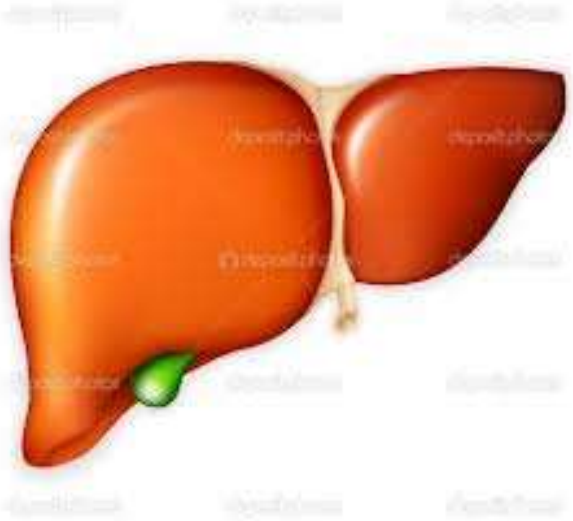
Liver Function Tests (LFT)

- The liver is a large organ located in the upper right-hand part of the abdomen behind the lower ribs. It takes up drugs and toxic substances from the blood and renders them harmless.
- It produces proteins, including enzymes and blood clotting factors, helps maintain hormone balance and stores vitamins.
- The liver produces bile, a fluid that is transported through ducts to the gallbladder to be stored and then to the small intestine to help digest fats.



What is being tested?

- **Alanine aminotransferase (ALT)** – an enzyme mainly found in the liver; the best test for detecting hepatitis
- **Aspartate aminotransferase (AST)** – an enzyme found in the liver and a few other places, particularly the heart and other muscles in the body
- **Total bilirubin** – measures all the yellow bilirubin pigment in the blood
- **Conjugated bilirubin** - measures the form made only in the liver and is often requested with total bilirubin in infants with jaundice
- **Alkaline phosphatase (ALP)** – an enzyme related to the bile ducts; often increased when they are blocked, either inside or outside the liver
- **Albumin** – measures the main protein made by the liver and tells how well the liver is making this protein
- **Total protein** - measures albumin and all other proteins in blood, including antibodies made to help fight off infections
- Other tests that can help to assess liver function include **gamma-glutamyl transferase (GGT)**, 5'-nucleotidase (5'-NT) **and prothrombin time (PT)**, together with **bilirubin and urobilinogen in urine**.

- Liver function tests are used to help determine the cause of symptoms such as jaundice that may be due to liver disease. They are also used to screen for potential liver damage, for example in alcoholics or people exposed to the hepatitis virus, and also to monitor changes in abnormal liver function.

- These tests are used when symptoms suspicious of a liver condition are noticed.
- These include: jaundice, dark urine and light-coloured stools; nausea, vomiting and diarrhoea; loss of appetite; vomiting of blood; bloody or black stools; swelling or pain in the belly; unusual weight change; and fatigue or loss of stamina, exposed to a hepatitis virus; has a family history of liver disease; has excessive alcohol intake; or is taking a drug that can cause liver damage.

Heat Labile and Heat Stable ALP

- Test based on differential heat sensitivities of bone, liver and heat stable isoenzymes.
- Bone ALP is most heat labile and deteriorates after 15 minutes at 56 degrees.
- Heat stable (placental or malignancy) is heat stable even at 56 degrees. Liver deteriorates logarithmically at 56 degrees.
- Since serum from most individuals contains bone and liver in equal proportions (50%), mathematical equations can be used to quantitate the two isoforms.
- Fasting sample is preferred to minimise overestimation of liver isoform as intestinal ALP has similar heat stability as liver.

