Jaundice in the acute setting

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Abstract

Jaundice is the result of accumulation of bilirubin in plasma, sometimes from overproduction from senescent erythrocytes but more usually through failure of the liver to remove it from the plasma or excrete it into the intestine via the bile ducts. Overproduction (haemolysis) or reduced conjugation through a defective uridine diphosphate-glucuronyl transferase in Gilbert's syndrome results in a modest elevation of unconjugated bilirubin (<100 mmol/litre) and absence of bile from the urine. Liver disease and extrahepatic obstruction result in conjugated jaundice with dark urine. With modern imaging, initially transabdominal ultrasound, it is usually possible to identify extrahepatic obstruction, particularly from malignancy, but bile duct stones can be difficult to visualize and can cause minimal duct dilatation. Spiral computed tomography, endoscopic ultrasound and magnetic resonance scanning with computerized reconstruction of the cholangiogram almost always resolve uncertainties about extrahepatic obstruction. More invasive endoscopic retrograde cholangiopancreatography can be reserved for therapeutic interventions such as sphincterotomy and removal of bile duct stones. Where there is no extrahepatic cause, jaundice can be an important presentation of acute or chronic liver disease, and attention should be paid to features of deteriorating liver function that might require specialist care.

Keywords Acute hepatitis; bilirubin; Gilbert's disease; jaundice; liver imaging

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Key points

- Jaundice is a result of increased bilirubin concentrations in the plasma caused by either excess production, such as from haemolysis, or inability of the liver to process and excrete it.

  Transabdominal liver imaging allows biliary obstruction to be distinguished from parenchymal hepatic or prehepatic causes of jaundice

- Magnetic resonance cholangiopancreatography, endoscopic ultrasound and spiral computed tomography should be the investigations of choice to identify the cause of biliary obstruction where this is not apparent on transabdominal ultrasound.

  Endoscopic retrograde cholangiopancreatography should be not be used to diagnose the cause of biliary obstruction.

  Very high concentrations of alanine aminotransferase or aspartate aminotransferase (>1000 U/litre) are never encountered in alcoholic hepatitis, so other causes such as toxins (drug-induced liver injury), viral hepatitis, hypoxia and autoimmune liver disease should be excluded.

  The presence of significantly deranged clotting results, acidosis, renal dysfunction and altered mental state in acute-onset jaundice without biliary obstruction warrants urgent referral to a specialist liver centre.

Definition and epidemiology

Jaundice is the yellowish discoloration of the skin, sclera and mucous membranes caused by the deposition of excessive bilirubin pigments. It is usually clinically detectable when serum bilirubin concentrations rise to more than 50 micromol/litre. The incidence of jaundice in primary care in adult patients aged 45 and over in the UK is 0.74 per 1000 patients per year. Jaundice or icterus is a clinical symptom and sign that can vary in its significance from trivial to life-threatening, and warrants further assessment.

Pathophysiology

The significance of jaundice is best understood through the pathophysiology (Figure 1). Bilirubin is a degradation product of haemoglobin. It is transported to the liver in its unconjugated form tightly bound to albumin, and as such is not excreted into the urine. In the liver, it is taken up by active transport and conjugated within the hepatocytes to form bilirubin monoglucuronides and diglucuronides. These are water-soluble, excreted into bile and further metabolized by gut bacteria into urobilinogen (partly reabsorbed via the enterohepatic circulation) and the various stercobilins that produce the brown pigmentation of stool.

Jaundice can be subdivided into unconjugated and conjugated types. Alternatively, it can be subdivided anatomically into prehepatic (overproduction of bilirubin or difficulty extracting it from the blood), hepatic (caused by intrinsic liver disease) and

