum bilirubin should include a direct fraction (which is not always routine in the hospital setting). Unconjugated hyperbilirubinaemia in a well patient without evidence of haemolysis

Figure 1. Scleral icterus and Kayser–Fleischer rings in a patient with Wilson's disease.

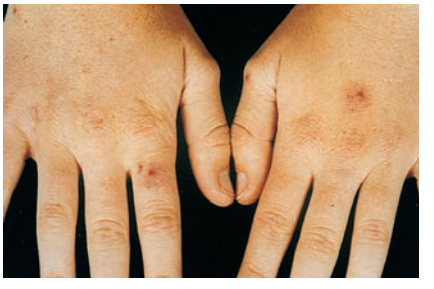


Figure 2. Spider naevi on the hands of a patient with established cirrhosis.

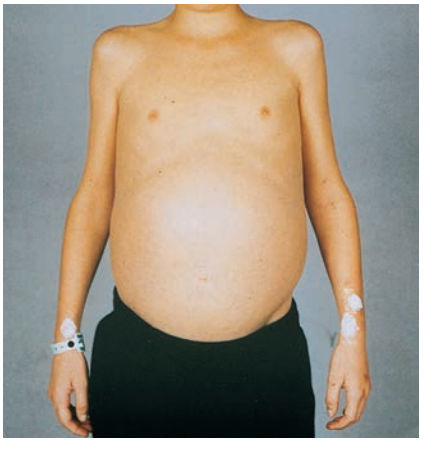


Figure 3. A boy with end-stage cirrhosis, with jaundice, wasting and ascites.

is likely to be Gilbert's disease. A full blood count and a blood film will indicate acute haemolysis. Haemolysis can also occur in patients with fulminating Wilson's disease because of the toxic effect of copper on red blood cells.

Measurement of alanine transaminase, gamma glutamyltranspeptidase and alkaline phosphatase will provide some clues to the degree of liver injury. The pattern of abnormalities may suggest a possible aetiology (for example, towering transaminases may suggest paracetamol or other toxic injury; high gamma glutamyltranspeptidase, a biliary problem such as stones).

Assessment of synthetic function is mandatory. Low serum albumin, or abnormal coagulation not responding to vitamin K, indicates liver synthetic failure – this is an urgent priority.

A drug screen and/or paracetamol levels are important in children with suspected drug ingestion or where one obtains a history of paracetamol ingestion.

Abdominal ultrasound is a useful screening test for biliary disorders such as gallstones, dilatation of the biliary tree and pancreatic disease. Abnormalities detected with this modality will need further imaging studies. Endoscopic retrograde cholangiopancreatography (ERCP) is usually the investigation of choice in adult patients, but this requires general anaesthetic in a child and a high degree of operator expertise. It is not routinely performed in paediatric hospitals. The introduction of magnetic resonance cholangiopancreatography (MRCP) has allowed for noninvasive examination of the biliary tree, with greater than 90% sensitivity and specificity for the diagnosis of biliary disorders when compared with ERCP. MRCP is the preferred option for the diagnosis of anatomical disorders of the pancreaticobiliary system in childhood.

Serology for hepatitis A, B and C is routinely available. Negative serology should not lead to the diagnosis of 'non A, non B, non C hepatitis' – it is essential to search for alternative diagnoses. A small battery of readily available investigations will diagnose or exclude most of the alternative disorders. In autoimmune hepatitis, serum immunoglobulins, antinuclear antibody, and anti-smooth muscle and anti-liver kidney microsomal antibodies may be elevated. In Wilson's disease, ceruloplasmin and copper are usually low and 24-hour urinary copper is usually elevated – it is essential to perform the urine collection in special de-coppered containers. Serum alpha-1-antitrypsin level and phenotyping looking for the PiZZ phenotype will exclude alpha-1-antitrypsin deficiency.

Liver biopsy is occasionally required to establish a diagnosis, such as in drug-induced hepatitis, Wilson's disease or autoimmune hepatitis, or less commonly to assess the degree of liver injury.

Conclusion

In general, the diagnosis of childhood liver disease presenting with jaundice can be ascertained by clinical assessment and simple noninvasive investigations. Because of the life-threatening nature of some of the conditions that present with jaundice, children with hepatobiliary disorders will usually require referral to a tertiary paediatric centre for assessment. MT

Suggested reading

1. Lee WM. Drug induced hepatoxicity. N Engl J Med 1995; 333: 1118-1127.
2. Kelly DA, ed. Diseases of the liver and biliary system in children. Oxford: Blackwell Science, 1999.