Interpretation of Liver Function Tests

Patterns

- **Acute hepatitic picture**: ALT/AST in 1000s (alcoholic a bit lower), ALP mildly raised
- **Chronic hepatitic picture**: ALT/AST in 100s, ↓albumin
- **Cholestatic (obstructive) picture**: ALP upto 1000s, ALT/AST mildly raised, ↑bilirubin
- **Alcoholic**: ↑γGT, ↑MCV

Liver enzymes

Enzymes leak from damaged liver cells; hence, they reflect liver injury (not function)

Aminotransferases (alanine aminotransferase (ALT) and aspartate aminotransferase (AST))

- ALT sources: specific to liver
- AST sources: liver, heart, skeletal muscle, kidneys, pancreas
- **Marked increase** (e.g. 1000s):
    1. Toxin/drug-induced hepatitis (e.g. paracetamol)
    2. Acute viral hepatitis (Hep A/B/E, EBV, CMV)
    3. Liver ischaemia
- **Modest increase** (300-500): chronic/alcoholic/autoimmune hepatitis, biliary obstruction
- **Mild increase** (<300): cirrhosis, non-alcoholic fatty liver disease, hepatocellular carcinoma, haemochromasosis/Wilson's
- Ratio of ALT:AST
    - ALT>AST: chronic liver disease
    - AST>ALT: + in established cirrhosis, ++ in alcoholic liver disease

Alkaline phosphatase (ALP)

- Sources: biliary ducts, bone (Paget's disease, bony metastasis, fractures, osteomalacia, renal bone disease); less so: placenta (pregnancy), small intestine (fatty meals), kidneys (CRF)
- γGT can be used to confirm if ALP is of hepatic origin and isoenzyme analysis may also be used to confirm source
- **Marked increase** (>4x normal): cholestasis (e.g. gallstones, PBC, PSC, pancreatic CA, drugs)
- **Moderate increase** (<3x normal): hepatitis, cirrhosis, infiltration (e.g. hepatocellular carcinoma, abscess etc)

Gamma-glutamyltransferase (γGT)

- **Mirrors ALP** so can be used to confirm if a rise in ALP is of hepatic origin
- Raised with alcohol abuse and enzyme-inducing drugs

Bilirubin

Extravascular haemolysis results in the breakdown of Hb → globulin (further broken down to amino acids) + haem (further broken down to bilirubin). This unconjugated bilirubin is then conjugated by the liver so it can be excreted in bile.

- **Unconjugated hyperbilirubinaemia** (indirect bilirubin fraction >85%)
    - Increased RCC breakdown (haemolytic anaemia – see FBC interpretation)
    - Impaired hepatic uptake (drugs, CCF)
    - Impaired conjugation (Gilbert's syndrome, physiological neonatal jaundice)
- **Conjugated hyperbilirubinaemia** (direct bilirubin fraction >50%)
    - Hepatocellular dysfunction (liver diseases)
    - Impaired hepatic secretion (cholastasis)

Functional liver tests

Albumin

Albumin half-life is **20 days** so changes happen in weeks.

- ↓albumin + ↓protein = advanced cirrhosis, alcoholism, protein malnutrition, chronic inflammation, renal/gut/skin loss
- ↓albumin + normal protein = infection (negative acute phase reactant)
- ↓albumin + ↑protein = myeloma

Prothrombin time/INR

PT/INR is dependent on vitamin K-dependant clotting factors and fibrinogen which are made in the liver. Some clotting factors have short half lives (e.g. **6-8 hours**) so changes can occur rapidly.

- Raised INR: liver disease (with impaired function), vitamin K deficiency, consumptive coagulopathy (e.g. DIC)

Other tests

FBC clues

- Anaemia = GI bleeding
- Macrocytosis = alcohol
- Thrombocytopenia = effect of alcohol on bone marrow, hypersplenism, liver fibrosis or DIC

Further investigations to find cause

Blood tests

- Viral
  - Hepatitis A IgM
  - Hepatitis B surface antigen
  - Hepatitis C IgG
  - Hepatitis E
  - CMV PCR/IgM
  - EBV PCR
- Autoimmune liver screen
  - Anti-smooth muscle (auto-immune hepatitis type 1)
  - Anti-mitochondrial (primary biliary cirrhosis)
  - Anti-liver-kidney microsomal (auto-immune hepatitis type 2, hepatitis C/D, drug-induced hepatitis)
  - Anti-nuclear (auto-immune hepatitis type 1, SLE)
- Tumour markers – if cirrhosis/weight loss
  - α-FP (hepatocellular carcinoma)
- Infiltrative
  - Ferritin and transferrin saturation (>55%) (haemochromatosis) – *but be aware ferritin is also an acute phase reactant*
  - Serum copper and caeruloplasmin ± 24 hour urinary copper (Wilson's disease)
  - Fasting glucose and lipids (fatty liver disease)
- Metabolic
  - α_1-antitrypsin (α_1-antitrypsin deficiency)
  - Immunoglobulins and protein electrophoresis (IgM raised in PBC, IgA raised in alcoholic liver disease, IgG raised in autoimmune hepatitis)
  - TTG (Celiac disease)
- Toxins
  - Paracetamol level (paracetamol overdose)

Imaging

- Abdominal ultrasound – 1st line imaging (quick and cheap) that is useful for determining liver texture, size and presence of any gallstones or cholecystitis
- Abdominal CT – can confirm pancreatitis or tumour

Procedures

- Ascitic tap – if ascites present (see ascitic fluid interpretation)
- Liver biopsy

Some non-hepatic causes of raised LFTs

In addition to any described above…

- Drugs
  - **Hepatitis**: RIP (of RIPE) tuberculosis Abx, sodium valporate, methotrexate, methyldopa, amiodarone, statins, paracetamol, phenytoin, ketoconazole, nitrofurantoin
  - **Cholestasis**: carbamazepine, chlorpromazine, co-amoxiclav, erythromycin, sulphonylureas, flucloxacillin
- Right heart failure
- Sepsis
- Coeliac disease
- Haemolysis
- Hyperthyroidism
- Right lower lobe pneumonia