Unit Eight

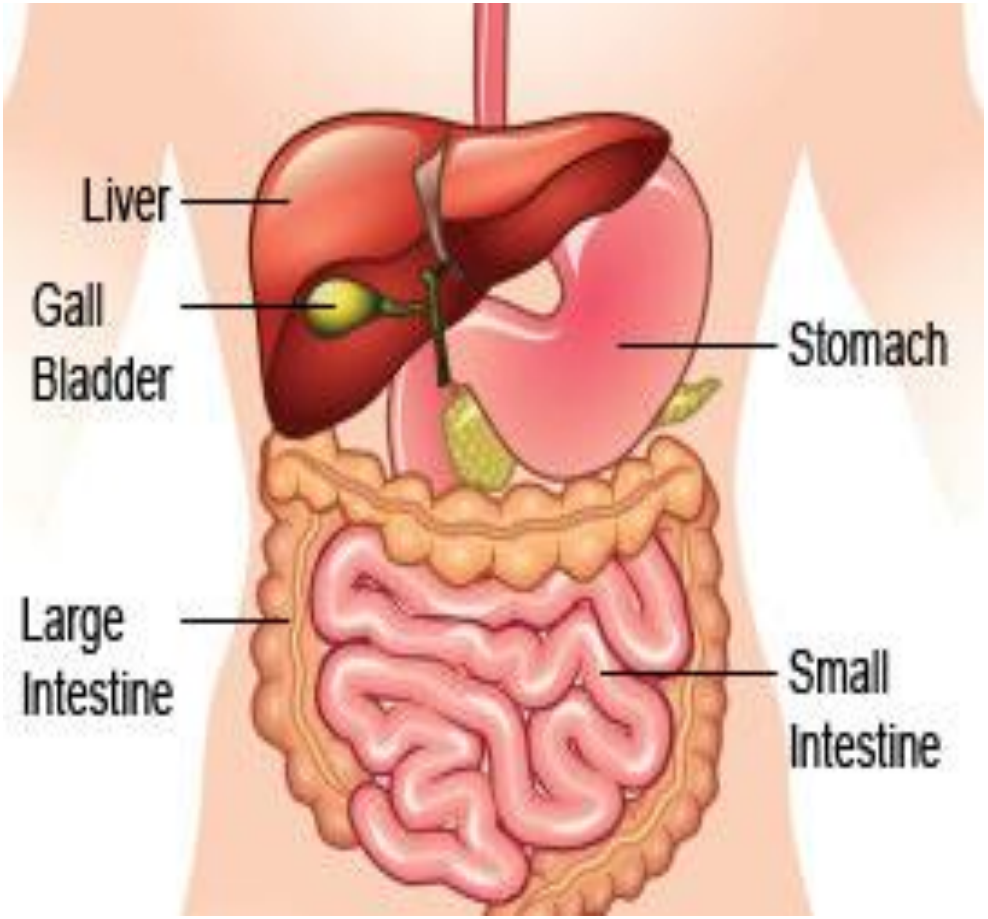
Liver Function Test

Assist. Lec. Sadoun Abbas Alsalimi
Department of Basic Sciences
College of Nursing
University of Basrah

Unit 8. Liver Function Test

Definition of Liver

The liver is an organ only found in vertebrates which detoxifies various metabolites, synthesizes proteins and produces biochemicals necessary for digestion and growth. In humans, it is located in the right upper quadrant of the abdomen, below the diaphragm. Its other roles in metabolism include the regulation of glycogen storage, decomposition of red blood cells, and the production of hormones. The liver's highly specialized tissue, consisting of mostly hepatocytes, regulates a wide variety of high-volume biochemical reactions, including the synthesis and breakdown of small and complex molecules, many of which are necessary for normal vital functions. Estimates regarding the organ's total number of functions vary, but textbooks generally cite it being around 500.



