

Overview of Diagnostic Tests for Viral Hepatitis (Summary)

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Viral hepatitis is the cause of about 80-90% of all cases of both acute and chronic hepatitis. As such, patients with either of these disorders require laboratory testing to evaluate for the presence of infection with one of the viruses that particularly damage the liver. This presentation provides an overview of serologic and virologic tests used for diagnosis and monitoring of acute and chronic hepatitis.

Acute hepatitis is a disorder characterized by damage to hepatocytes, the major functioning liver cells; it is usually recognized by elevation of hepatocyte enzyme activities, particularly AST and ALT. In most cases, the disease is undiagnosed, but between 10 and 30% of patients developed impaired function and become jaundiced, leading to a clinical diagnosis. The frequency of acute viral hepatitis has been gradually declining due to virtual elimination of post-transfusion hepatitis by donor testing, improved sanitation measures, and availability of vaccines against hepatitis A and B, the most common causes. There is hope that universal immunization of children may virtually eliminate acute hepatitis B in this country in the near future.

Acute hepatitis A (HAV), the most common cause in children, causes about 35% of acute hepatitis. The diagnostic laboratory test is IgM anti-HAV, which develops before onset of illness and remains positive for 3-6 months. Total anti-HAV (mainly IgG) is positive in almost 40% of Americans; although rare in children < 5 years, it is found in 75% of adults over age 50. For this reason, use of total anti-HAV is not recommended as a diagnostic test for acute HAV; it may be useful as a screen in low prevalence populations (children), with confirmation with IgM anti-HAV in case of positive results.

Acute hepatitis B (HBV), responsible for almost 50% of cases of acute hepatitis, primarily affects individuals from teenage years through adulthood. The first marker to appear after infection is a protein termed surface antigen (HBsAg), which appears 1-2 months after infection. The initial antibody response to HBV is antibody to the core antigen (anti-HBc), which precedes onset of clinical hepatitis. IgM anti-HBc antibodies are relatively specific for acute hepatitis, although rarely they persist in chronic HBV infection; they are considered the diagnostic test for acute HBV infection. Clearance of infectious virus is indicated by loss of HBsAg and appearance of anti-HBs. In a small percent of cases, at the time of diagnosis HBsAg and anti-HBs are roughly in equivalence, so that no detectable level of either is present; the only marker present is IgM anti-HBc, sometimes termed the "core window". This phenomenon is seen rarely with current, sensitive assays.

Acute hepatitis C (HCV), responsible for about 15% of acute hepatitis, primarily affects young adults, particularly with a history of injection drug use. Before availability of testing, it was also a common cause of post-transfusion hepatitis. In contrast to HAV

and HBV infections, antibody to HCV (anti-HCV) is not uniformly present before onset of clinical hepatitis; it is found in less than 60% of patients at onset of illness, and takes up to 2-3 months after infection to reach 95% sensitivity. IgM anti-HCV is found in both acute and chronic hepatitis, and is not helpful in differential diagnosis. Anti-HCV is felt to persist for life, even with recovery from hepatitis.

In most cases, patients with acute hepatitis A and B recover completely; recovery is usually indicated by return of AST, ALT, and bilirubin to normal. In HBV and HCV infection, however, chronic hepatitis may develop, either following an episode of acute hepatitis or without it. Chronic hepatitis is much more common than acute hepatitis; approximately 1 million Americans have chronic hepatitis B, while 3.5-4 million have chronic hepatitis C (representing almost 2% of the population). While infants almost always develop chronic HBV infection when exposed, in teenagers and adults about 1-3% of infections become chronic. In contrast, an estimated 85% of those infected with HCV develop chronic hepatitis.

Chronic hepatitis is usually recognized by elevated ALT or, less commonly, AST; symptoms, if present, are mild and non-specific. Over the course of 20-30 years, about 20% of those with chronic hepatitis will develop cirrhosis (the 9th leading cause of death in the U.S.), and may also develop hepatocellular carcinoma, an otherwise rare

will likely improve testing. There are several subspecies (genotypes) of HCV RNA that can be identified by nucleotide sequencing.

Effective therapy for HCV with combined ribavirin and interferon has recently become available. Decisions on duration of therapy are based on laboratory test results. Before treatment, quantitative HCV RNA and genotype are performed. Genotypes 2 and 3, which represent about 25% of infections in the U.S., respond well to 6 months of treatment, and longer therapy is no more effective. In patients with the common genotype 1, viral load is an important prognostic variable. With high ($> 2 \times 10^6$ copies/mL) viral load, treatment is given for 6 months, and ALT and qualitative HCV RNA are measured. If either is abnormal, treatment is stopped; if both are normal, treatment is continued for another 6 months. In all patients treated, qualitative HCV RNA is measured at end of treatment and, if negative, 6 months after completing treatment; negative results on both indicate high likelihood of permanent virologic remission.