Isoenzymes of ALP

50% - Pre-Beta ALP (Heat Labile)

25% - Alpha-2 Heat Labile ALP

1% - Alpha-2 Heat Stable ALP

10% - Alpha-1

10% - Gamma-ALP

Leukocyte Alkaline Phosphatase (LAP)

Elevated

- liver disease (liver fraction of AP...heat stable):
  - obstructive jaundice (even pericholangitis as in abdominal inflammation., IBD
  - hepatocellular jaundice
  - hepatic venous outflow obstruction with biliary changes can give AP >1000[4]
  - space occupying liver lesions, diffuse or segmental
- bone disease (bone fraction...heat labile):
  - tumors
  - increased bone turnover (hyperparathyroidism; rickets; Paget's disease; healing fractures)
- placental disease (syncytial trophoblastic fraction...PLAP):
  - pregnancy (especially 3rd trimester).
  - ovarian, testicular, and germ tumors.
- other:
  - intestinal epithelial damage (strangulation/obstruction).
  - kidney/renal tubule damage/tumors...RCC.
  - hyperthyroidism
  - congestive heart failure.
  - 1-3 weeks after pulmonary infarct.
  - pancreatitis.
  - CMV & EBV mononucleosis.
  - dozens of medications

Decreased

- hypothyroidism
- pernicious anemia/low serum B12 (osteoblasts need T4 & B12)
- milk alkali syndrome
- malnutrition
- hypophosphatasia of any cause
- celiac disease
- Whipple disease
- folic acid deficiency
- hypoparathyroidism
- lactosuria
- chondrodystrophy
- zinc deficiency of any etiology (dialysis or TPN, etc.)
- trifluoperazine

Bilirubin

- Metabolism of Bilirubin is a process that begins in the blood, with the...

- **Erythrocytes**
- Contain haemoglobin. Run around the body in the blood until passing into the spleen…

- **Spleen**
- Breaks up the old blood cells, cracking apart the haemoglobin to produce haem, then biliverdin and then unconjugated bilirubin. It then chucks the whole lot out into the portal vein which passes to the liver

- **Liver**
- It gets conjugated (and so becomes water soluble). The conjugated bilirubin then passes out into the gut…

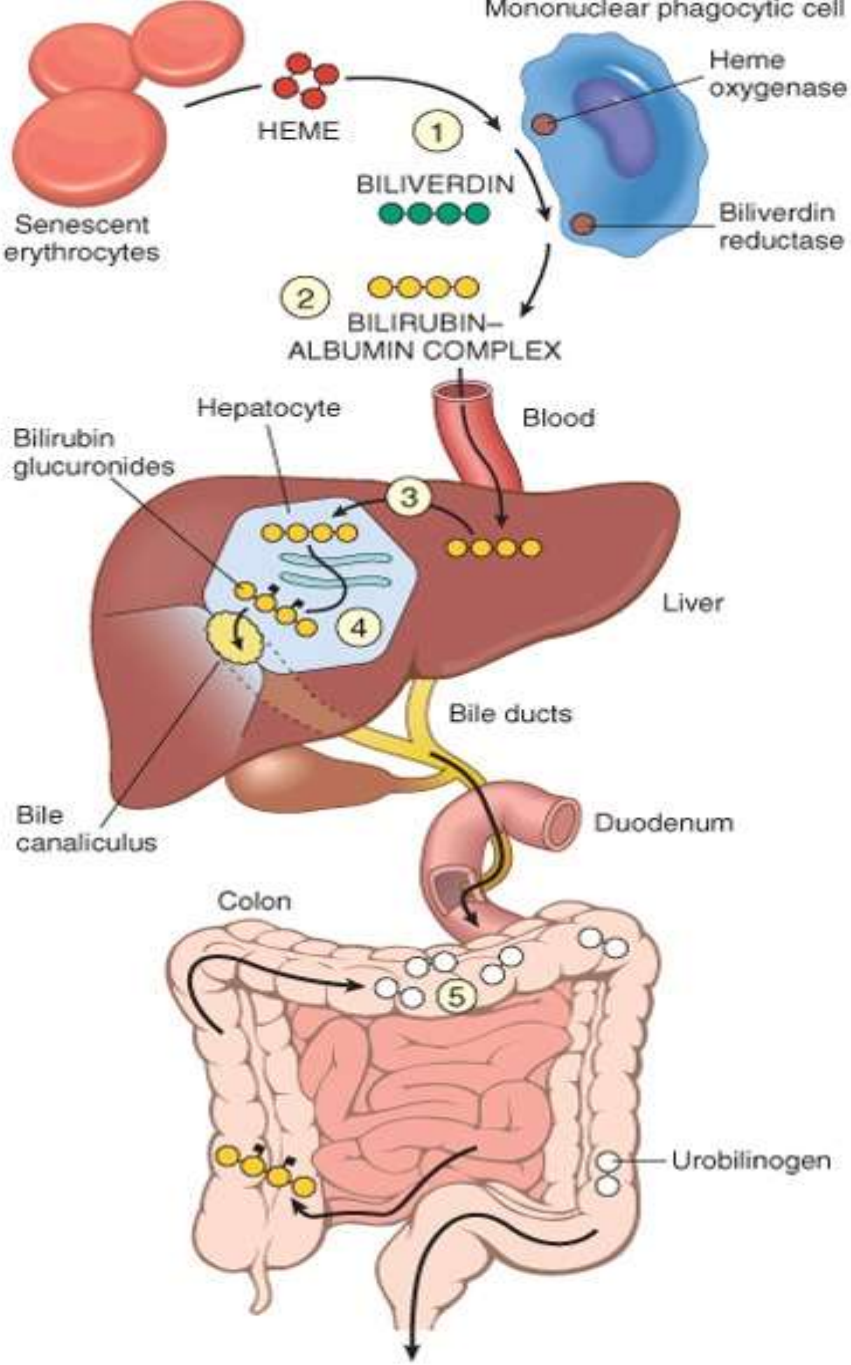
- **Gut**
- In the gut, jolly old conjugated bilirubin is converted by bacteria into urobilinogen. Some leaves in urine, much is reabsorbed into the enterohepatic circulation then a large amount of it is oxidised to stercobilinogen, and excreted in the faeces…

