Abnormal Liver EnzymesTesting for Hepatitis B Virus

David Wong, MD Affiliations: University of Toronto (Assistant Professor of Medicine, Department of Medicine, Division of Gastroenterology)

Hepatitis B virus (HBV) is one of the most common viral infections in the world. Over two billion people have been infected worldwide, leaving 400 million with chronic, lifelong infection. Chronic HBV infection is endemic in most parts of the world, with the exception of North America and Western Europe. In Canada, the prevalence of chronic HBV infection exceeds 2% in northern Inuit communities and in large cities where the number of foreign-born individuals is high. Chronic HBV infection is asymptomatic until end stage cirrhosis or very advanced liver cancer develops. It is estimated that 25% to 35% of those with chronic HBV infection will die of a liver-related cause. Men are at higher risk of liver-related complications than women (Table 1).

Pregnant women are routinely screened for chronic HBV infection as neonatal transmission can be prevented with active (HBV vaccine) and passive (HBIg) immunization. Infants born to HBV-infected mothers should be screened 1-2 months after the completion of at least 3 doses of HBV vaccine series. Note: testing should NOT be done before the age of 9 months or within one month of the most recent vaccine dose. Persons needing immunosuppressive therapy, such as chemotherapy (particularly with the use of anti-CD20 agents), immunosuppression related to transplantation, rheumatologic or gastroenterologic conditions should be screened for hepatitis B. Immunosuppression can lead to a fatal HBV reactivation.

Meet George

George, 52, felt well but a routine visit to his family physician uncovered abnormal liver enzymes. In retrospect, his liver enzymes had been intermittently but mildly abnormal for many years, with Alanine Aminotransferase (ALT) ranging from 30 to 50. He also had a mildly low platelet count of 145, Complete Blood Count (CBC) otherwise normal. An abdominal ultrasound showed a “fatty” liver and a 3.5 cm nodule in the right lobe. Subsequent investigations uncovered chronic hepatitis B infection, CT scan confirmed cirrhosis complicated by liver cancer (biopsy not required for diagnosis). George was treated with an antiviral agent and underwent surgical resection for his liver cancer. He now has ongoing surveillance for tumor recurrence, for which he may require a liver transplant.

Table 1

Who to screen for Hepatitis B

The following should be routinely screened for hepatitis B:

- Persons born in HBV endemic areas (every where except North America and Western Europe)
- Sexual and household contacts of persons with chronic HBV infection
- Injection drug users (current or past history)
- Exposure to multiple different sexual partners
- HIV positive persons
- Persons with elevated Alaine Aminotransferase / Asparate Aminotransferase ALT/AST of unknown origin
- Hemodialysis patients

Screening for Hepatitis B

While all other viral hepatitides are diagnosed with an antibody test, hepatitis B is unique in that there are tests for several different viral proteins and antibodies.

a. HBV surface antigen or envelope (HBsAg) is produced in great excess compared to the number of complete viral particles. HBsAg is the most sensitive test for ongoing HBV infection, even more sensitive than Polymerase Chain Reaction (PCR) testing.

b. Antibody to HBsAg (anti-HBs) is detectable after successful vaccination or after resolution of HBV infection. Anti-HBs titers can fall with time persons with resolved HBV infection or prior successful HBV vaccination can become anti-HBs negative.

c. Antibody to HBV core protein (anti-HBc (total)) is the most durable antibody response and least likely to fall to negative values after resolved infection. Anti-HBc is only positive with natural infection, either resolved acute infection or ongoing chronic infection and is not positive after vaccination.

Table 2

Screen for HBV with HBsAg, anti-HBs, and anti-HBc (total)

- HBsAg POSITIVE: Infected
- HBsAG NEGATIVE
  - i. Anti-HBc POSITIVE: prior infection
  - II. Anti-HBc Negative and anti-HBs NEGATIVE i.e. Not immune, vaccinate if still at risk for HBV infection

Evaluating for activity of liver injury

Over time, HBV infection can be inactive, where no liver injury occurs, or active, where liver injury can lead to cirrhosis. Activity of HBV can be assessed with simultaneous testing of: ALT/AST levels, HBeAg and anti-HBe sta tus, and HBV DNA (viral load).

1. HBV is very likely inactive and does not require antiviral therapy if:

a. HBV DNA (viral load by PCR) is persistently low 1,000 (1E3) IU/mL

2. HBV is very likely active and MAY require antiviral therapy if:

a. HBV DNA is higher > 1,000 (1E3) IU/mL and ALT levels are elevated Note: Higher HBV DNA levels do not necessarily mean that HBV is actively damaging the liver. Referral to a specialist with expert knowledge on HBV is warranted when HBV DNA levels are high.

Evaluating for severity of liver injury

Cirrhosis is associated with increased risk of liver-related complications such as esophageal varices, ascites, liver failure, and liver cancer. Liver biopsy is a good test for liver fibrosis but it is not uniformly available. Abdominal ultrasound can also recognize cirrhosis at very late stages. Platelet count < 150 or lower is often the earliest sign of advanced liver fibrosis or cirrhosis.

Table 3
Take Home Message

- Chronic HBV infection is asymptomatic until end stage liver failure or end stage liver cancer develops
- Persons from HBV-endemic regions of the world (where estimated prevalence exceeds 2%), essentially everywhere except North America and Western Europe, should be routinely screened for chronic HBV infection.
- Screening should be done with three tests: HBsAg, anti-HBs, and anti-HBc (total)

i. HBsAg being positive identifies the HBV-infected individual

ii. HBsAg, anti-HBs and anti-HBc ALL being negative identifies the individual who is at risk for HBV infection if exposed. If there are risk behaviors for infection, this individual should be offered the HBV vaccine.

- The HBsAg positive individual should be further evaluated for

i. Disease activity with blood tests for ALT/AST, HBeAg/anti-HBe, and HBV DNA

ii. Disease severity (signs of liver cirrhosis) with CBC looking for platelet count <150, International Normalized Ratio (INR) elevation, Albumin low, Bilirubin elevation. An abdominal ultrasound should also be done to look for signs of advanced cirrhosis, liver cancer

iii. Anyone with cirrhosis, men older than 40, women older than 50 should be routinely screened for liver cancer using ultrasound every six months. Serum AFP is no longer recommended.

- Antiviral treatment for those with high HBV DNA levels >1,000 (1E3) IU/mL

a. Is indicated for those with cirrhosis, both compensated (asymptomatic) and decompensated (symptomatic)

- Should be considered for those without advanced liver fibrosis

Conclusion

HBV is a common infection without symptoms until it is too late. Screening is required for diagnosis. Once HBV infection is identified, anti-viral therapy should be considered for those with high HBV DNA levels. The decision to initiate therapy should not be taken lightly because HBV is not a curable infection and lifelong therapy may be required. Referral to a specialist with expert knowledge of HBV is indicated. A platelet count of 150 or lower should raise the clinical suspicion of established cirrhosis in anyone with chronic HBV infection or any other chronic liver disease.

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Resources

1. Weinbaum C: Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. MMWR Recommendations and Reports 57(RR-8):1, 2008

David Wong, MD is an Assistant Professor of Medicine from the Department of Medicine, Toronto University, in the Division of Gastroenterology