Jaundice

See also Abnormal Liver Function Tests.

Definition

Yellow discolouration caused by accumulation of bilirubin in tissue. Normal serum bilirubin is 3-20µmol/l. Jaundice not usually apparent until serum bilirubin > 35 µmol/l.

Pathophysiology

- Bilirubin is produced from the breakdown of haemoglobin via biliverdin in the RES.
- 95% of the circulating bilirubin is unconjugated (***indirect*** bilirubin) and bound to albumin.
- Bilirubin-albumin complex is broken down by hepatocytes leaving free albumin circulating.
- Bilirubin is conjugated with 2 x glucuronic acid catalysed by UDP-glucuronyl transferase.
- Most bilirubin diglucuronide is pumped into the bile canaliculi & stored in the GB.
- Normally only a small amount escapes into the blood (conjugated or ***direct*** bilirubin).
- Gut bacteria aid conversion of bile bilirubin diglucuronide to urobilinogen & a small amount enters the enterohepatic circulation.
- Urobilinogen is then either reabsorbed (~1%) and excreted in the urine or broken down by colonic bacteria to urobilins (brown colour) & excreted in the stool.

Jaundice results from interference in these processes and can be classified as:

- **Prehepatic** causes (unconjugated hyperbilirubinaemia)
- **Hepatocellular disease**
- **Posthepatic**: Intrahepatic & Extrahepatic cholestasis

Presentation

History:

- Flu-like prodrome (infective hepatitis)
- Pain. (Sudden→?gallstones. Painless + wt loss/anorexia/back ache→Ca.)
- Dark urine/pale stools. (Viral hepatitis & obstructive jaundice)
- Pruritus.
- Weight loss.
- Travel. (Hepatitis A)
- Alcohol consumption.
- IVDA.
- Blood transfusions.
- Contact with jaundiced patients.
- Medication history. (Amitriptyline, chlorpromazine, chlorpropamide, erythromycin, halothane, imipramine, indomethacin, isoniazid, methyldopa, MAOIs, OCP, rifampicin, salicylates, sulphonamides, thiouracil)
- PMHx: (chronic active hepatitis, previous biliary surgery, malignancy)
- Occupational history. (Chemicals)
- Family history of jaundice (Gilbert's)

Examination:

- Most easily recognised in fair-skinned individuals, difficult in darkly pigmented patients
- Most easily seen in the sclera, under tongue
- Yellow-green in appearance in chronic, severe obstructive jaundice (biliverdin).
- Check for signs of the underlying chronic liver disease.
- If gallbladder palpable, then stone disease unlikely (Courvoisier's law)
- Splenomegaly is suggestive of cirrhosis, haematological disorders or reticulosis

Differential Diagnosis

Prehepatic (unconjugated hyperbilirubinaemia)

- Gilbert's syndrome (AD, 5% pop, underactive UDP-glucuronyl transferase [UDP-GT] or ↓liver bilirubin uptake. Worsened by infection, fatigue & fasting).
- Haemolytic anaemias (E.g. spherocytosis, pernicious anaemia).

- Thalassaemia
- Trauma
- Crigler-Najjar syndromes (I: AR, inborn, no UDP-GT→rapidly fatal; II: AD, ↓↓UDP-GT, Rx: **phenobarbitone**)
- Glucose-6-phosphate deficiency ± oxidative drugs

Hepatocellular disease (may cause unconj or conj hyperbilirubinaemia)

- Viral hepatitis (including type A and B). Other infections such as the zoonotic diseases (Leptospirosis, brucellosis and Coxiella burneti) and glandular fever.
- Alcoholic hepatitis
- Autoimmune hepatitis (10-20% of chronic hepatitis).
- Drug induced hepatitis. E.g. paracetamol, Ecstasy and halothane.
- Hepatotoxic chemicals. E.g. phosphorous, CCl_4 and phenol
- Decompensated cirrhosis
- Rare disorders: Dubin-Johnson Syndrome (AR, conj J, ↓excretion of conj bili, liver deposits), Rotor syndrome (AD, conj J, sim. To Dubin-Johnson but no deposits)

Intrahepatic cholestasis

- Primary biliary cirrhosis (PBC)
- Drugs (for example phenothiazines)
- Primary sclerosing cholangitis

Extrahepatic cholestasis. From within lumen, in the duct wall or external compression.

- Common duct stone
- Pancreatitis
- Cancer of the gallbladder/pancreas
- Bile duct strictures (benign or malignant)
- Tumour of the ampulla of Vater

Investigations

- Urinalysis:
  - Urinary bilirubin, and absent or ↓↓urobilingen suggests obstructive jaundice.
  - ↑Urinary bilirubin and ↑urobilinogen suggests hepatocellular failure.
  - No urinary bilirubin, ↑urinary urobilinogen suggests haemolytic jaundice.
  - NB: False neg for urinary bilirubin if rifampicin or urine not fresh. False pos with phenothiazines. False positives for urobilinogen occur in acute porphyria.
- LFTs:
  - ↑Unconjugated (indirect) bilirubin→Gilbert's, haemolysis (also ↑reticulocytes, ↓serum haptoglobin), mild chronic hepatitis, or Crigler-Najjar syndrome
  - ↑Conjugated (direct) bilirubin (>10) suggests obstructive jaundice, including: liver disease, biliary atresia, pancreatic disease, Dubin-Johnson syndrome
  - ALP: ↑↑extrahepatic/intrahepatic disease. (Gallstones, pancreatic ca, drugs)
  - AST & ALT: ↑↑hepatocellular disease (e.g. viral hepatitis), modest ↑ in chronic hepatocellular damage and obstruction.
    - AST>ALT in cirrhosis, liver Ca, haemolytic jaundice and EtOH hepatitis.
    - ALT>AST in acute hepatitis and in extrahepatic obstruction.
  - Gamma-glutamyl transferase (GGT). Sensitive but not specific for excess alcohol. ↑↑ biliary obstruction & hepatic malignancies ↑GGT + ↑ALP → cholestasis.
- FBC (haemolysis), Hepatitis serology, INR (vitamin K corrects def in cholestasis but not in parenchymal liver disease), serum ANA & anti-smooth muscle antibody (ASMA) for PBC, Alpha-1 antitrypsin levels, ferritin (screens for haemochromatosis).
- Imaging USS, CT, MR cholangiopancreatography (MRCP), ERCP
- Liver biopsy