

# Medical Writers' Circle

a series of articles

written by medical  
professionals about  
the management  
and treatment of  
Hepatitis C

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## The Importance of Laboratory Test Results in Hepatitis C Infection

Most people with hepatitis C feel well and have no specific findings on physical examination that would lead a health care provider to suspect liver disease. Even the vast majority of people with liver disease that has advanced to cirrhosis have a normal physical examination. Therefore, the evaluation and treatment of liver disease, in particular hepatitis C, places a large emphasis on laboratory tests results to diagnose, stage and predict and evaluate response to therapy.

The liver has several general functions and it is often called both the body's manufacturing center and its filtering plant. Blood tests used to evaluate the liver can be divided into those representing liver cell damage, cholestasis or liver function. The serum aminotransaminases, alanine aminotransferase (ALT or SGPT) and aspartate aminotransferase (AST or SGOT) are part of most automated blood chemistry panels. Elevation of these enzymes is caused by damage to the hepatocyte or liver cell. The degree of elevation may be important in acute disease but is unimportant in chronic disease. The most common causes of elevated aminotransaminases are fatty liver, viral hepatitis, medication induced hepatitis, autoimmune hepatitis and alcoholic liver disease. The tests are a reflection of cell damage and death but are not

liver function tests. Although many patients and physicians refer to these tests as "liver function tests", this term is incorrect and they do not reflect the liver's ability to either synthesize or metabolize various chemicals. Therefore, an abnormality in these tests does not mean that the liver is not functioning. In fact, the vast majority of patients with elevated aminotransaminases, regardless of degree, have normal liver function.

Cholestatic liver disease is any condition leading to the obstruction of bile ducts in either the liver or biliary tree. Elevation of the enzymes alkaline phosphatase and gamma-glutamyl transpeptidase are indicative of this type of disease. Conditions that commonly lead to the elevation of these enzymes include primary biliary cirrhosis, primary sclerosing cholangitis and gallstone disease.

Bilirubin is the final breakdown product of heme, the majority of which comes from hemoglobin. Bilirubin can be elevated in many liver-related and non-liver-related conditions and it may be elevated in conditions which lead to liver cell damage and cholestasis. The level of serum bilirubin is not a sensitive indicator of liver function and it may not accurately reflect the degree of liver damage.

Albumin and blood clotting factors are proteins made in the liver. Blood tests such as the serum albumin and prothrombin time are measures of these

proteins. As these tests evaluate the functional integrity of the liver, they can be correctly called "liver function tests". Abnormalities of these tests are of concern and are indicative of extensive liver damage.

The most common laboratory abnormality seen in chronic hepatitis C infection is an isolated, elevated alanine aminotransferase (ALT) although as many as 60% of hepatitis C infected patients will have a normal ALT level. *The level of serum ALT elevation does not correlate with histological disease and may be normal in any stage of chronic hepatitis C.* Therefore, patients with minimal ALT elevations should be evaluated for the presence of chronic hepatitis. In advanced disease, an increase in alkaline phosphatase and total bilirubin as well as thrombocytopenia (low platelets) may be seen.

In the patient with risk factors for hepatitis C or an abnormal ALT, the most practical method of diagnosing HCV infection is by obtaining a second generation enzyme linked immunosorbent assay (EIA) antibody to hepatitis C (anti-HCV). False-positive results may occur at a rate of 10-20% and are usually seen in the presence of autoimmune disease, hypergammaglobulinemia and low-risk blood donors. False negative results may occur in immunosuppressed patients, including people infected with the human immunodeficiency virus. In early infection, anti-HCV testing may be negative, as antibodies may not develop until

4-6 weeks after exposure. Unfortunately, a positive hepatitis C antibody does not distinguish acute from chronic disease or active from past infection nor is it a sign of immunity or protection. Therefore, a positive EIA anti-HCV test is a marker that hepatitis C may be present and it must be followed by confirmatory viral load testing.

