Jaundice

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Abstract

Jaundice is yellow discolouration of the skin, sclera and mucous membranes due to raised plasma bilirubin. Jaundice occurs due to an imbalance between the production and clearance of bilirubin and thus an understanding of bilirubin metabolism is required to evaluate a jaundiced patient. Jaundice can be classified as pre-hepatic, hepatic or post-hepatic according to the site of disruption of bilirubin metabolism. Following history, examination and initial blood tests, an abdominal ultrasound scan is usually the next investigation, with sequentially more invasive tests being undertaken as required. Jaundiced patients usually require management by a multidisciplinary team.

Keywords Bilirubin; cancer; cholestasis; gallstones; jaundice; liver

Definition

Jaundice refers to yellow discolouration of the skin, sclera and mucous membranes due to a raised plasma bilirubin. The normal range for plasma bilirubin is 5–19 μmol/litre and jaundice is usually apparent when this is greater than 50 μmol/litre. The term is derived from the French 'jaunisse', meaning 'yellow disease'. The Latin root is 'galbinus' meaning 'greenish yellow', a colour then associated with bitterness or envy. An alternative term is 'icterus', derived from the Greek 'ikteros' meaning jaundice. A greenish tinge to a patient's skin colour indicates longstanding jaundice, due to oxidation of bilirubin to biliverdin. Another cause of yellow discolouration of the skin, especially on the palms and soles, but not of the sclera or mucous membranes is carotenaemia, the presence of the orange pigment carotene in the blood, due to ingestion of carrots.

Bilirubin metabolism

Jaundice occurs due to an imbalance between the production and clearance of bilirubin. Thus an understanding of bilirubin metabolism (Figure 1) is needed in order to evaluate a jaundiced patient. Bilirubin is a breakdown product of haem, derived from haemoglobin. In the reticuloendothelial system, haem is initially oxidised to form biliverdin and then reduced to unconjugated bilirubin. Unconjugated bilirubin is insoluble in plasma and is thus transported bound to albumin, to the liver. In the hepatocytes, unconjugated bilirubin is conjugated with glucuronic acid to increase water solubility. This conjugation is catalysed by uridine diphosphoglucuronosyl transferase (UDPG). Conjugated bilirubin is excreted into the bile canaliculi by an ATP-dependent pump, the C-MOAT transporter, belonging to the multidrug-resistant protein 2 (MRP2) as a component of bile. Bile is stored and concentrated in the gallbladder and then released into the duodenum. In the small bowel, some of the bilirubin is hydrolysed to yield unconjugated bilirubin and glucuronic acid. Most unconjugated bilirubin is reduced by colonic bacteria to stercobilinogen and urobilinogen, some of which are reabsorbed and returned to the liver for re-conjugation (enterohepatic circulation) or otherwise excreted in the stool or urine.

Composition and function of bile

Bile composition is very complex and varies according to the nutritional state of the individual. Bile is formed by hepatocytes and its composition modified in the biliary canaliculi. It is 95% water, in which is dissolved bile salts (also called bile acids), phospholipids, cholesterol, bilirubin (mostly in its conjugated form), inorganic salts (potassium, sodium and bicarbonate), steroids, vitamins, heavy metals, exogenous drugs and environmental toxins.[1]

Bile serves a number of important functions. It excretes bilirubin, bile salts and potentially harmful exogenous drugs and allows the elimination of cholesterol. Bile salts emulsify dietary fats and aid in their absorption. It also has a role in the immune system, by protecting patients from enteric infections by excreting immunoglobulin A, inflammatory cytokines, and stimulating the innate immune system in the intestine.

Classification and causes of jaundice, according to disorders in bilirubin metabolism

Jaundice can be broadly classified as pre-hepatic (resulting from excessive haemolysis), hepatic (due to congenital or acquired liver disorders causing impaired intra-hepatic bilirubin metabolism) or post-hepatic/cholestatic. Cholestasis is impairment in the flow of bile from the hepatocytes into the duodenum. It may be intra-hepatic or extra-hepatic, according to the site of obstruction.

Pre-hepatic jaundice

This occurs due to increased haemolysis. Its aetiology is either congenital (spherocytosis, thalassaemia, sickle cell anaemia) or acquired, for example due to autoimmune haemolysis, blood transfusion or trauma (Figure 1). Pre-hepatic or haemolytic jaundice usually causes a mild increase in bilirubin levels (68–102 μmol/litre) without significant alteration of liver function, together with raised urobilinogen levels in the urine and raised unconjugated bilirubin in the blood. The clinical findings will vary depending on the pathology leading to the erythrocyte disruption.

