

Does your patient have chronic hepatitis B?

Coleman I. Smith, MD, hepatologist, answers questions often asked by physicians

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Hepatitis B virus (HBV) markers and their significance

HBsAg	Patient is infected with the virus.
anti-HBs (surface antibody)	Patient is immune due to natural infection or vaccine.
HBeAg	Patient has active viral replication, ongoing liver disease (usually), and is highly infectious.
anti-HBe	Patient has reduced viral replication, inactive liver disease (in the presence of HBsAg) (usually), and is less infectious than if HBeAg were positive (rarely, anti-HBe may be associated with active viral replication). The absence of HBeAg does not exclude active viral replication. Some mutant strains of the virus are unable to synthesize HBeAg, despite active viral replication as detected by high levels of HBV DNA.
HBV DNA	Patient has active viral replication, ongoing liver disease (usually), and is highly infectious.
HbCag	This antigen is not detectable in the serum, and there is no available test.
anti-HBc (core antibody)	Patient has been in contact with HBV and may or may not still be infected.
IgM anti-HBc	Patient has been infected with HBV within the last six months.

How do I diagnose chronic HBV infection?

Chronic HBV infection is diagnosed by the presence of HBsAg in the serum for six months or more. It can also be diagnosed by the presence of HBsAg with the additional finding of anti-HBc with no evidence of IgM anti-HBc (using standard commercially available assays).

What happens if a person develops chronic HBV?

When an individual develops chronic hepatitis B, a variety of outcomes are possible, ranging from a chronic carrier state with very little, if any, liver damage, to ongoing chronic hepatitis of varying degrees of severity. The latter may at times progress to cirrhosis with all its clinical sequelae. Liver cancer is another possible outcome of chronic hepatitis B virus infection.

What happens to the liver when a person becomes chronically infected?

During the early phase of chronic infection, there is

often significant viral replication and ongoing liver damage as manifested by HBeAg positivity and elevated transaminases. HBeAg often disappears after a variable period of time, although it may take some years for this to occur. When HBeAg does disappear, the liver disease becomes more quiescent and the patient is less infectious. It is in this stage that hepatocellular carcinoma (HCC) may complicate long-standing chronic HBV infection.

If HBeAg disappears, do I stop following the patient closely?

No. Even after HBeAg has disappeared and the liver disease has become relatively inactive, the whole process may be reactivated. Multiple cycles of reactivation may occur. Episodes of reactivation may occur spontaneously or may be precipitated by a course of immunosuppressant therapy (such as steroids or chemotherapy given for an unrelated illness). Such an event may result in worsening of the liver disease and a potentially severe outcome. Thus, one has to watch closely any person chronically infected with HBV who requires immunosuppressant therapy. An additional reason to continue to follow these patients closely is to monitor them for the development of complications of cirrhosis and/or HCC. The disappearance of HBeAg may be associated with ongoing high levels of HBV DNA and thus signify the emergence of an HBeAg negative mutant strain. These people still have active viral replication despite a negative HBeAg.

How do I manage patients who are chronically infected with HBV?

Do the following for patients who have chronic hepatitis B virus infection:

- Take a clinical history (including family history), looking in particular for evidence of symptomatic liver disease in the patient, family, household members, or sexual partner(s).
 - Do a physical exam to look for evidence of liver disease such as spider nevi, jaundice, ascites, etc.
 - Order biochemical tests to assess liver status (AST, ALT, alkaline phosphatase, bilirubin, albumin, prothrombin time). All should be repeated every six months.
 - Measure HBeAg and HBV DNA every six months to assess if active viral replication is present.
 - Assess HBsAg and anti-HBs yearly to see if viral clearance has occurred.
 - Refer individuals who are HBV DNA positive to a physician experienced in the management of chronic liver disease for further assessment. Also refer persons with clinical evidence of liver disease (e.g., jaundice, ascites, variceal hemorrhage). Consideration should be given to liver biopsy. In those with liver disease and active viral replication (HBV DNA positivity), treatment with antiviral medications should be considered.
 - Monitor all chronically infected persons for the development of hepatocellular carcinoma. A reasonable approach is to do a right upper quadrant ultrasound and alpha-fetoprotein (a tumor marker) estimation every six months, especially if the infection has been present for ten years or more. Individuals at increased risk are those who acquired their infection at or soon after birth, males, persons with a family history of hepatocellular carcinoma, and persons born in Africa.
 - Test family members of chronically infected persons (including non-sexual contacts), as well as any sexual partners who are at risk of acquiring hepatitis B. If found susceptible or if they have an indeterminate serologic pattern (an isolated anti-HBc+), they should be vaccinated against hepatitis B, even if pregnant.
 - Evaluate patients for the presence of antibody to hepatitis A (total anti-HAV). Those with a negative antibody are susceptible and should receive hepatitis A vaccine.
 - Educate every chronically infected person about hepatitis B. Also educate his/her household members and sexual partners. Brochures to assist with education are available in many languages from the Hepatitis B Coalition, a program of the Immunization Action Coalition. (See website and mailing address below.)
- What kinds of treatment modalities are available for chronic HBV infection?**
- Patients with chronic HBV and ongoing viral replication may benefit from treatment with antiviral medications. There are now a number of different treatment options for patients with chronic hepatitis B infection. Treatment should be carried out by a physician with experience in antiviral treatment of chronic hepatitis. Clinical trials of other antivirals are ongoing.

For clinical trial information, visit:

[www.hepb.org/patients/
hepatitis_b_clinical_trials.htm](http://www.hepb.org/patients/hepatitis_b_clinical_trials.htm)

www.clinicaltrials.gov