The recombinant immunoblot assay (RIBA) is another type of antibody test with limited utility. As with EIA antibody tests, it does not distinguish between acute or chronic disease or between past and active infection. Therefore, it

viral levels are usually expressed as thousands or millions of international units. Of note, quantitative viral testing may be falsely negative if viral levels are below the lower limit of detection of the assay being used. Therefore, qualitative HCV-RNA testing is used for diagnosis while quantitative testing should be reserved for use during treatment. It is important to note that the level of virus does not correlate with prognosis, underlying liver histology or how ill a person feels. Therefore, a patient with a viral level of 3,000,000 international units does not have a

behave differently than the HCV mono-infected person. Quantitative viral load testing should not be repeated yearly or more often as it adds little to the care of the untreated patient other than increased expense and anxiety. These tests, however, should be followed serially in someone undergoing anti-viral therapy, as the goal of therapy is the loss of detectable serum HCV-RNA.

Several other liver tests are frequently obtained in patients with hepatitis C. The serum alpha-fetoprotein is a marker of liver cancer but it may be mildly elevated

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adds little to the care of a patient with a positive hepatitis C antibody by the EIA method and known risk factors except extra expense. The NIH consensus conference on hepatitis C has recommended that it be used as a confirmatory test in patients without known risk factors who test positive for the EIA anti-HCV to eliminate the possibility of a false positive EIA. RIBA testing is not influenced by the presence of autoimmune disease or hypergammaglobulinemia. In clinical practice, this test has little if any utility and, except for rare exceptions, it should not be obtained.

Confirmatory tests for the presence of hepatitis C infection are those tests that determine the presence of hepatitis C viral particles (HCV-RNA) in the blood. A positive HCV-RNA in the serum confirms the diagnosis of active hepatitis C. This type of viral testing may be either qualitative or quantitative. Qualitative testing is more sensitive and specific than quantitative testing and results are reported as either positive or negative. Quantitative testing reports on the actual measured amount of viral particles in the serum and the

worse prognosis nor is the person any sicker than someone with a viral count of 200,000 international units. Small fluctuations in HCV-RNA level are equally unimportant. A patient whose viral level has decreased from five to one million international units has shown no significant change in viral level and should not be rejoicing. The converse is also true and an elevation from one to five million international units should not lead a patient to be upset. It is important to understand the relative lack of importance of viral level in the untreated hepatitis C patient. Misconceptions about viral levels often lead to tremendous angst among patients who insist on comparing numbers in the waiting room, are upset by the initial level of viremia or feel falsely relieved or upset with small changes in HCV-RNA viral load. Recently, however, it has been suggested that in the population co-infected with hepatitis C and HIV, a higher hepatitis C viral load is associated with a more rapid progression to advanced disease. As regards viral level and its significance, the co-infected patient appears to

in patients with chronic hepatitis C in the absence of liver cancer. If it is elevated, this test should be followed closely. Autoimmune markers may be present in as many as 25% patients with hepatitis C without the presence of autoimmune disease. These markers include an anti-nuclear antibody, smooth muscle antibody, anti-mitochondrial antibody or anti-thyroid antibodies. The presence of these antibodies does not appear to influence disease progression. Patients in whom autoimmune disease is suspected should be adequately evaluated before the presence of autoantibodies is attributed to HCV infection.

The adequate interpretation of laboratory test results is very important to understand the evaluation of hepatitis C infection. Unfortunately, in the majority of cases, these blood tests are unable to accurately predict current disease stage or possible disease progression. Therefore, despite all these advanced tests, the performance of a liver biopsy cannot be emphasized enough as this is the best test to accurately stage the disease and predict disease progression.

# Medical Writers' Circle

*is a program of the  
Hepatitis C Support Project.*

The Mission of the Hepatitis C Support Project is to offer support to those who are affected by the hepatitis C Virus (HCV) and HIV/HCV coinfection.

Support is provided broadly, through information and education, as well as access to support groups. The (Project) seeks to serve the HCV community as well as the general public.

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