Hepatic jaundice

Hepatic jaundice is due to congenital or acquired hepatocellular disorders causing impaired uptake of bilirubin from plasma, conjugation and excretion (Figure 1). Congenital causes of hepatic jaundice include Crigler–Najjar syndrome, Gilbert's syndrome, Rotor's syndrome, Dubin–Johnson's syndrome, haemochromatosis, Wilson's disease and α-1-antitrypsin

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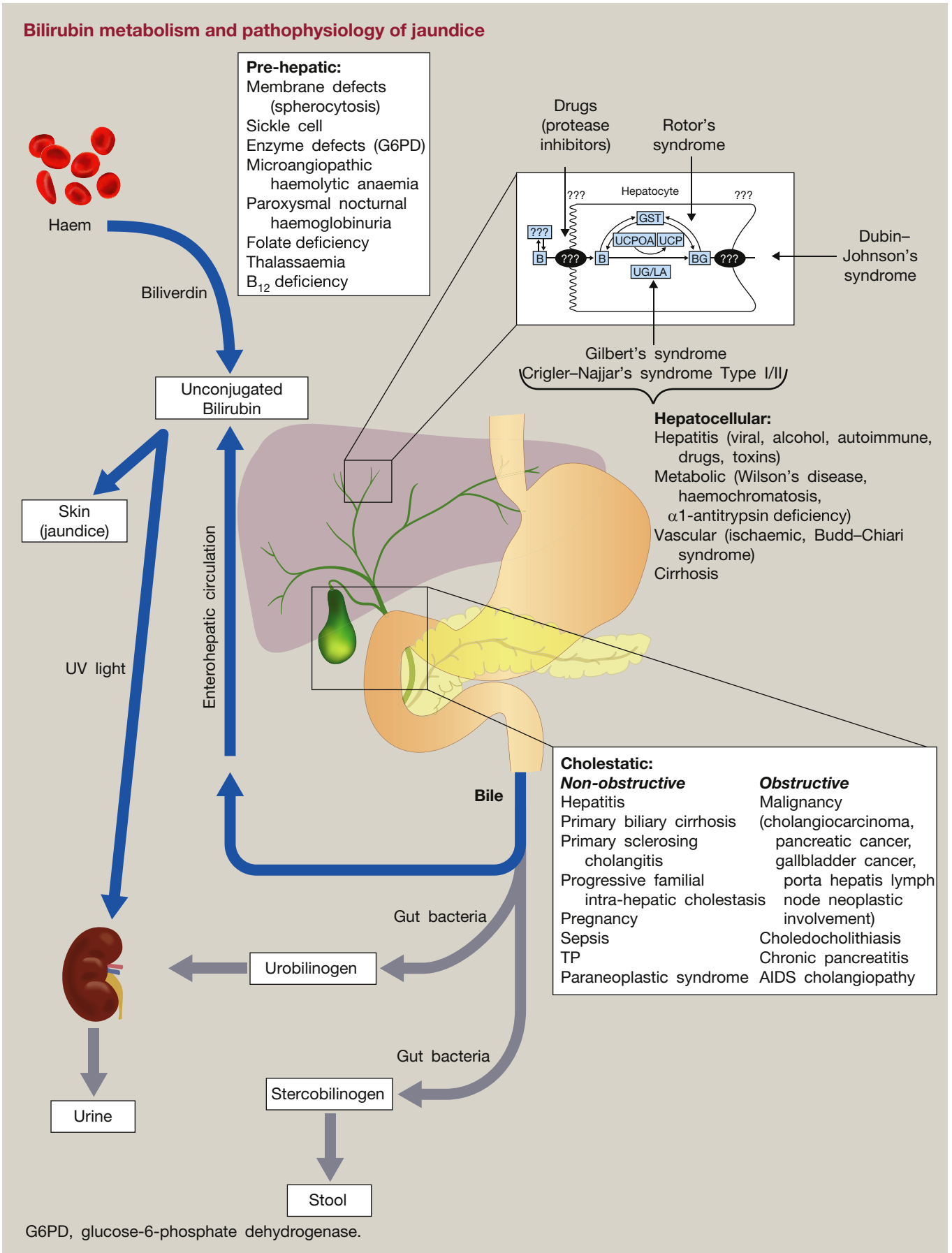

Figure 1

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