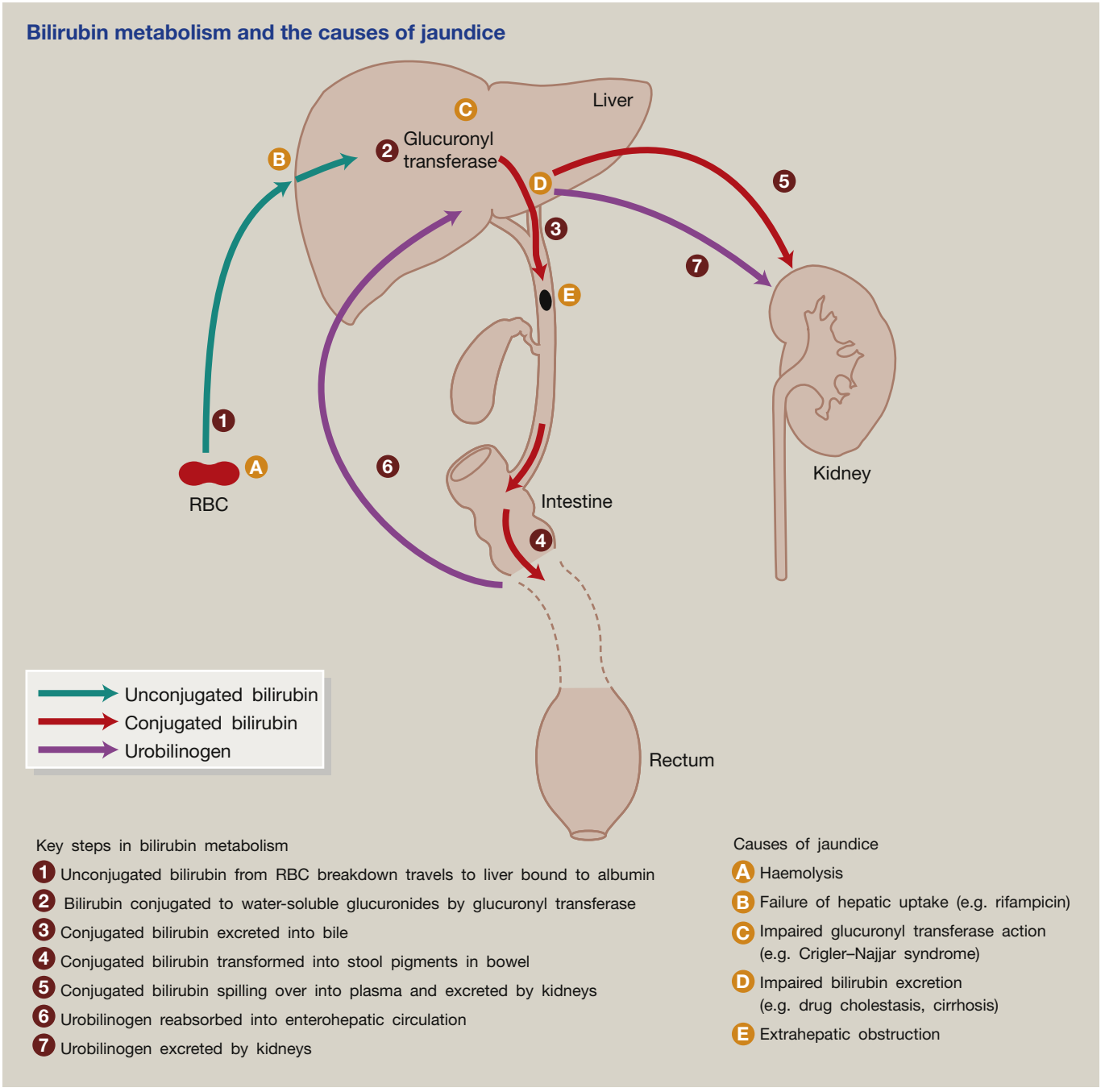

Figure 1

post-hepatic (from extrahepatic obstruction). Hepatic and post-hepatic causes have an excess of predominantly conjugated bilirubin. Routine chemical methods of differentiating unconjugated (indirect) bilirubin from conjugated (direct) bilirubin are unreliable; it can be useful to demonstrate the presence of bile in urine as evidence of conjugated jaundice. However, dipsticks for urinary urobilinogen can be unreliable.

Jaundice becomes clinically apparent when serum total bilirubin concentration is two to three times normal. In unconjugated jaundice in adults, a serum total bilirubin over 100 mmol/litre (normal <18 mmol/litre) is uncommon. Deep jaundice in adults is always predominantly conjugated.

Causes of jaundice

Unconjugated jaundice

Increased bilirubin production results from any form of haemolysis and is sometimes termed ‘acholuric jaundice’ to emphasize the absence of bile from the urine. Causes can be hereditary (e.g. hereditary spherocytosis) or acquired (e.g. malaria). Impaired hepatic uptake of bilirubin leads to unconjugated jaundice, with drugs a predominant cause; they compete for protein binding or for uptake receptors. Impairment of glucuronyl transferase, the enzyme that converts bilirubin into a polar, water-soluble glucuronide suitable for excretion into bile, is