INTRODUCTION

As antiretroviral therapies continue to improve, patients infected with HIV are living longer, and the health problems that are of primary concern to these patients are changing in recent years. Before the advent of highly active antiretroviral therapy (HAART), HIV-infected patients were most likely to succumb to opportunistic bacterial or fungal infections, secondary to HIV-induced immune suppression. With longer survival times, liver disease and hepatocellular carcinoma (HCC) are becoming increasingly important in these patients.\textsuperscript{1,2} In fact, approximately 10–15\% of deaths in HIV patients are now due to liver disease. In patients with HIV, most liver disease is due to chronic viral hepatitis. This is not surprising considering that agents causing viral hepatitis, like the hepatitis B virus (HBV) and hepatitis C virus (HCV), are transmitted through similar routes as HIV. An additional complication involving the liver in HIV-infected patients is the fact that many anti-HIV drugs cause hepatotoxicity, which is further exacerbated by viral hepatitis.

CHRONIC HBV AND HCV INFECTIONS

Worldwide, there are over 500 million people who are chronically infected with HBV or HCV, or both. HBV is a small, enveloped DNA virus that belongs to the \textit{Hepadnaviridae} family. HBV is unusual for a DNA virus in that replication of the viral DNA genome is through the reverse transcription of a RNA intermediate.\textsuperscript{3} The small, 3.2 kb HBV genome encodes four open reading frames (ORFs) (Fig. 1),
which are translated to make the viral core (C) protein, the main constituent of the viral nucleocapsid; the reverse transcriptase (RT), the enzyme responsible for DNA replication via reverse transcription; and three envelope glycoproteins. In addition, the HBV X (HBx) protein has a number of pleotropic effects on viral and cellular gene expression, cell signaling, cell cycle, and apoptosis, although the significance of these in viral replication or pathogenesis remains unresolved. HBV is transmitted by contact with blood or other body fluids of an infected person in the same way as HIV. However, HBV is 50–100 times more infectious than HIV.

Of the two billion people who have been infected with HBV, more than 350 million have chronic, lifelong infections.\textsuperscript{5,5} In the US alone, there are 1.25 million chronic HBV carriers. In some areas of Asia and Africa, where HBV is endemic, 10–20\% of the whole population is chronically infected with HBV (Fig. 2). In these parts of the world, HBV infections are acquired mainly perinatally or early in childhood and have a high (up to 90\%) probability of becoming chronic. In contrast, 5–15\% of adults who acquire HBV infection will become chronic carriers of the virus. Patients who are chronically infected with HBV are at high risk of premature death from cirrhosis of the liver and HCC, a highly malignant liver cancer. The risk of death from HBV-related liver cancer or cirrhosis is approximately 25\% for persons who become chronically infected. Together, these diseases kill about one million persons each year worldwide.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{HBV_genome.png}
\caption{HBV genome organization. Solid lines, the partially double stranded, relaxed circular DNA genome; dotted lines, viral RNA transcripts; solid arrows, encoded proteins. Core, core protein; S, surface protein, RT, reverse transcriptase; X, X protein. Triangle, the RT protein covalently linked to the genome; checked box, the ε RNA packaging signal; ovals, direct repeat 1 and 2, \textit{cis}-acting elements involved in reverse transcription}
\end{figure}