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Functions of Liver

1. Synthetic Function:

a. Synthesis of plasma proteins (albumin, coagulation factors, many globulins)

b. Synthesis of cholesterol. c. Synthesis of triacyl glycerol. d. Lipoprotein synthesis

2. Metabolic Function:

a. Carbohydrates : Glycolysis; glycogen synthesis; glycogen breakdown; gluconeogenesis

b. Ketogenesis; fatty acid synthesis and breakdown. c. Protein catabolism.

d. Citric acid cycle, production of ATP

3. Detoxification and Excretion:

a. Ammonia to urea. b. Bilirubin (bile pigment)

c. Cholesterol. d. Drug metabolites

4. Homeostasis: Blood glucose regulation

5. Storage Function: Vitamin A, D, K, B12

6. Production of Bile Salts: help in digestion

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Liver Function Tests

Biochemical tests are of immense value in diagnosis and monitoring of liver diseases. These tests are usually referred to as "liver function tests" (LFT). LFTs are the most widely performed biochemical tests in the laboratory. Often abnormal liver function will lead to jaundice. Nowadays, only clinically useful tests are being done. These liver function tests are broadly classified as:

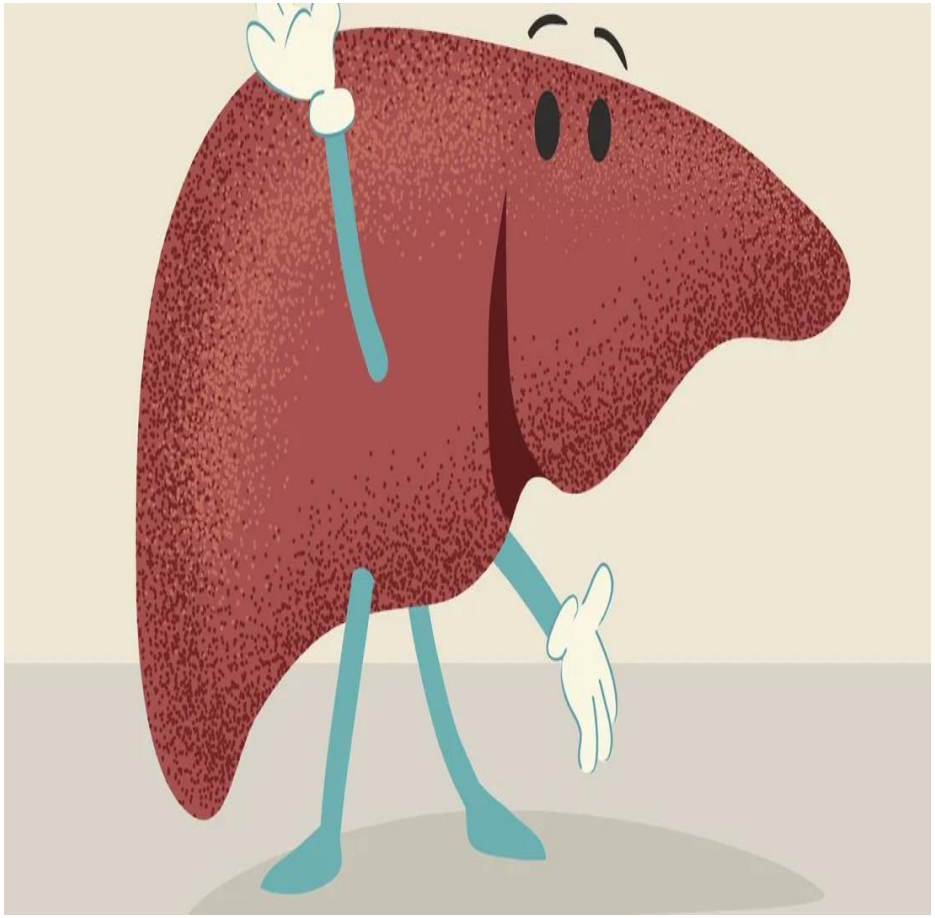
1- Tests to detect hepatic injury:

a. To detect the disease, whether mild or severe; whether acute or chronic.

b. To assess the nature of liver injury; hepatocellular or cholestasis.

2- Tests to assess hepatic function.

Normal LFT values need not indicate absence of liver disease, because liver has very large reserve capacity. Asymptomatic people may have abnormal LFT results. So interpretation should be based on clinical picture.



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Classification of Liver Function Tests

1. Classification based on laboratory findings:

A- Tests of hepatic excretory function: Serum bilirubin and Urine bile pigments (bile salts and urobilinogen).

