CHAPTER 36. LIVER FUNCTION

A. Background: Read over gross, microscopic & ultrastructure of the liver and be familiar with terminology.

B. Biochemical functions of the liver
   1. Hepatic excretory function – removal of organic compounds both endogenous and exogenous via metabolism followed by excretion through bile duct.
      a. Bilirubin – review bilirubin metabolism (Chapter 30)
      b. Bile Acid metabolism: important aspect in cholesterol homeostasis. Also important in digestion of fats. Reabsorbed in terminal ileum (enterhepatic circulation).
         1. Cholesterol metabolized to cholic acid and chenodeoxy-cholic acid (primary bile acids), see fig. 36-2. Important in facilitating the excretion of cholesterol. Prior to excretion, bile acids are conjugated with either taurine or glycine lowering pK_a's to 2 & 4, respectively. This ensures that the acids are charged in the intestinal lumen (pH 5 – 8). Glycine conjugate predominates (3 or 4:1). Secondary bile acids formed from action of intestinal bacteria on primary bile acids.
      c. Hepatic bile formation: 5 – 15% total solids with bile acids major solid component. Bile formed in bile caniculi. Osmotic water flow is major factor regulating bile formation and secretion. Cholesterol & phospholipids are not secreted in absence of bile acid secretion. Bile acids solubilize these substances in mixed micelles dispersing them in the aqueous phase.
      d. Enterohepatic circulation: See fig. 36-4. Micelles facilitate fat absorption in jejunum by solubilizing hydrolytic products of fat digestion & delivering them to intestinal mucosa.
      e. Abnormalities of bile metabolism: See table 36-1
         1. Abnormalities of bile acid delivery to the intestine
         2. Interruption of the enterohepatic circulation of bile acids
         3. Disturbances of bile acid metabolism with hepatocellular disease
      f. Analytical methodology & clinical significance
         1. GLC, HPLC, enzymatic analysis, RIA, ELISA all used to quantify
         2. ↑ serum bile acids in fasting state suggest impaired hepatic uptake or portosystemic shunting. Should be confirmed by standard liver function tests. Serial serum bile acid assays may be used to monitor individuals with suspected or proven hepatic disease.
      g. Xenobiotic metabolism & excretion
         1. Phase I and Phase II metabolites.

2. Hepatic synthetic function – see chapters 19, 23, & 24 for role in synthesis and regulation of carbohydrate, lipid, and protein metabolism.

C. Clinical Manifestations of Liver Disease
   1. Jaundice: See table 36-2
   2. Portal hypertension
   3. Bleeding esophageal varices
   4. Ascites – analyses. Serum/ascites albumin gradient > 1.1 g/dL is diagnostic of portal hypertension
   5. Portosystemic encephalopathy
   6. Altered drug metabolism
   7. Nutritional and metabolic abnormalities
   8. Disordered hemostasis: disseminated intravascular clotting (DIC), other clotting abnormalities
   9. Enzymes released (review Chapter 20 for individual enzyme assays)

D. Diseases of the Liver
   1. Mechanisms and patterns of injury: necrosis vs apoptosis
   2. Fibrosis
   3. Patterns of injury: hepatocellular, cholestatic, acute, chronic
   4. Disorders of bilirubin metabolism (review Chapter 30)
   5. Acute hepatitis: see fig. 36-6
      a. Toxic
      b. Acute Viral: See Table 36-3
         1. Hepatitis B. Time course (see fig. 36-7)
         2. Hepatitis A, D, C, E, G
   6. Chronic viral: see table 36-4. B, C, autoimmune chronic
   7. Alcoholic Liver Disease: see table 36-5
   8. Cirrhosis
   9. Drug-induced liver disease
   10. Metabolic liver disease
      a. Hemochomatosis
      b. Wilson's disease
      c. α_1-antitrypsin inhibitor deficienct
      d. The glycogenosis
      e. Cholestatic liver disease
      f. Primary biliary cirrhosis
      g. Primary sclerosing cholangitis
      h. Post-bone marrow transplant cholangiopath
      i. Acute graft vs host disease
      j. Chronic graft vs host disease
      k. Biliary sludge syndrome
      l. Post liver tansplant cholangiopathy

m. AIDS cholangiopathy

11. Nutritional liver disease and fatty liver
    a. Fatty liver: see tables 36-6,-7
    b. Reye's syndrome
    c. Obesity
    d. Diabetes
    e. Nonalcoholic steatohepatitis
    f. Hepatic tumors: See table 36-8
    g. Hepatocellular carcinoma
    h. Biliary tract diseases
        1. gallstones
        2. cholecystitis

E. Diagnostic Strategies: See table 36-9 for tests of hepatic function, fig. 36-9 for algorithm for the use of abnormal liver function tests to classify and diagnose various types of liver disease
    1. Serum enzymes: see fig. 36-10 for differential diagnostic testing triggered by ↑ serum alkaline phosphatase
    2. Serum albumin
    3. Prothrombin time
    4. Serum bilirubin – see fig. 36-11