Investigation of jaundice

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Abstract

Jaundice is a clinical sign that reflects accumulation of bilirubin in blood. It can result from increased bilirubin production, inability of the liver to conjugate bilirubin or failure to excrete bilirubin into the biliary tree. Appropriate investigation of jaundice starts with a history of associated symptoms, and risk factors for liver disease. Clinical examination should look for stigmata of chronic liver disease and signs of specific liver diseases. Initial blood tests should assess liver injury and synthetic function. A combination of urinalysis and the pattern of abnormal liver function tests can indicate whether the jaundice is likely to be hepatitic or cholestatic, and guide further investigations. This review will describe bilirubin metabolism, the causes of jaundice, and the appropriate investigation of jaundice.

Keywords Biliary obstruction; cirrhosis; haemolytic anaemia; hepatitis; hyperbilirubinaemia; jaundice; liver injury

What's new?

- Cholangiography using fibreoptic/videoendoscopes can be combined with ERCP to distinguish accurately between benign and malignant biliary strictures
- Intraductal ultrasound can aid the detection of small stones in dilated ducts, where conventional imaging has failed

Definition of jaundice

Jaundice describes yellow discolouration of the skin, mucous membranes and sclera. It becomes clinically apparent when serum bilirubin is >34 μmol/L. Jaundice can signify underlying hepatobiliary or pancreatic disease that requires systematic investigation.

Pathology and pathogenesis

An understanding of bilirubin metabolism and clearance can aid effective management of jaundice (Figure 1).

The majority of bilirubin (80%) is formed following the breakdown of red blood cells. The typical life span of a red blood cell is 120 days after which it is destroyed in the reticuloendothelial system. Haem, from haemoglobin, is converted to biliverdin and then (unconjugated) bilirubin. Bilirubin circulates in blood bound to albumin, until it is taken up by hepatocytes.

Within the hepatocyte, bilirubin is conjugated with glucuronic acid by UDP-glucuronosyltransferase, rendering it water-soluble. Conjugated bilirubin can be excreted into bile and pass into the gut. Only 2% of bilirubin in the gut is absorbed, the remainder being degraded by colonic bacterial enzymes to form urobilinogen. Some urobilinogen re-enters the liver, but about 90% is converted into stercobilinogen, which is excreted in the faeces.

Determining whether the hyperbilirubinaemia is conjugated or unconjugated can reveal where bilirubin metabolism/clearance is defective and therefore give clues to the underlying aetiology.

Unconjugated hyperbilirubinaemia can result from overproduction of bilirubin, impaired hepatic uptake, or abnormalities of bilirubin conjugation (Table 1).

Conjugated hyperbilirubinaemia may be due to hepatocellular injury, intrahepatic cholestasis, or biliary obstruction (Table 2).

Diagnostic work-up in jaundice

The initial diagnostic work-up of the jaundiced patient includes a thorough history and examination.

History

Enquire about:

- associated symptoms (itch, loss of appetite, weight loss, pale stools, steatorrhoea, dark urine, fever and abdominal pain)
- history of obesity or the metabolic syndrome
- drug history
- family history (jaundice, liver disease, cancer or haemolytic anaemia)
- social history (alcohol consumption, occupation)
- risk factors for viral hepatitis and HIV (sexual contacts, blood transfusions, intravenous drugs, tattoos, country of birth, foreign travel).

Examination

Physical examination may reveal signs of chronic liver disease, such as:

- finger clubbing
- leuconychia
- palmar erythema
- Dupuytren's contracture
- bruising
- scratch marks
- spider naevi
- gynaecomastia
- caput medusae
- hepatomegaly
- splenomegaly
- hepatic encephalopathy.

