LIVER PHYSIOLOGY

Synthetic functions

Synthesis of plasma protiens
- Acute phase protiens
- Albumin
- Clotting factors
- Binding protiens (eg haptoglobin)

Other synthetic functions
- see other headings
  - gluconeogenesis
  - cholesterol/lipoprotiens
  - immunological
  - hormones
  - urea and bile production

Endocrine Functions

Activation of vitamin D
Conversion of thyroxine (T_4) to T_3
Secretes angiotensinogen
Metabolises hormones

Storage

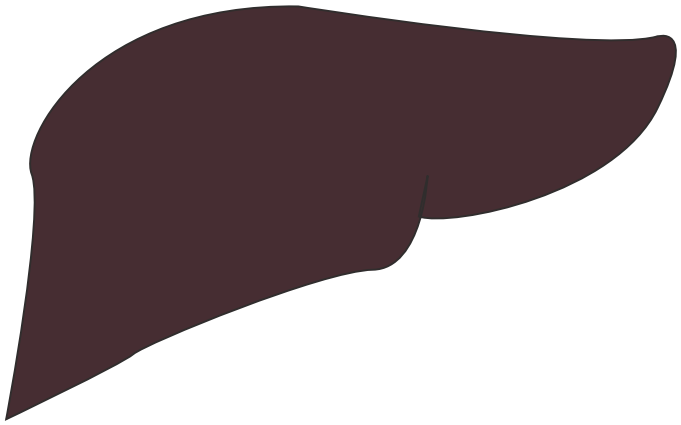
Stores vitamins ADEK B_{12}
Iron
Copper
Glycogen
Important blood reservoir

Metabolic Functions

Carbohydrate metabolism
- Converts glacatose/frctose to glucose
- Gluconeogenesis
- Contains 100g of glycogen for release

Lipid metabolism
- Fatty acid oxidation
- Synthesis of cholesterol/lipoprotiens
- Production of ketoacids

Protien metabolism
- Amino acid production
- Turnover of protiens



Immunological/protective

Reticuloendothelial component
- Filters the portal blood from bacteria
- Importance in antigen presentation
- Phagocytoses via Kupffler cells
- Removes haemolysis products

Inactivation of toxins and drugs
- Phase I (oxidation, reduction, hydrolys)
- Phase II (conjugation/
- Cytochrome P450 system

Other functions

Important role in acid base regulation
Digestive role via bile salts
Bile neutralises acid in the duodenum

Laboratory assessment of liver function. Assessment of liver function with laboratory tests requires serial measurements of parameters related to different hepatic functions, interpreted in a clinical context. Bilirubin metabolism is assessed by plasma conjugated and unconjugated bilirubin, assessing the conjugation and excretion functions. Elevated conjugated bilirubin can also be detected by dipstick testing of urine. Hepatocellular enzyme levels in plasma are used to assess cellular injury. Aminotransferases (AST and ALT) reflect cellular injury. ALT is more specific to liver tissue and is less elevated in alcoholic hepatitis, an AST to ALT ratio of 2:1 or greater is strongly suggestive of an alcohol related aetiology (especially in association with a doubling of GGT). Alkaline phosphatase is not specific to liver tissue but is elevated in cholestasis of any cause. γ-Glutamyl transferase (GGT) is a sensitive indicator of biliary disease and is elevated by all causes of induction of microsomal enzymes. Serum proteins provide an indicator of the synthetic function of the liver. Albumin has a half-life of about 20 days and is reduced in severe cirrhosis, and also by malnutrition, nephrotic syndrome and other causes. Clotting factors II, VII, IX, X, V and fibrinogen are produced in the liver. A prolonged INR may indicate a failure of synthesis of these factors (especially VII) due to hepatic failure or vitamin K malabsorption. Other tests include blood ammonia, which is elevated in hepatic failure due to impairment of the urea cycle and correlates with encephalopathy. Elevated triglycerides and abnormal lipoproteins may also reflect impaired lipid metabolism. Specific tests for causes of liver disease include hepatitis serology, antimicrosomal antibody (PBC), antinuclear antibodies (SLE), α-fetoprotein (hepatoma), Fe studies (haemochomatosis), ceruloplasmin (Wilson's disease), and dozens of other specific tests.α

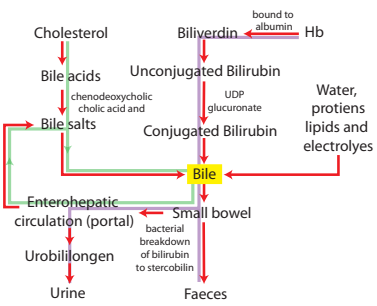
Hepatocellular injury
- ALT, AST (more cell injury)
- GGT, ALP (more cholestatic)

