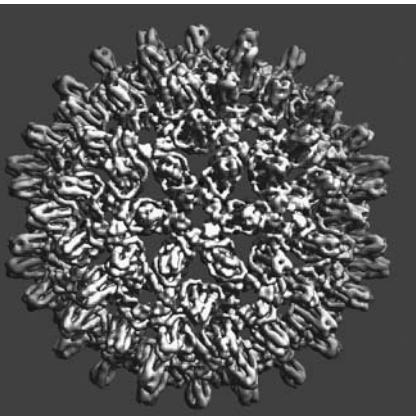
The ABCs of hepatitis

Hepatitis B often overlooked by PWAs

by R. Paul Kerston



Hepatitis B core protein shell

More than 5% of the world's population has chronic hepatitis B, which is caused by the hepatitis B virus (HBV). Hepatitis B can cause serious or even fatal damage to the liver. Despite available vaccines and treatments, hepatitis B remains a serious disease.

In developed countries such as Canada, HBV is usually transmitted through contact with blood, semen, vaginal fluids, or saliva or from mother to baby before or during birth. HBV is considered much more infectious than HIV. In young people, HBV infection is more likely to lead to chronic infection and long-term liver problems than in older persons.

Symptoms

When initially infected by HBV, symptoms range from absolutely nothing—in most cases—to more severe symptoms such as jaundice, loss of appetite, pain in the abdomen, nausea, vomiting, muscle and joint aches, and fever.

Frequently, HBV-infected persons develop a protective immunity, often without their knowledge. However, in a minority of people, HBV continues to reproduce within the body long after the initial infection. Some of these people will become chronic carriers of the disease, which means that they can infect others for the rest of their lifetimes. This carrier status can occur despite the infected person experiencing no symptoms whatsoever. Of these chronic carriers, approximately one-quarter eventually develop chronic liver inflammation, which leads to increased risk for diseases such as cirrhosis or cancer of the liver. HIV-positive persons who contract HBV are at greater risk of becoming chronic hepatitis B carriers.

With hepatitis B, liver damage is not caused by the virus itself, but by the body's own immune system response of destroying the liver cells that host the virus. As a result of their already-impaired immune systems, HIV-positive individuals co-infected with HBV may experience less liver damage than others. Acute liver inflammation may occur in individuals with immune reconstitution from taking HAART (highly active antiretroviral therapy). However, because the body's impaired immune system doesn't clear HBV from liver cells as effectively in HIV-positive people, such individuals are thought to be more infectious than their HIV-negative counterparts.

Diagnosis

One way to diagnose hepatitis B is by detecting antibodies developed by the immune system. If antibodies are detected, the body has rid itself of the virus after infection—often without one's knowledge. However, chronic carriers will have HBV surface antigens in their blood, instead of antibodies, for at least six months. Some of these persons also test e-antigen positive, which means that they are highly infectious. Twenty-five percent of people with HBV have both antigens and antibodies, which also indicates carrier status.

Another diagnostic test is measurement of alanine aminotransferase (ALT), a liver-specific enzyme whose level is usually elevated in chronic HBV infection. Bilirubin levels also rise. *(See the article on interpreting liver test results on page 26.)*

Drug treatments

Four drug treatments for chronic hepatitis B are available, including the use of lamivudine (also known as Epivir or 3TC), the very same nucleoside analog antiretroviral drug often prescribed in combination HIV therapy (HAART). Lamivudine blocks HBV replication. In HIV, lamivudine is usually prescribed at 150mg, twice daily. For hepatitis B, the standard dose of lamivudine is 100mg daily for one year. It is recommended that this drug be stopped after a sustained period of more than two months of hepatitis B e-antigen (HbeAg) loss or the detection of antibodies to these antigens in the blood (seroconversion).

