Glossary of terms

Acute Hepatitis B Viral Infection

Acute infection occurs when people are first infected with the hepatitis B virus. Symptoms may or may not be present.

In some people the infection resolves itself, but in other cases the infection may persist lifelong, causing chronic hepatitis B.

ALT (Alanine Aminotransferase)

A liver enzyme found in the blood that is a marker of liver inflammation. Elevated levels of ALT usually indicate liver cell damage. Normalization or reduction in ALT levels suggests improvement of liver inflammation.

ALT Flare

A spike in ALT levels that if left unresolved can have potentially fatal consequences.

ALT Normalization

The return of ALT levels from elevated (an indicator of cell death and liver damage) to normal (suggesting improvement of liver inflammation).

Antibody

A protein produced by the body in response to an infection or vaccination. Antibodies help the immune system fight off disease.

Antigen (Ag)

Part of an invading microorganism, such as a virus, that may cause tissue damage (in hepatitis, to the liver), and that also stimulates the body's immune system to produce antibodies.

Biopsy

The surgical removal of tissue from living patients for diagnostic examination. In patients with chronic hepatitis B it is primarily used to assess liver disease (cirrhosis, inflammation, and liver cancer).

Chronic Hepatitis B

Chronic hepatitis B is a disease of the liver that can progress to cirrhosis (scarring of liver tissue), liver cancer, liver failure, and death. It is caused by persistent infection with the hepatitis B virus (HBV).

A patient who tests positive for HBV for more than six months is considered to have a chronic HBV infection.

Symptoms may include jaundice, fatigue, abdominal pain, loss of appetite, nausea, vomiting, and joint pain.

Cirrhosis

A serious liver condition characterized by scarring of the liver that can lead to liver failure and death. In addition to hepatitis B, other common causes of cirrhosis are chronic alcohol use, hepatitis C, blocked bile ducts, and inherited disease.

Compensated Liver Disease

A situation in which the liver continues to function normally despite the presence of disease that damages liver cells.

Decompensated Liver Disease

Advanced liver disease, with the liver damaged to the extent that liver function is impaired.

E Antibody (HBeAb Or Anti-HBe)

A substance produced by the body in response to hepatitis B infection. Seroconversion from e antigen positive to e antibody positive indicates a positive response to treatment.

E Antigen (HBeAg)

E antigen is a viral protein that is secreted by HBV-infected cells. Its presence is often associated with a high amount of virus in the blood.

Historically, HBeAg-positive patients are easier to treat than HBeAg-negative patients because they are able to achieve seroconversion. Seroconversion from e antigen positive to e antibody positive indicates a positive response to treatment.

Patients with HBeAg-negative hepatitis B are often older, with more advanced liver disease. They are more difficult to manage clinically because they usually require years of therapy.

HBeAg-Positive Patients

Patients who test positive for the hepatitis B e antigen.

HBeAg-Negative Patients

HBeAg-negative disease generally occurs due to a mutation of the hepatitis B virus, and patients who are negative for the e antigen are generally older, tend to have more advanced liver damage, have more comorbid conditions and have been infected with HBV for a longer period of time.

E Antigen Loss

The loss of the e antigen from the blood. E antigen loss can be a precursor of e antigen seroconversion, a therapeutic goal in the treatment of HBeAg-positive patients. However, rare mutations may cause the loss of e antigen and may require further follow-up.

E Antigen Seroconversion

Conversion from e antigen positive to e antibody positive. E antigen seroconversion that occurs during treatment indicates a positive response.

Enzyme

Protein produced by the body that acts as a catalyst for chemical reactions. ALT is an enzyme released from damaged liver cells and other tissues. Elevated levels in the blood are usually a sign of liver inflammation that can lead to progressive liver damage, with potentially serious consequences.

Fibrosis

Abnormal formation of fibrous connective tissue in organs, including the liver, usually due to scarring that results from chronic inflammatory damage.

HAI - Histology Activity Index

A scoring system used to measure liver inflammation and fibrosis, through microscopic examination of liver tissues obtained by liver biopsy.

HBV DNA (Deoxyribonucleic Acid)

Genetic material of the hepatitis B virus. Levels in the blood are associated with the amount of virus present, which in turn provides information about the risk of progressive liver disease.

Hepatitis B Virus Infection

An infection caused by the hepatitis B virus. Infection can be either *acute* (lasting less than six months) or *chronic* (often lasting a lifetime). It is spread primarily through blood, unprotected sex, shared needles, and from an infected mother to her newborn during the delivery process.