B- Liver enzyme panel which are markers of liver injury and/or cholestasis: Alanine amino transferase (ALT), Aspartate amino transferase (AST), Alkaline phosphatase (ALP) and Gamma glutamyl transferase (GGT).

C- Plasma proteins (Tests for synthetic function of liver): Total proteins, Serum albumin, globulins, A/G ratio and Prothrombin time (PT).

D- Special tests: Ceruloplasmin, Ferritin, Alpha-1-antitrypsin (AAT), and Alpha fetoprotein (AFP).

2. Classification based on clinical aspects:

A- Markers of Liver Dysfunction: Serum bilirubin, Urine Bile pigments (bile salts and UBG), Total protein, serum albumin and A/G ratio, Prothrombin time and Blood ammonia (when indicated).

B- Markers of hepatocellular injury: Alanine amino transferase (ALT) and Aspartate amino transferase (AST).

C- Markers of cholestasis: Alkaline phosphatase and Gamma glutamyl transferase.

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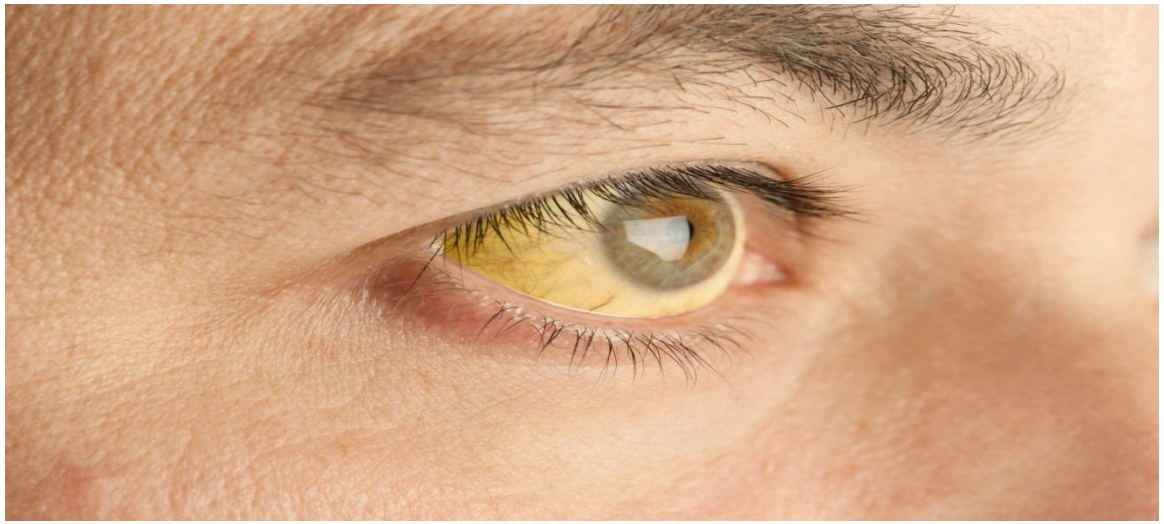
Indications for Liver Function Tests

1. Jaundice
2. Suspected liver metastasis
3. Alcoholic liver disease
4. Any undiagnosed chronic illness
5. Annual checkup of diabetic patients
6. Coagulation disorders
7. Therapy with statins to check hepatotoxicity



Clinical Manifestations of Liver Dysfunction

1- Jaundice: It is the yellowish discoloration of sclera, skin and mucous membrane. It is characteristic of liver disease but it will occur when rate of hemolysis is increased leading to elevation of serum bilirubin.

2- Portal Hypertension.

