# What You Need To Know: Interpreting Hepatitis B Viral Markers

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Hepatitis B is associated with a myriad of viral markers – HBsAg, anti-HBs Ab, anti-HBc IgM, anti-HBc IgG, HBeAg, anti-HBe Ab, DNA polymerase and last but not least, HBV DNA. These all represent products of the HBV genome and their antibodies.

How do we interpret and use these markers? Perhaps for the usual cases of jaundice seen by the general practitioner, one needs to be aware only of the markers of acute and chronic hepatitis B.

Acute hepatitis B is hallmarked by a positive HBsAg and anti-HBc IgM. However, there may be a "window" period after the disappearance of HBsAg when anti-HBc IgM may be the only positive marker of infection. The other exception when HBsAg may be absent during acute hepatitis B is in fulminant cases when the hyperactivated immune system clears and "mops" up all the circulating HBsAg.

Chronic hepatitis B carriers, defined as the presence of HBsAg for more than 6 months, do not have anti-HBc IgM. Instead, anti-HBc IgG is positive, indicating "past" infection. Anti-HBc IgG may be considered to be a serological scar of hepatitis B infection, never to disappear unlike the other markers.

What about the other markers?

Anti-HBs Ab is the antibody to the HBsAg. It appears soon after an acute infection and in patients who do not become chronic HBsAg carriers, the antibody clears all the antigen within 6 months. Conversely, in chronic HBsAg carriers, the HBsAg "wins" and therefore there is no anti-HBs Ab.

To complicate matters, there are occasional patients who are positive for both HBsAg and anti-HBs Ab. This conundrum is explained by the anti-HBs Ab belonging to a strain of hepatitis B virus different from the HBsAg that is circulating in the blood. Alternatively, the individual could be at the recovery period of an acute hepatitis B infection, when the HBsAg is on the way down whilst the anti-HBsAg titre is up. In such a case, the HBsAg would be present in a low titre.

A positive anti-HBs Ab can mean one of two scenarios – post-hepatitis B vaccination or past hepatitis B infection. As the hepatitis B vaccine consists of recombinant HBsAg coats without any genetic material, individuals successfully vaccinated against hepatitis B will be positive only for anti-HBsAb and no other hepatitis B marker. If the anti-HBc IgG is positive together with the anti-HBs Ab, then the individual had been infected by hepatitis B previously and has now cleared the HBsAg.

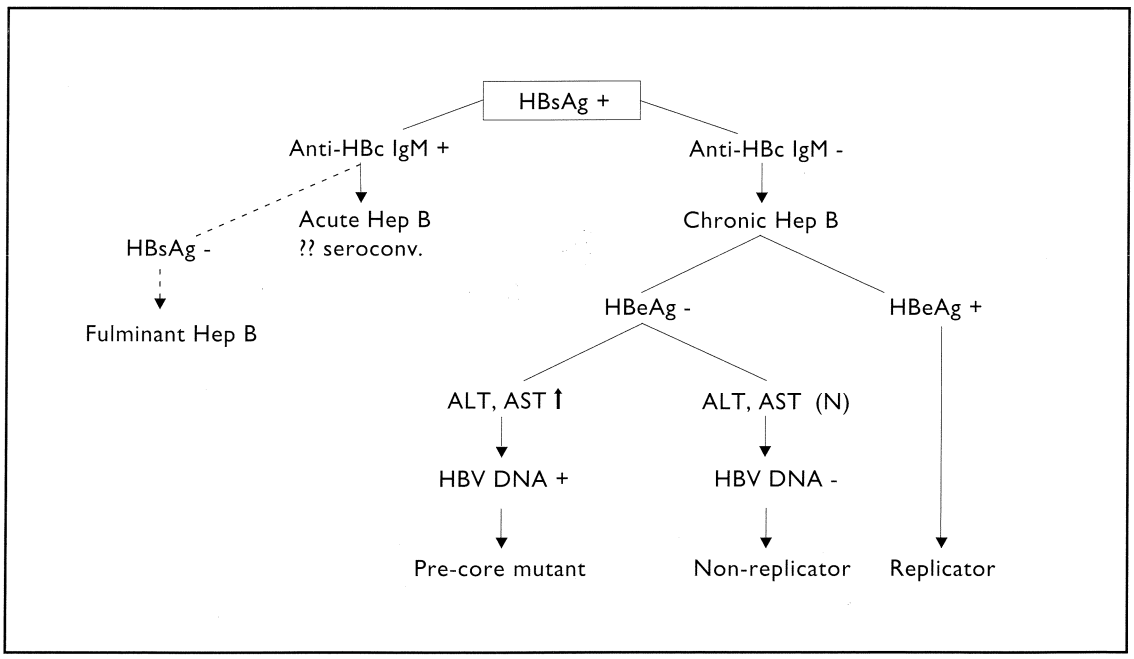


**Fig 1** – Assessing a patient wiith hepatitis B

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The titre of anti-HBs Ab is important in determining if one is immune to hepatitis B. Immunity is conferred when the titre of anti-HBs Ab is >10 mIU/mL. Booster doses and hepatitis B immunoglobulin (HBIg) injections are indicated if there is a needle-stick injury and the anti-HBs Ab is <10 mIU/mL.

The HBeAg is a marker of active replication of the hepatitis B virus. Thus it is positive in acute hepatitis B and infectious chronic carriers. Because of its implication of infectivity, babies of mothers who are HBeAg positive receive both hepatitis B vaccination and HBIg at birth, as opposed to only hepatitis B vaccination for babies of mothers who are anti-HBe Ab positive.

From simple reasoning, one would think the converse, that is, anti-HBe Ab positivity, denotes a non-replicating carrier. However, this is not true because there are pre-core mutant hepatitis B strains that are not able to produce HBeAg even though they are actively replicating, but are instead anti-HBe Ab positive.

The natural history of a chronic hepatitis B carrier is to become anti-HBe Ab positive after a "seroconversion". After seroconversion, necro-inflammatory activity in the liver is minimal as the virus is no more replicating.

During seroconversion, there may be a flare of the hepatitic activity. And during this flare, anti-HBc IgM may become positive again. Thus one may misinterpret the seroconversion episode as an acute hepatitis B event as the liver enzymes are elevated, the patient is icteric and HBsAg and anti-HBc IgM are both positive. However, in such an instance, the anti-HBc IgM is of a low titre and of a subtype different from that of acute infection (monomer versus pentamer).

There are two other useful markers of active HBV replication – HBV DNA polymerase (HBV DNA pol) and HBV DNA. HBV DNA pol used to be a surrogate marker for the presence of HBV DNA before commercial kits for detection of the latter became widely available. Now, with the flourish of HBV DNA kits, the use of HBV DNA pol has taken a back-seat.

The presence of HBV DNA is the gold standard for proving active hepatitis B viral replication. When interpreting the result of a HBV DNA assay, one must be aware of the method used. Four main methods are commonly used – in increasing order of sensitivity – dot blot, liquid hybridisation, Chiron branched-DNA and PCR. The most notoriously insensitive test is the dot blot test, as HBV DNA negative by this method has often been tested positive by other methods.

The demonstration of HBV DNA is especially relevant in cases of pre-core mutant strains where the anti-HBe Ab is positive and in cases under consideration for liver transplantation.

With all these in mind, Fig 1 delineates the diagnostic workup of an individual who has hepatitis B.