Hepatitis B: The Other Hepatitis Virus

Prevention, diagnosis and treatment of HIV/HBV co-infection - Part One of Two

by James Learned

In recent years, a lot has been written about hepatitis C virus (HCV) infection in people who also have HIV (co-infection). HCV is a significant problem for many people with HIV, but it isn't the only virus that can cause hepatitis (inflammation of the liver). HIV/hepatitis B virus (HBV) is another common co-infection and, like HIV/HCV co-infection, can cause severe liver damage and death.

HIV/HBV co-infection is relatively common because the viruses are transmitted similarly, although HBV is transmitted more easily. Through blood-to-blood contact, for example, HBV is 100 times more infectious than HIV and 10 times more infectious than HCV. And HBV is much more likely to be transmitted through unprotected sex than HCV. In the U.S. and Europe, most people with HIV (up to 95%) either have had HBV at some time in the past or are currently co-infected.

HBV can cause both short-term (acute) and long-term (chronic) infection. Our immune system usually fights off (clears) HBV within six months of initial infection, but this doesn't always happen. If the immune system doesn't clear the virus within six months, a person is considered to have chronic HBV. In chronic infection, the virus continues to reproduce in the liver, which can cause severe liver damage over time, such as cirrhosis (scarring) and liver cancer (hepatocellular carcinoma or HCC).

Overall, about 95% of adults infected with HBV clear the virus following initial (acute) infection. The remaining 5% don't clear the virus and have chronic HBV. The probability of developing chronic HBV infection depends on certain factors, especially age and the strength of the immune system. About 90% of infants infected at birth develop chronic infection; the rate falls to about 30% for children infected between the ages of one and five, and falls further to about 5% for adults with healthy immune systems. Chronic infection is more likely to occur in people with weakened immune systems—people taking immunosuppressive drugs after a transplant, people receiving hemodialysis, chemotherapy, or corticosteroid treatment, and people with HIV.

The likelihood of clearing HBV is generally lower for people who are HIV-positive than for those who are HIV-negative. Up to 10% of people with HIV in the U.S. also have chronic HBV, compared to .05% of those without HIV. People with low CD4 counts (below 200) infected with HBV are much more likely to develop chronic infection than people with higher CD4 counts. Of additional concern, HIV/HBV co-infection can cause more health problems than having chronic HBV alone, including faster progression of liver disease, difficulty tolerating some HIV medications, and higher death rates due to liver failure.

Transmission

Anyone recently infected or who has chronic HBV can transmit the virus to other people depending on their behaviors. HBV is present in semen, vaginal fluids, and blood and can be transmitted:

- through unprotected sex (accounting for up to 60% of new infections),
- by sharing injection drug equipment (needles, syringes, cookers, cotton, tourniquets, water, etc.),
- through tattooing if unsterilized needles or shared ink pots are used,
- through a needlestick,
- by sharing anything that might have another person's blood on it (razors, toothbrushes, nail clippers and, possibly, cocaine straws or crack pipes),
- through contact with open sores of someone with HBV, or
- from a mother to her baby during birth.

In the U.S., rates of mother-to-child transmission have decreased to historic lows. Women are routinely tested for hepatitis B during pregnancy, and infants born to women with chronic HBV are vaccinated and given hepatitis B immune globulin (HBIG) shortly after birth to avoid infection.

You *cannot* get HBV by sharing cups, glasses, silverware, and other kitchen items.

Prevention

The best way to prevent HBV infection is to be vaccinated. The hepatitis B vaccine has been around for almost 25 years and has significantly reduced the number of new infections. In the U.S., new infections have dropped from about 260,000 each year in the 1980s to about 73,000 in 2003. The biggest reduction has been in children and adolescents due to routine vaccination of newborns and children up to age 18. Most

new infections occur in people in their 20s, 30s, and 40s.

The hepatitis B vaccine is a series of three shots injected into the muscle of the upper arm over a six-month period. It's effective in more than 95% of healthy adults and children who receive all three doses. The antibodies that the immune system creates in response to the vaccine protect you from infection for at least 15 years—probably longer. HBV vaccination is available at doctors' officers and at many STD clinics, AIDS service organizations, drug treatment programs, and syringe exchanges.

For various reasons, some people don't get all three doses of the vaccine. But getting even the first dose is effective in about 50% of healthy people. The general idea is that one dose is better than none, two doses are better than one, and it's best to get all three. If you miss a dose or fall behind schedule, get the next dose as soon as you can. You don't need to start over if the time between doses is longer than suggested. It's also fine—and not dangerous—to be vaccinated if you've been vaccinated before or had HBV some time in your life. If blood tests show that you're protected from hepatitis B infection, the vaccination isn't necessary.

The vaccine is also extremely safe. If side effects occur, the most common are soreness where the shot was given (usually lasting a day or two) or mild flu-like symptoms. You shouldn't get the vaccine if you've ever had a severe allergic reaction to baker's yeast (used to make bread) or to an earlier dose of the vaccine. Allergic reactions are very rare, and there have been no reported deaths attributed to the vaccine.

