Liver Function Test

Liver function tests represent a broad range of normal functions performed by the liver. The diagnosis of liver disease depends upon a complete history, complete physical examination, and evaluation of liver function tests and further invasive and noninvasive tests. Many patients become confused regarding the meaning of a liver function test. This section is designed to describe the basic liver function tests and the meaning for patients.

The hepatobiliary tree represents hepatic cells and biliary tract cells. Inflammation of the hepatic cells results in elevation in the alanine aminotransferase (ALT), aspartate aminotransferase (AST) and possibly the bilirubin. Inflammation of the biliary tract cells results predominantly in an elevation of the alkaline phosphatase. In liver disease there are crossovers between purely biliary disease and hepatocellular disease. To interpret these, the physician will look at the entire picture of the hepatocellular disease and biliary tract disease to determine which the primary abnormality is.

Alanine Aminotransferase (ALT):

ALT is the enzyme produced within the cells of the liver. The level of ALT abnormality is increased in conditions where cells of the liver have been inflamed or undergone cell death. As the cells are damaged, the ALT leaks into the bloodstream leading to a rise in the serum levels. Any form of hepatic cell damage can result in an elevation in the ALT. The ALT level may or may not correlate with the degree of cell death or inflammation. ALT is the most sensitive marker for liver cell damage.

Aspartate Aminotransferase (AST):

This enzyme also reflects damage to the hepatic cell. It is less specific for liver disease. It may be elevated and other conditions such as a

myocardial infarct (heart attack). Although AST is not a specific for liver as the ALT, ratios between ALT and AST are useful to physicians in assessing the etiology of liver enzyme abnormalities.

Alkaline Phosphatase:

Alkaline phosphatase is an enzyme, which is associated with the biliary tract. It is not specific to the biliary tract. It is also found in bone and the placenta. Renal or intestinal damage can also cause the alkaline phosphatase to rise. If the alkaline phosphatase is elevated, biliary tract damage and inflammation should be considered. However, considering the above other etiologies must also be entertained. One way to assess the etiology of the alkaline phosphatase is to perform a serologic evaluation called isoenzymes. Another more common method to asses the etiology of the elevated alkaline phosphatase is to determine whether the GGT is elevated or whether other function tests are abnormal (such as bilirubin) Alkaline phosphatase may be elevated in primary biliary cirrhosis, alcoholic hepatitis, PSC, gallstones in choledocholithiasis.

Gamma Glutamic Transpeptidase (GGT):

This enzyme is also produced by the bile ducts. However, it is not very specific to the liver or bile ducts. It is used often times to confirm that the alkaline phosphatase is of the hepatic etiology. Certain GGT levels, as an isolated finding, reflect rare forms of liver disease. Medications commonly cause GGT to be elevated. Liver toxins such as alcohol can cause increases in the GGT.

Bilirubin:

Bilirubin is a major breakdown product of hemoglobin. Hemoglobin is derived from red cells that have outlived their natural life and subsequently have been removed by the spleen. During splenic degradation of red blood cells, hemoglobin (the part of the red blood cell that carries oxygen to the tissues) is separated out from iron and

cell membrane components. Hemoglobin is transferred to the liver where it undergoes further metabolism in a process called conjugation. Conjugation allows hemoglobin to become more water-soluble. The water solubility of bilirubin allows the bilirubin to be excreted into bile. Bile then is used to digest food.

As the liver becomes irritated, the total bilirubin may rise. It is then important to understand the difference between total bilirubin, which has undergone conjugation (that is hepatic cell metabolism), and at portion of bilirubin which has not been metabolized. These two components are called total bilirubin and direct bilirubin. The direct bilirubin fraction is that portion of bilirubin that has undergone metabolism by the liver. When this fraction is elevated, the cause of elevated bilirubin (hyperbilirubinemia) is usually outside the liver. These types of causes are typically gallstones. This type of abnormality is usually treated with surgery (such as a gallbladder removal or choleycystectomy). If the direct bilirubin is low, while the total bilirubin is high, this reflects liver cell damage or bile duct damage within the liver itself.

Albumin:

Albumin is the major protein present within the blood. Albumin is synthesized by the liver. As such, it represents a major synthetic protein and is a marker for the ability of the liver to synthesize proteins. It is only one of many proteins that are synthesized by the liver. However, since it is easy to measure, it represents a reliable and inexpensive laboratory test for physicians to assess the degree of liver damage present in the in any particular patient. When the liver has been chronically damaged, the albumin may be low. This would indicate that the synthetic function of the liver has been markedly diminished. Such findings suggest a diagnosis of cirrhosis. Malnutrition can also cause low albumin (hypoalbuminemia) with no associated liver disease.

Prothrombin time (PT):

Another measure of hepatic synthetic function is the prothrombin time. Prothrombin time is affected by proteins synthesized by the liver. Particularly, these proteins are associated with the incorporation of vitamin K metabolites into a protein. This allows normal coagulation (clotting of blood). Thus, in patients who have prolonged prothrombin times, liver disease may be present. Since a prolonged PT is not a specific test for liver disease, confirmation of other abnormal liver tests is essential. This may include reviewing other liver function tests or radiology studies of the liver. Diseases such as malnutrition, in which decreased vitamin K ingestion is present, may result in a prolonged PT time. An indirect test of hepatic synthetic function includes administration of vitamin K (10mg) subcutaneously over three days. Several days later, the prothrombin time may be measured. If the prothrombin time becomes normal, then hepatic synthetic function is intact. This test does not indicate that there is no liver disease, but is suggestive that malnutrition may coexist with (or without) liver disease.

Platelet count:

Platelets are cells that form the primary mechanism in blood clots. They are also the smallest of blood cells. They derived from the bone marrow from the larger cells known as megakaryocytes. Individuals with liver disease develop a large spleen. As this process occurs platelets are trapped with in the sinusoids (small pathways within the spleen) of the spleen. While the trapping of platelets is a normal function for the spleen, in liver disease it becomes exaggerated because of the enlarged spleen (splenomegaly). Subsequently, the platelet count may become diminished.

Serum protein electrophoresis:

This is an evaluation of the types of proteins that are present with in a patient's serum. By using an electrophoretic gel, major proteins can be separated out. This results in four major types of proteins. These

are 1) albumin, 2) alpha globulins, 3) beta globulins and 4) gammaglobulins. This test is useful for evaluation of patients who have abnormal liver function tests since it allows a direct quantification of multiple different serum proteins. If the gamma globulin fraction is elevated, autoimmune hepatitis may be present. In addition a deficiency in the alpha globulin fraction can result in the diagnosis, or a clinical clue, to A. alpha-1 antitrypsin deficiency. This is a simple blood test that is commonly performed by hepatologists.