3- Ascites: It is due to effusion of serous fluid into the abdominal cavity. It is a common presenting feature of cirrhosis. Most often it accompanies peripheral edema. Ascites may be due to causes not related to any pathology of liver

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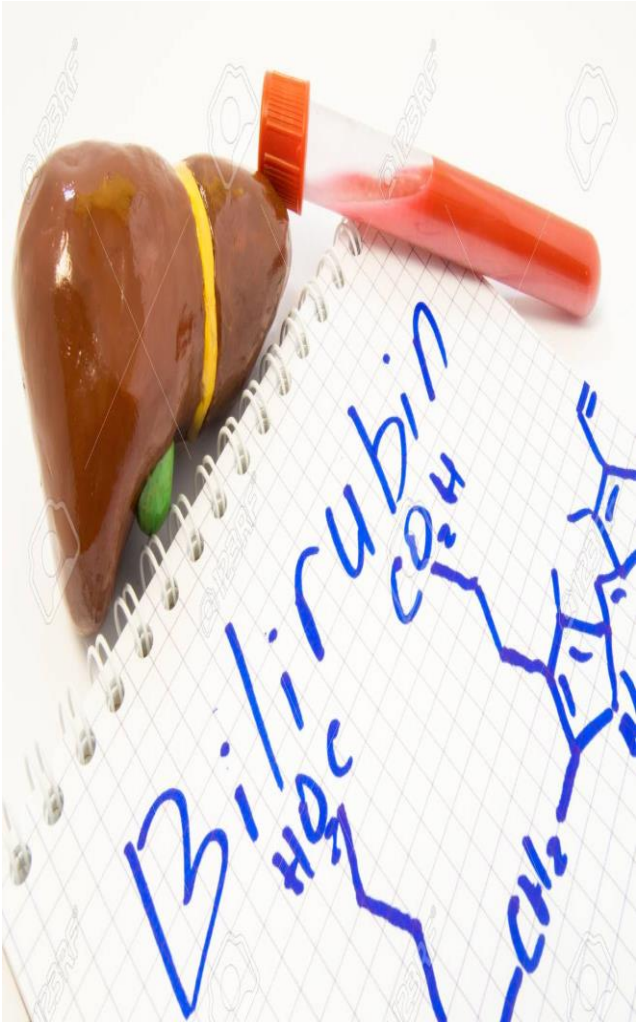
Measurement of Bilirubin

It is the test of Excretory Function of Liver. Bilirubin is the excretory product formed by the catabolism of heme. It is conjugated by the liver to form bilirubin diglucuronide and excreted through bile. Its subsequent breakdown products, such as stercobilin, cause the brown color of feces. Another breakdown produced Urobilinogen which converted to Urobilin which is the main component of the straw-yellow color in urine. Measurements of bilirubin as well as detection of bilirubin and urobilinogen in urine are important tests of liver function. Normal serum bilirubin level varies from 0.2 to 0.8 mg/dL. The unconjugated bilirubin (bilirubin-albumin complex) (free bilirubin) (indirect bilirubin) varies from 0.2–0.7 mg/dL and conjugated bilirubin (direct bilirubin) 0.1–0.4 mg/dL. A rise in serum bilirubin above 1 mg/dL is abnormal (latent jaundice); but jaundice appears only if the level goes above 2 mg/dL. In all cases of jaundice, urine should be examined for the presence of bile pigments (bilirubin), bile salts and urobilinogen. In cases of obstruction, bile is not reaching the intestine and urobilinogen may be decreased or absent in urine. The most common cause for hepatocellular jaundice is infection with hepatitis viruses (viral hepatitis) such as hepatitis A virus (HAV) and hepatitis B virus (HBV).