There are some considerations regarding the HBV vaccine for people with HIV. The Centers for Disease Control and Prevention (CDC) and various treatment guidelines strongly recommend HBV vaccination for everyone with HIV. Unfortunately, people with HIV are less likely to have an effective response to the vaccine. It's unlikely to produce the desired antibody response in people with CD4 counts below 200, but it works in about 70% of those with CD4 counts above 500. Therefore, it's best to get the vaccine when your CD4 count is within a healthy range (above 200). HIV-positive or not, if you're sick when you're scheduled to get a dose of the vaccine, wait until you recover before getting the shot. For people with any kind of immunodeficiency, including HIV, it's a good idea to have blood work done after being vaccinated to make sure that it was successful.

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Being vaccinated for hepatitis A is also strongly recommended for people with HIV. A combined hepatitis A and hepatitis B vaccine called Twinrix provides protection against both infections. Like the HBV vaccine, Twinrix is given as three shots over six months.

Other than vaccination, ways to reduce HBV transmission are similar to those that reduce transmission of HIV and/or hepatitis C:

- using latex barriers during vaginal and anal sex,
- avoiding shared injection drug equipment (needles, syringes, cookers, cotton, tourniquets, water—the works),
- avoiding shared implements that might have another person's blood on them (razors, toothbrushes, nail clippers, unsterilized tattoo or piercing equipment, snorting straws, etc.),
- following standard precautions in occupations that involve possible blood exposure, and
- cleaning up blood spills with a mixture that's 10% bleach and 90% water.

Acute hepatitis B

Many people who've recently been infected with HBV (acute infection) have no symptoms, while others have symptoms that can range from mild to severe. Few people who have symptoms connect them to HBV because they're similar to the symptoms of other viral infections like the flu—feeling tired, fever, nausea, diarrhea, vomiting, loss of appetite, and sore joints. Some people develop symptoms that are clear signs of a liver problem—jaundice (yellowing of the skin and whites of the eyes), dark urine, pale feces, and pain in the upper-right abdomen.

If symptoms occur, they usually appear six to twelve weeks after exposure to the virus, and they can last from a couple of weeks to several months. In some cases, you feel so sick and run down that you can't do anything but rest for weeks or even months. A very small number of people with acute HBV—less than 1%—suffer fulminant hepatitis, which can cause very quick liver failure and death.

There's no specific treatment for acute HBV except for getting lots of rest, drinking plenty of fluids, and taking over-the-counter pain relievers. Avoid acetaminophen—found in Tylenol and other pain relievers—especially in high doses, because it can be tough on the liver. If you experience any serious symptoms or think that you've recently been exposed to HBV, see your healthcare provider as soon as possible. If you were exposed within the past two

weeks (at most), an injection of hepatitis B immune globulin (HBIG) may prevent the development of HBV infection, or it may reduce the length and severity of illness. But HBIG provides only temporary protection, so the first dose of the hepatitis B vaccine should be administered at the same time.

The best thing to be said for acute HBV infection is that if the immune system clears the virus within six months, your immune system will protect you from future infection and HBV vaccination isn't needed.

Chronic hepatitis B

Hepatitis B doesn't directly cause most of the liver damage that people with HBV can experience. Rather, the immune system's response to the virus causes the damage. T-cells and cytokines—chemicals created by white blood cells—attack and kill infected liver cells.

Chronic HBV is usually a slowly progressive disease, but isn't something to be ignored or taken lightly. It can take years or decades for serious liver damage to occur. Between 25% and 40% of people with chronic HBV develop serious liver damage during their lives (cirrhosis and/or liver cancer), and 15-25% die because of liver disease.

Liver damage often occurs more quickly and is more serious in people who also have HIV. Two studies that looked at large numbers of people over time found that those co-infected with HIV and HBV were far more likely to die of liver disease than people with chronic HBV alone.

Most people with chronic HBV don't have any physical symptoms for many years (if ever), while others have symptoms that come and go. The liver doesn't usually let us know that it's in trouble until liver damage is severe. Liver problems can usually be detected during routine blood work before noticeable symptoms occur. With serious liver damage, physical symptoms can include fatigue (sometimes severe), weight loss, rash, hives, loss of muscle mass, arthritis, and many others. Other signs of serious liver damage include vitamin deficiencies that can lead to reduced bone mass (osteopenia) and other conditions that aren't apparent unless special tests are performed or the damage is so critical that they affect bodily functions.

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Diagnosing HBV

Blood tests are the only way to know whether you have (or had) hepatitis B. Various laboratory tests are used to diagnose HBV infection and to monitor people with chronic HBV. Hepatitis B is the most complicated hepatitis virus to interpret based on blood work. Diagnosing HBV isn't like diagnosing HIV, which is done based on the presence or absence of specific antibodies. HBV infection is diagnosed by looking at a combination of antigens (fragments of the virus) and antibodies in the blood. The immune system produces specific antibodies to respond to specific antigens. Different combinations of antigens and antibodies mean very different things. The presence or absence of certain antigens and antibodies can also help a provider determine the status of an individual's chronic HBV.

