

Presentation of Jaundice

Pathophysiology of jaundice

- Pre-hepatic
 - Increased breakdown of red cells leads to increased serum bilirubin. This unconjugated bilirubin isn't water-soluble so can't be excreted in the urine. Intestinal bacteria convert some of the extra bilirubin into urobilinogen, some of which is re-absorbed and IS excreted by the kidneys – hence urinary urobilinogen is increased.
- Hepatic
 - Disorders of uptake, conjugation or secretion of bilirubin.
 - Usually divided into conjugated or unconjugated bilirubinaemia.
- The various causes of jaundice are traditionally classified into pre-hepatic, hepatic and post-hepatic (or cholestatic) groups according to the mechanism of the jaundice.

Pre-hepatic causes of jaundice

- Congenital red cell issues
 - Cell shape
 - Sickle cell disease
 - Hereditary spherocytosis
 - Hereditary elliptocytosis
 - Enzyme
 - G6PD deficiency
 - Pyruvate kinase deficiency
 - Haemoglobin
 - Thalassemia
- Autoimmune haemolytic anaemia
- Drugs
 - Penicillins
 - Sulphasalazine
- Infections
 - Malaria
- Mechanical
 - Metallic valve prostheses
 - DIC
- Transfusion reactions
- Paroxysmal nocturnal haemoglobinuria

Hepatic causes of jaundice

- Conjugated causes:
 - Cirrhosis (see chronic liver disease for further causes)
 - Malignancy
 - Primary or metastases
 - Viral hepatitis
 - Drugs
 - Hepatitis
 - Isoniazid, rifampicin, atenolol, enalapril, verapamil, nifedipine, amiodarone, ketoconazole, cytotoxics, halothane
 - Cholestasis

- Ciclosporin, azathioprine, chlorpromazine, cimetidine, erythromycin, nitro, ibuprofen, hypoglycaemics
 - Enzymes
 - Dubin-Johnson syndrome (DJS)
 - Autosomal recessive (cMOAT gene) with excretion of conjugated bilirubin.
 - Leads to pigmented liver.
 - Increase in conjugated bilirubin with no other enzyme changes
 - High coproporphyrin
 - Rotor syndrome
 - Similar to DJS
 - Liver not pigmented
 - Normal coproporphyrin
- **Unconjugated causes of jaundice** (sometimes classified as pre-hepatic causes)
 - Gilbert's syndrome
 - Congenital hypo-activity of conjugation enzyme UGT-1. Benign and common (5%)
 - Normal LFTs except mildly elevated bilirubin, especially in times of physiological stress/illness
 - Normal life expectancy
 - Crigler-Najar syndrome
 - Autosomal recessive (type I) or dominant (type II). Severe unconjugated hyperbilirubinaemia.
 - Congenital absence (I) or decrease (II) of glucuronyl transferase.
 - Normal liver histology.
 - Treatment is liver transplant (only type II survive to adulthood)

Post-hepatic causes of jaundice

- Biliary tree obstruction
 - Gallstones
 - Compression e.g. pancreatitis, pancreatic tumour, lymph nodes, biliary atresia
 - Cholangiocarcinoma
 - Post-operative stricture
- Primary biliary cirrhosis (**see PBC section**)
 - M:F = 1:9
 - ANA and Anti- mitochondrial antibodies
 - And anti-centromere for prognosis (though more association with CREST)
- Primary sclerosing cholangitis (**see PSC section**)
 - 80% of PSC have UC
 - ANCA, anti-smooth muscle antibodies
 - Association with cholangiocarcinoma

Pregnancy-associated jaundice

- Obstetric cholestasis
 - 0.1-0.2% of pregnancies
 - Presentation
 - Itching – jaundice later
 - Raised liver markers, esp ALP
 - Issues
 - Fetal mortality 3.5%
 - Often recurs in further pregnancies

- Treatment
 - Ursodeoxycholic acid
- HELLP (Haemolysis, Elevated Liver enzymes, Low Platelets)
 - Occurs in 1-2 out of 1000 pregnancies and 10-20% of severe pre-eclampsia
 - Leads to a variant of DIC
 - Needs steroids and prompt delivery
 - Maternal mortality 1-24%
- Fatty liver of pregnancy
 - All LFTs including synthetic function go off
- Hyperemesis gravidum
- Pre-eclampsia
 - Associated with abnormal LFTs in 20% cases

History in jaundice

- History of presenting complaint
 - Onset of jaundice
 - Pain/Painless
 - Fevers
 - Constitutional symptoms
 - Bowel symptoms
 - Dark urine/Pale stools
- Past medical history
 - IBD
 - Viral hepatitis
 - Blood transfusions
 - Heart valve surgery
 - Autoimmune disorders
- Medications
 - See drug causes above
- Allergies
- Family history
 - Thalassaemia/Sickle cell/
- Social history
 - Alcohol consumption
 - Travel history: viral hepatitis, malaria
 - Ideas; concerns; expectations

Examination in jaundice

- Features of chronic liver disease:
 - Ascites
 - Hands: clubbing, Dupuytren's contracture, palmar erythema
 - Spider naevi
 - Gynaecomastia
 - Portal hypertension: splenomegaly and caput medusae
 - Encephalopathy
- Cachexia
- Abdominal masses
- Lymphadenopathy
- Splenomegaly

Initial management of jaundice

- Blood tests:
 - Liver function tests (including bili, ALP, ALT, AST, GGT)
 - Full blood count, urea and electrolytes
 - Clotting screen
 - Liver screen
 - Autoimmune screen (ENA, ANA, ANCA)
 - Viral screen (Hep A,B,C)
 - Alfafetoprotein (AFP)
 - Serum caeruloplasmin
 - Ferritin
 - Blood film
- Ultrasound of the abdomen

Further management of jaundice

- Further investigation and management will be dictated by the aetiology – see the various sections for more information on this.

Common questions concerning jaundice

How are the causes of jaundice classified?:

- Pre-hepatic, hepatic and post-hepatic

What are the pre-hepatic causes of jaundice?

- Congenital cell issues
 - Cell shape
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 - Thalassemia
- Drugs
 - Penicillins
 - Sulphasalazine
- Infections
 - Malaria
- Autoimmune
 - Warm/cold
- Mechanical
 - Metallic valve prostheses
 - DIC
- Transfusion reactions
- Paroxysmal nocturnal haemoglobinuria

What are the hepatic causes of jaundice?

Conjugated causes include:

- Cirrhosis (see chronic liver disease for further causes)
- Malignancy
- Viral hepatitis
- Drugs
 - Hepatitis: isoniazid, rifampicin, atenolol, enalapril, verapamil, nifedipine, amiodarone, ketoconazole, cytotoxics, halothane
 - Cholestasis: Ciclosporin, azathioprine, chlorpromazine, cimetidine, erythromycin, nitro, ibuprofen, hypoglycaemics
- Enzymes
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What tests are in a routine liver screen

- Assuming FBC, U&E, liver function (ALP,ALT,AST, GGT) and clotting has already been done
 - Autoimmune screen (ENA, ANA, ANCA)
 - Viral screen (Hep A,B,C)
 - Alfafetoprotein (AFP)
 - Serum caeruloplasmin
 - Ferritin

- Consider

What three blood tests examine synthetic liver function?

- Clotting (PT)
 - Examining vitamin-K dependent clotting factors
- Platelets
- Albumin
- The rest of the LFTs reflect liver processing ability. The synthetic function tests are the most important in assessing how well the liver is working. Note, for example, that ALT and AST can be normal or low in advanced liver failure.