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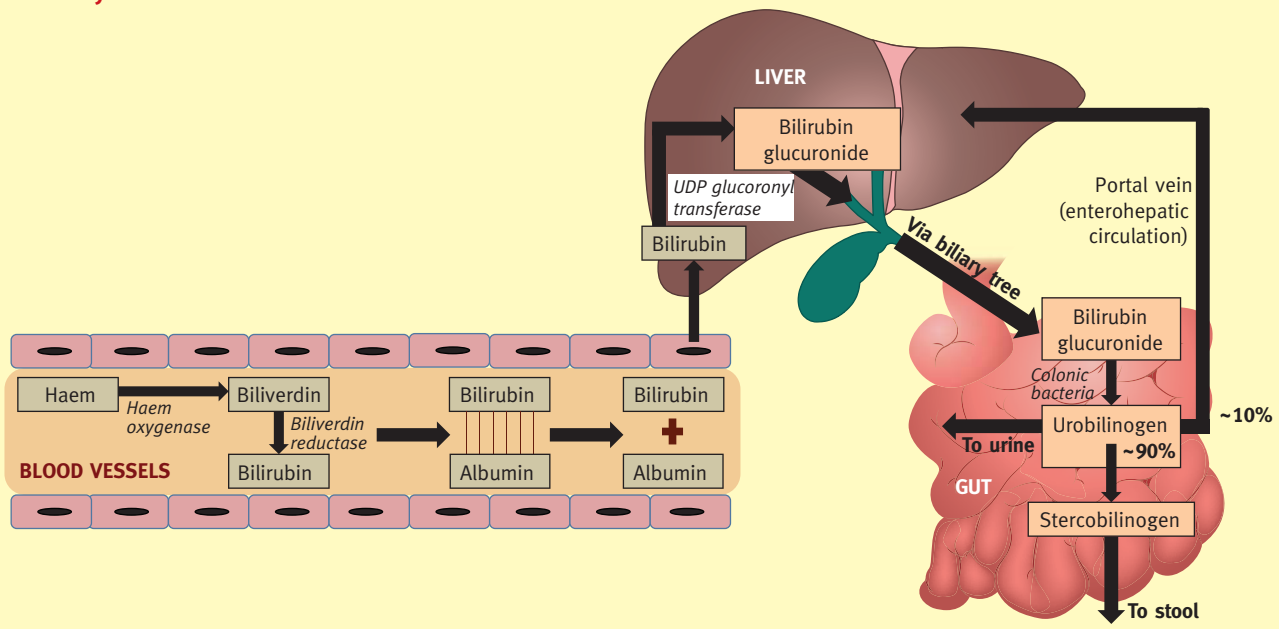
Summary of bilirubin metabolism



The key steps involved in bilirubin metabolism. Unconjugated bilirubin from red blood cell breakdown travels to the liver bound to albumin. Bilirubin is taken into hepatocytes, where it is conjugated and transported to the gut via bile.

Figure 1

Causes of unconjugated hyperbilirubinaemia

Increased bilirubin production	Impaired hepatic bilirubin uptake	Impaired bilirubin conjugation
Extravascular haemolysis	Hepatic failure	Gilbert's syndrome
Haematoma	Portosystemic shunts	Crigler–Najjar syndrome
Intravascular haemolysis (haemolytic anaemia, hereditary spherocytosis)	Medications (rifampicin, probenecid)	Neonates
	Congestive cardiac failure	Advanced cirrhosis
		Hyperthyroidism
		Medications (ethinyl oestradiol)

Table 1

Causes of conjugated hyperbilirubinaemia

Intrahepatic cholestasis	Hepatocellular injury	Extrahepatic cholestasis
Primary biliary cirrhosis	Viral hepatitis	Choledocholithiasis (gallstone disease)
Alcoholic hepatitis	Alcoholic hepatitis	Neoplasia (e.g. pancreatic cancer, cholangiocarcinoma)
Non-alcoholic steatohepatitis	Non-alcoholic steatohepatitis	Primary sclerosing cholangitis
Viral hepatitis	Autoimmune liver disease	Acute or chronic pancreatitis
Drugs (e.g. steroids, antibiotics and neuroleptic medications)	Drugs (including idiosyncratic drug reactions)	Benign strictures
Herbs/toxins (e.g. Jamaican bush tea, arsenic)	Neoplasia (e.g. hepatocellular carcinoma)	
Infiltrative diseases (e.g. lymphomas, sarcoidosis)	Infiltrative diseases (e.g. lymphomas, sarcoidosis)	
Pregnancy	Vascular (e.g. Budd–Chiari syndrome, severe heart failure)	
Hereditary conditions	Metabolic/hereditary conditions	

Table 2