The results of blood work for HBV can tell whether:

- you've never been infected with hepatitis B and haven't been vaccinated (consider getting the vaccine);
- you were probably infected within the past six months and the virus is still active;
- you were probably infected within the past six months and the virus is in the process of clearing;
- you were probably infected more than six months ago and your immune system cleared the virus;
- you were vaccinated at some time and the antibodies that are present will successfully prevent HBV infection; or
- you have chronic HBV infection.

If you have chronic HBV, further tests help you and your provider understand more about the status of your infection. One blood test looks for a particularly important antigen—the hepatitis B envelope antigen (HBeAg)—and the hepatitis B e antibody (anti-HBe), which the immune system produces in response to that antigen.

If HBeAg is positive and anti-HBe is negative, hepatitis B virus is replicating in liver cells. If HBeAg is negative and anti-HBe is positive, it usually means that the virus is inactive. This isn't always the case, though. Some people with chronic hepatitis B, especially those who have been infected for many years, may have what's called a "precore mutant" of HBV. This can cause HBeAg to be negative and anti-HBe to be positive, even though hepatitis B virus is still actively replicating in the liver.

Liver function tests

Liver function tests (LFTs) are also important if you have chronic HBV. Among other things, liver function tests measure levels of liver enzymes in the blood, specifically alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The liver releases these enzymes all the time. High levels indicate that something's going on in the liver. For example, ALT levels are usu-

ally higher than normal during acute HBV infection—often very high—although that doesn't necessarily mean that your liver will have permanent damage. Within six months of initial infection, ALT levels usually return to normal if you've cleared HBV and have no other liver problems.

Getting liver enzymes monitored regularly, especially ALTs, is important in chronic HBV infection. The levels may be periodically or consistently high. They don't necessarily predict what will happen to the liver in the future, but consistently elevated ALT levels over time and a failure to return to normal levels can indicate a higher risk of long-term liver damage. ALT levels are also important to take into account when considering treatment for chronic HBV.

HBV viral load

As with HIV and hepatitis C, HBV viral load tests are available to measure the amount of HBV or, more accurately, HBV-DNA in the blood. HBV-DNA levels help tell whether the virus is actively replicating in the liver and, if so, the degree of replication. Depending on which viral load test is used, the results can come back between undetectable (less than 100 or 1,000 copies/mL) and millions of copies/mL.

HBV-DNA levels predict the likelihood of developing hepatocellular carcinoma (liver cancer) over time. The higher the HBV-DNA levels the more likely it is that a person will develop liver cancer, regardless of ALT levels, the presence of cirrhosis, and other factors.

An HBV-DNA count above 100,000 copies/mL is generally the cut-off used to indicate that virus is replicating and treatment is needed. What consistently low HBV-DNA levels mean for any single individual isn't clear. Some people with consistent HBV-DNA levels below 100,000 have severe liver disease. To figure out what's going on and what to do, viral load results, liver enzyme levels, and the presence or absence of hepatitis B antigens and antibodies all need to be taken into account.

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Other tests and procedures

Healthcare providers sometimes order further tests for people with chronic HBV: alpha-fetoprotein screening, ultrasound, and, sometimes, liver biopsy.

Cancerous liver cells produce high levels of alpha-fetoprotein (AFP) in the blood. AFP screening can help detect the presence of a tumor early on, but AFP screening alone doesn't provide enough information. An abdominal ultrasound, which is painless, may also be done. A transducer, which looks like a wand, is moved back and forth over the upper abdomen to get a sense of what the liver looks like and to see whether there are any abnormalities. Using AFP screening and ultrasound together is more likely to detect liver cancer than using either test alone. Some providers suggest that these tests be done every six months in people with chronic HBV who have a higher risk of developing liver cancer—older men (over 45 years old), people with cirrhosis, people who consume a lot of alcohol, people with a family history of liver cancer, and people with HIV and/or chronic hepatitis C.

A liver biopsy may be recommended to determine the extent of liver damage. Not everyone with chronic hepatitis B needs a liver biopsy. Healthcare providers have different opinions as to when and whether it should be done. The need varies from person to person and, ideally, the decision should be made after discussion with your provider.

The biopsy is a short outpatient procedure performed while you're awake. A needle is inserted just below the right ribs and into the liver, and a small tissue sample is removed and examined. A biopsy doesn't damage the liver. People respond very differently to a biopsy—some find it painful, while others are surprised at how little pain they feel. Many people find the procedure boring because you have to lie still for a long time afterwards to avoid internal bleeding.

Moving forward

Treatment isn't necessary for everyone with chronic HBV. Decisions are based on the results of the tests described above and other considerations. Some of the medications used to treat HIV have an effect on HBV and vice versa, making treatment more complicated for people co-infected with HIV and HBV.

Some healthcare providers who specialize in HIV also have a good understanding of hepatitis B, while others don't. To receive the best care possible, people with HIV/HBV co-infection might need to see a liver specialist (a gastroenterologist or hepatologist) in addition to their HIV provider.

The second part of this article will appear in the May/June issue of *Positively Aware*. It will discuss treatment considerations for people co-infected with HIV and hepatitis B.

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