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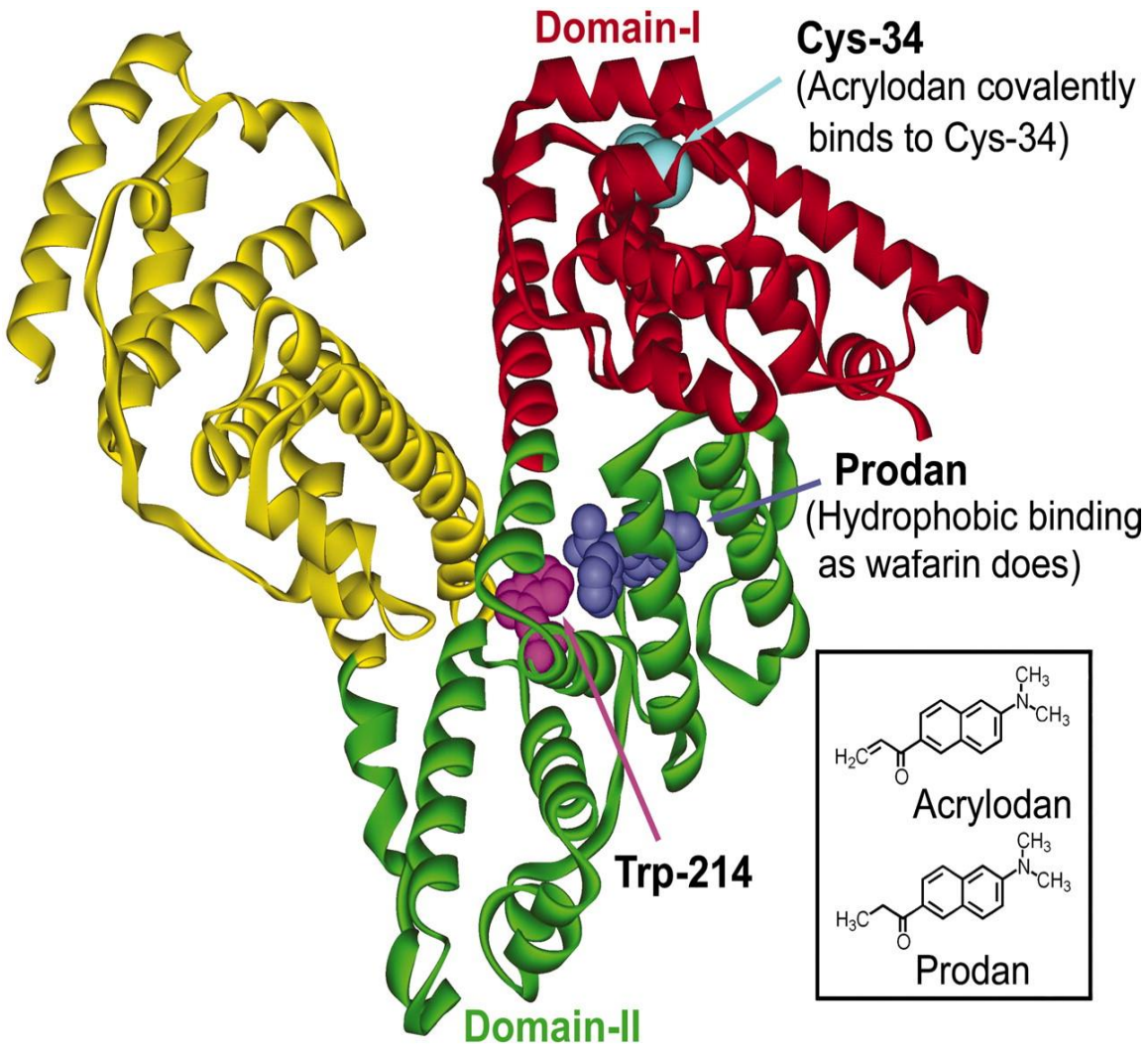
Measurement of Serum Albumin Level

Almost all the plasma proteins except immunoglobulins are synthesized by the liver. Serum albumin is quantitatively the most important protein synthesized by the liver, and reflects the extent of functioning liver cell mass. Since albumin has a fairly long half-life of 20 days, in all chronic diseases of the liver, the albumin level is decreased. A reversal in (albumin/globulin) A/G ratio is often the rule in cirrhosis, due to hypoalbuminemia and associated hypergammaglobulinemia. Normal albumin level in blood is 3.5 to 5 g/dL; and globulin level is 2.5 to 3.5 g/dL.