People must be monitored closely to identify reactivation, which is an indication for re-treatment. Lamivudine has few side effects and discontinuation of such therapy is rarely necessary for such reasons. HBV treated with lamivudine often results in what is known as a 4-log suppression of HBV DNA. In other words, this suppression is equal to going from

100,000 copies of the virus to only 10. Seventeen percent of patients using lamivudine for one year, prescribed as above, seroconverted; 32% showed loss of the e-antigen. Flare-ups of hepatitis B in persons co-infected with HIV/HBV upon switching off lamivudine to a new combination for HIV treatment are possible.

Two nucleotide drugs that were originally developed as HIV treatments are also active against HBV. Adefovir dipivoxil is a nucleotide that was discontinued from further development as an HIV treatment for safety reasons. It can be taken in lower doses for HBV treatment, thereby avoiding major toxicity. Another nucleotide, tenofovir, is not yet licensed as an HIV treatment in Canada but is available through expanded access.

Interferon

The other drug for HBV treatment is interferon alfa/alpha (IFN). Interferons are proteins produced by host cells in response to viral infection. Of the three different types of interferon, only those produced by B lymphocytes and monocytes (two types of white blood cells) have been shown to be effective against HBV. Unlike lamivudine, IFN both augments the host immune response and works on the virus itself. The dosage is 5 million units daily, or 10 million units three times per week, given subcutaneously (under the skin) for four months. Side effects are common, including flu-like fever and chills.

Not everybody is considered suitable for IFN therapy. Doctors recommend waiting for more than six months before commencing IFN therapy because 5–10% of HBV e-antigen positive persons develop their own antibodies. Untreated cirrhosis of the liver is one reason not to initiate IFN treatment.

IFN is intended to permanently suppress viral replication or eliminate the infection completely. Twenty-five to 40% of patients in trials had e-antigens and HBV DNA disappear after treatment with IFN for 4–6 months. With those persons in whom therapy results in e-antigen negative status, the result is an inactive HbsAg carrier state—meaning they are not infectious—and about one-third of these people eventually lose the HbsAg altogether on their own. Side effects with IFN require close monitoring, optimally every 2–4 weeks, with complete ALT and AST testing plus a complete blood cell count.

HIV and HBV co-infection

HIV-positive persons who are co-infected with HBV may not respond well to IFN. Lamivudine is better for such persons. In fact, lamivudine is considered safe and convenient, and it achieves a >30% HbeAg loss compared with IFN treatment's 30–40%. IFN requires uncomfortable injections and is associated with many side effects.

However, lamivudine requires longer treatment: one year compared with four months on IFN. One other drawback to lamivudine is the emergence of viral variants and thus, resistance that has been measured at between 15–30% after one year of therapy, 50% after three years.

Data on combination therapy with both IFN and lamivudine is currently very limited.

Other treatment options

Liver transplantation, another treatment option, is considered when the liver is seriously damaged. Earlier disappointments, including rejection, have been minimized by the use of drugs such as lamivudine and famciclovir.

Although some may consider a range of Chinese medicinal herbs, few trials have been conducted to date, and the evidence is currently considered too weak to make recommendations.

HBV is one of the leading causes of liver cancer in the world. Vaccination prevents not only hepatitis and cirrhosis caused by HBV, but also liver cancer. Universal vaccination for HBV has been adopted in 80 countries. In the US, universal vaccination was introduced for all newborns in 1991, although the vaccine became available as early as 1982.

Adults should take 10mg doses upon diagnosis, at 1–2 months, and at 6 months. Effectiveness is considered achieved in 95% of those who complete the full program of the three vaccinations. In those individuals who develop HBV antibodies as a result of vaccination, efficacy approaches 100% and such immunity lasts at least 10 years, if not for life. Lifetime immunity is believed to occur despite antibody levels dropping in a large number of such individuals after the 10-year mark.

A major issue of concern to health professionals treating co-infection of HIV and HBV is not only the effects of the two diseases on the liver, but also the side effects of drugs associated with treatment, or hep atoxicity. Liver enzymes help in the metabolization process and over-taxing this organ through high combinations of drugs can cause severe difficulties with high levels of these toxins not being properly metabolized or removed. Careful monitoring and consultation with health professionals is required. ⊕

R. Paul Kerston is a researcher with the BCPWA Society's Treatment Information Program.