Synthetic Function
- Albumin (long half life)
- Clotting factors and INR

Heaptic impairment
- Elevated bilirubin
- Elevated blood ammonia

Specific Tests
- ANA, αFP, Fe studies,
- Ceruloplasmin, Viral serologies

Physiological consequences of hepatic disease Carbohydrate metabolism: reduced ability to metabolize a glucose load, reduced sensitivity to insulin both in the liver and peripherally, reduced ability to metabolize lactate, reduced glycogen stores. Protein metabolism: disrupted metabolism of non-branched-chain amino acids, leading to elevation in circulating levels of aromatic amino acids, impairment of the urea cycle and a rise in plasma ammonia, secondary rise in ammonia due to poor excretion of urea and NH_3 by the kidneys with enterohepatic circulation of urea (converted in the gut to NH_3) and potentiation of the effect of NH_3 because of alkalosis. Lipid metabolism the pathogenesis of fatty liver is uncertain possibly reduced synthesis of apoproteins, causes accumulation of triglycerides possibly increased synthesis of lipids longstanding cholestatic disease causes increased LDL and cholesterol and reduced HDL. Synthetic functions reduced albumin synthesis, reducing plasma oncotic pressure and binding sites reduced clotting factor synthesis (II, V, VII, IX, X) except for fibrinogen. Metabolism of drugs and hormones portosystemic shunting, decreased phase I and II reactions and increased insulin, glucagon, oestrogens.



Bile production the liver produces about 1L of bile per day, this passes into the gallbladder where it is concentrated to about one-fifth of its volume. Bile consists of electrolytes, protien, bilirubin, bile salts and lipids. Bile acids (cholic acid and chenodeoxycholic acid) are produced in the liver from cholesterol. They combine with taurine and glycine to form the bile salts. The main function of the bile salts is the emulsification of dietary fat, this being essential for fat absorption. In addition bile salts are also important for the absorption of the fat soluble vitamins ADEK. Bile salts are reabsorbed from the portal circulation and recycled in the liver. Bilirubin is also an important component in bile production. Hb is broken down in the reticuloendothelial system to biliverdin. This is converted to bilirubin by a reductase enzyme. Bilirubin is bound to serum albumin and is transported to the liver. In the liver, the unbound bilirubin enters the hepatocyte and is conjugated with gluconorides rending it water soluble, and the conjugate is then secreted in the bile. In the gut, conjugated bilirubin is broken down by bacteria to form urobilinogen, which undergoes enterohepatic circulation and is excreted in the urine.

Splanchnic (including hepatic) blood flow the splanchnic system recieves approximately 1250ml of the CO which equates to approximately 25%. Anatomically the blood is derived from the coeliac, superior and inferior mesenteric arteries. It is unique in that it is partially in parallel (incl gastric, spleen, pancreas, small intestine and colonic) and partially in series. The liver is the reason for this, as it recieves 25% of its flow from the hepatic artery and the remainer from the portal system. The heaptic system has the capacity to increase flow arterial or portal flow if the reciprocal is decreased. The liver maintains a tightly controlled oxygen utilisation due to very effective variable extraction, and uses approximately 50ml O_2 per minute (20%). The splanchnic system is also an important reservoir with pooling occuring in the capacitance vessels of the mesentary, spleen and liver. Control of flow extrinsically is almost exclusively through sympathetic activity. Sympathetic activation results in increased venous constriction which increases the circulating blood volume, and increased resistance of the arterioles which diverts blood away from the digestive system to prioritised organs. Intrinsic blood flow control demonstrates significantly less autoregulation than other organs such as the kidney, brain and heart. It is present however in the hepatic artery in response to modulate the differences in pressures in the compared to the portal vein (100mmHg compared to 10mmHg) and to vary flow if portal return to decreased. Metabolic control is important however in regional control of blood flow, particularly in settings such as food ingestion and consumption with local release of hormones such as gastrin and cholecystokinin increasing flow to the digestive tract. The total flow from the portal vein is about 1.1 l/min at about 9 mmHg. All substances absorbed from the gut, with the exception of lipids which pass into the lymph, must pass through the liver before entering the systemic circulation. Cirrhosis or right heart failure cause an increased resistance to flow in the liver, leading to a rise in pressure in the portal venous system. This causes transudation of fluid into the gut and peritoneal cavity, and in the long term, dilatation of veins at the sites of portosystemic anastomosis: the lower oesophagus, bare area of the liver, umbilicus and anal canal.

Christopher Andersen 2012