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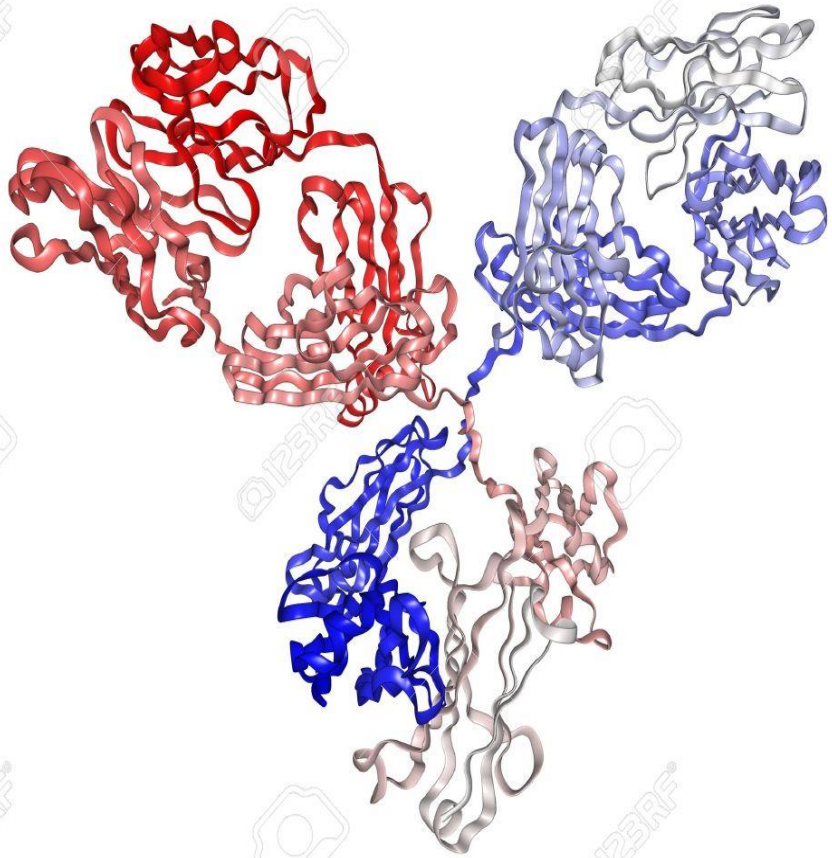
Immunological Tests in Liver Disease

Immunoglobulin G (IgG) level is increased in chronic hepatitis, alcoholic and autoimmune hepatitis. It shows a slow and sustained increase in viral hepatitis. Immunoglobulin M (IgM) shows marked increase in primary biliary cirrhosis and moderate increase in viral hepatitis and cirrhosis. Immunoglobulin A (IgA) is increased in alcoholic cirrhosis and primary biliary cirrhosis. The increase in these globulin fractions (IgM and IgG) may cause a reversal of A/G ratio.



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Measurement of Prothrombin Time (PT)

Since prothrombin is synthesized by the liver, it is a useful indicator of liver function. The half life of prothrombin is 6 hours only; therefore PT indicates the present function of the liver. PT is prolonged only when liver loses more than 80% of its reserve capacity. Vitamin K deficiency is also a cause for prolonged prothrombin time. In case of liver disease, the PT remains prolonged even after parenteral administration of vitamin K.

Measurement of Blood Ammonia

It is an index of urea synthesis by liver. It is a useful test in hepatic encephalopathy. The major source of ammonia in the blood is bacteria of gastrointestinal tract. It is produced by action of intestinal bacterial protease , urease and amino oxidase on the intestinal contents. The ammonia is later converted to urea by the liver, but this activity is considerably decreased in hepatic cell damage; or by the development of portocaval shunts causing portal blood to bypass the liver. The ammonia level is an indicator of the capacity of the liver to eliminate ammonia generated in intestine. Raised ammonia in the serum/plasma is suggestive of cirrhosis and/or development of collateral circulation. It may occur with portocaval anastamosis. Arterial blood should be used for blood ammonia estimation. Estimation of ammonia may be helpful to exclude or diagnose hepatic failure in patients with unexplained stupor or coma. In neonates suspected to have urea cycle disorders (and in organic acidurias), ammonia estimation is indicated.