Bilirubin

- **Faeces**
- Stercobilinogen is the main pigment in stool.

- **Urine**
- A small amount of conjugated bilirubin is absorbed straight from the liver. If the bile duct is blocked then a whole lot more goes into the urine, making it darker. A tiny amount of urobilinogen is absorbed from the gut. In early or recovering hepatitis, this results in pre-formed stercobilinogen appearing in the urine in excess as urobilinogen. Once the biliary obstruction is established this levels drops – hence it is a sensitive marker of early liver damage.

- **Enterohepatic Circulation**
- The urobilinogen is reabsorbed, and travels back through the liver and down the bile duct again. This returns the cholic acid and chenodeoxycholic acid to the liver, enhancing bile secretion.



Albumin

- produced only in the liver
- major plasma protein that circulates in the bloodstream
- essential for maintaining oncotic pressure in the vascular system
- important in the transportation of many substances such as drugs, lipids, hormones, and toxins that are bound to albumin in the bloodstream

Globulin

- Second major plasma protein in circulation after albumin.
- Important in immune system

A/G Ratio

- Normally, there is a little more albumin than globulins, giving a normal A/G ratio of slightly over 1, that is 0.8 - 2.0. Because disease states affect the relative amounts of albumin and globulin, the A/G ratio may provide a clue as to the cause of the change in protein levels.
- A low A/G ratio may reflect overproduction of globulins, such as seen in multiple myeloma or autoimmune diseases, or underproduction of albumin, such as may occur with cirrhosis, or selective loss of albumin from the circulation, as may occur with kidney disease (nephrotic syndrome).
- A high A/G ratio suggests underproduction of immunoglobulins as may be seen in some genetic deficiencies and in some leukemias. More specific tests, such as liver enzyme tests and serum protein electrophoresis, must be performed to make an accurate diagnosis.
- With a low total protein that is due to plasma expansion (dilution of the blood), the A/G ratio will typically be normal because both albumin and globulin will be diluted to the same extent.