Hepatocellular Carcinoma (HCC)

Liver cancer. 80% of the world's liver cancer is associated with chronic hepatitis B virus infection.

Ishak Fibrosis Score

A scoring system that measures the degree of fibrosis (scarring) of the liver, which is caused by chronic necroinflammation. A score of 0 represents no fibrosis, and 6 is established cirrhosis. Scores of 1 and 2 indicate degrees of portal fibrosis; stages 3 and 4 indicate bridging fibrosis. A score of 5 indicates nodular formation and incomplete cirrhosis.

Knodell Scores for Evaluation of Liver Histology

The Knodell scoring system, also called the Histologic Activity Index (HAI), classifies liver biopsy specimens according to scores into four categories of histologic features:

- Periportal and/or bridging necrosis (scores from 0 to 10)
- Intralobular degeneration and focal necrosis (scores from 0 to 4)
- Portal inflammation (scores from 0 to 4)
- Fibrosis (scores from 0 to 4)

The *Knodell Necroinflammatory Score* is the sum of scores from parts I-III, hence a range of 0 to 18, and measures the degree of acute necroinflammatory activity in the liver.

The *Knodell Fibrosis Score* (part IV, above) measures the degree of scarring in the liver. Scarring builds up over time due to chronic necroinflammatory activity, ultimately leading to cirrhosis.

Recently, the Ishak fibrosis score has become the preferred method for evaluating liver fibrosis because it rates fibrosis according to seven categories on a continuous integer scale, as opposed to the discontinuous 4-point Knodell fibrosis score.

Liver Histology

A microscopic study of liver tissues for evidence of liver damage.

Mutation

A spontaneous or induced change in the DNA of a virus that can lead to treatment resistance. A virus can mutate from one form to another, making treatment difficult.

Necroinflammation

Tissue inflammation and cell death. Measures of necroinflammation help determine the extent of liver damage.

Nucleoside Analog

A synthetic compound that closely mimics the components of DNA and disrupts the virus's ability to replicate by blocking the completion of the viral DNA chains. Nucleoside analogs are one form of hepatitis B treatment.

PCR (Polymerase Chain Reaction)

A highly sensitive test used to detect the amount of HBV DNA in blood or other tissues.

PCR Negativity

Reduction in viral DNA or RNA to below the limits of detection of the PCR assay. Assays vary in their ability to detect low levels of DNA or RNA. Some tests are more sensitive than others.

Resistance

Loss of sensitivity of an infection to treatment. In some cases this is caused by a mutation of the virus. There are various definitions of resistance as it pertains to hepatitis B treatment. In the GLOBE study, resistance was defined as rebound of viral DNA after initial suppression, with viral resistance mutations that emerged during treatment confirmed by genotypic analysis.

Surface Antibody (HBsAb Or Anti-HBs)

A protein produced by the body's immune system in response to a surface antigen or vaccination.

Surface Antigen (HBsAg)

A protein produced by the liver that indicates hepatitis B infection. When a surface antigen is present, it may indicate that the person is or has been infected.

Therapeutic Response

The primary clinical trial endpoint used in the GLOBE study to measure efficacy across virologic and serologic treatment markers. Therapeutic response is a composite endpoint. Reduction of HBV DNA to below 5 $\log_{10}$ copies/mL, coupled with either HBeAg loss or ALT normalization.

Treatment-Emergent Resistance

When a patient's viral levels rebound during treatment due to viral resistance mutations that became detectable only after treatment began (i.e., patient did not have the mutation present before starting treatment).

A virus mutation from one form to another, making treatment of these viruses difficult.

Treatment Failure

The failure of treatment to reduce the levels of viral DNA in the blood. In the GLOBE study, primary treatment failure was defined as viral DNA levels never below 5 $\log_{10}$ copies/mL.

Vaccine

A preparation that stimulates the production of antibodies to protect against a specific infection. The hepatitis B vaccine is only effective if given before infection occurs.

Viral Suppression

A clinically meaningful reduction in the levels of circulating virus, usually measured by blood levels of HBV DNA in the case of HBV.

Virologic Breakthrough

The return of higher levels of viral DNA following reductions achieved through the use of anti-viral therapy. Often indicates the emergence of resistance.

Virus

A tiny microorganism, much smaller than bacteria, which can invade the body's cells and cause disease. A virus can mutate from one form to another, making treatment of viruses difficult.