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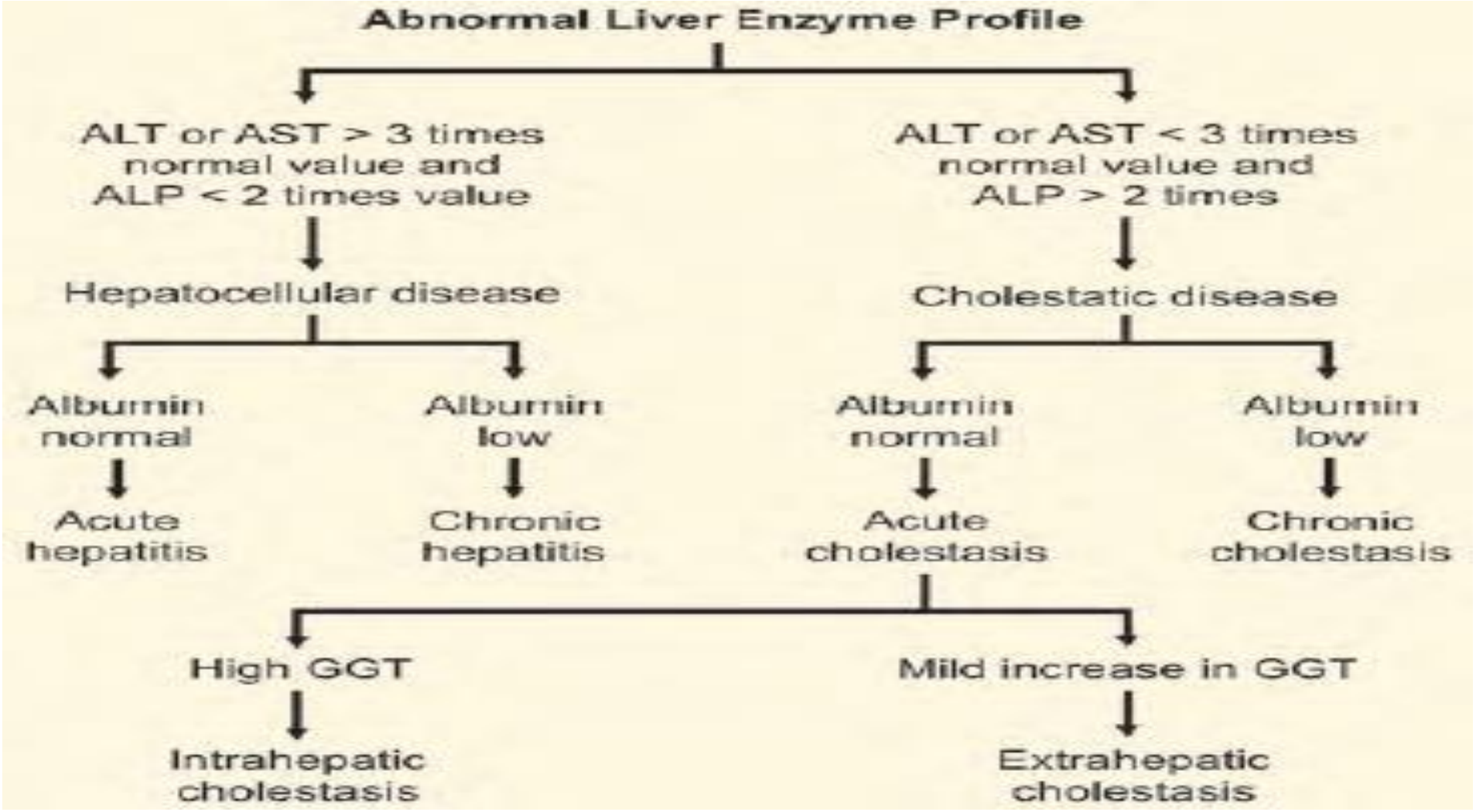
Algorithm for Diagnosis of Liver Diseases



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Clinical Features of Acute Liver Failure

1- Liver: Loss of metabolic function, Decreased gluconeogenesis leading to hypoglycemia, Decreased lactate clearance leading to lactic acidosis, Decreased ammonia clearance leading to hyperammonemia, Decreased synthetic capacity leading to coagulopathy and Portal hypertension.

2- Lungs: Adult respiratory distress syndrome

3- Adrenal Gland: Inadequate glucocorticoid production contributing to hypotension

4- Bone Marrow: Frequent suppression, especially in viral diseases

5- Circulating leukocytes: Impaired function contributing to sepsis

6- Brain: Hepatic encephalopathy, Cerebral edema and Intracranial hypertension

7- Heart: Subclinical myocardial injury

8- Kidney: Frequent dysfunction or failure