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Reply:

In their letter, Dr. Papatheodoridis and colleagues questioned the basis for selecting a cutoff level of hepatitis B virus (HBV) DNA higher than 2000 IU/ml to differentiate hepatitis B e antigen (HBeAg)–negative persons who should be evaluated for chronic hepatitis from those who are in the inactive carrier state. We chose this cutoff level on the basis of the available literature, which suggests that more than 95% of persons having chronic hepatitis B will have HBV DNA levels higher than 2000 IU/ml.[1-4] We agree that a small percentage of HBeAg-negative carriers who have persistently normal aminotransferases have serum HBV DNA levels that only intermittently exceed 2000 IU/ml. However, as Papatheodoridis and colleagues indicated, minimal or no inflammation and fibrosis have been found in these persons, and in our experience, HBV DNA levels persistently higher than 2000 IU/ml have not been observed among HBeAg-negative persons with persistently normal aminotransferases.

Papatheodoridis and colleagues also indicated that a small percentage of patients with HBeAg-negative chronic hepatitis have serum HBV DNA levels lower than 2000 IU/ml. However, their data and ours show that none of the HBeAg-negative patients with biopsy-documented chronic hepatitis B and abnormal aminotransferases have serum HBV DNA levels persistently lower than 2000 IU/ml.

We agree that there is no clear cutoff HBV DNA level that would differentiate inactive hepatitis B surface antigen carriers from patients with HBeAg-negative chronic hepatitis. Therefore, in the recent update of the American Association for the Study of Liver Diseases guidelines, we emphasized the importance of serial testing and the role of liver histology in patients who fall into gray zones.[5]

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Treating Acute Hepatitis B

To the Editor:

We read with interest the article by Kumar et al.[1] on a randomized controlled trial of lamivudine to treat acute hepatitis B.

The trial of lamivudine versus placebo revealed a greater decrease in HBV DNA levels in the lamivudine-treated group, but this did not translate into a biochemical or clinical improvement in the lamivudine-treated group. This is the first sound evidence to support the prevailing practice of not treating acute hepatitis B patients.

However, the development of antibodies to hepatitis B e antigen (anti-Hbe) and hepatitis B s antigen (anti-HBs) was lower in the lamivudine-treated group relative to placebo (87.5% versus 71 % for anti-HBe and 85% versus 67% for anti-HBs), although this did not reach statistical significance. It is an important observation and its long-term significance in terms of potential flaring of hepatitis B in these patients remains to be determined. It seems plausible that interruption of the protective immune response may be a consequence of pharmacologic therapy. How this translates into future risk of reactivation needs examination. We hope they will follow the groups in the long term to see if any differences evolve.

The second noteworthy outcome from this study is that there was no difference in the 2 groups regarding outcome of severe or fulminant hepatitis B. This suggests that lamivudine treatment of patients with acute hepatitis B may not be harmful in this setting. Clearly, the number of patients is too small to make definitive conclusions. The results may encourage use of lamivudine in a small subset of patients with acute hepatitis B who have a more severe presentation with potential need for liver transplantation. The use of lamivudine in this subset may rescue such patients by increasing chances of spontaneous recovery without liver transplantation. A 2002 German study of fulminant hepatitis B showed that 7 of 8 patients treated with lamivudine (after 2000) avoided death or transplantation compared to a historical group (before 2000) where only 5 of 21 patients not treated with lamivudine avoided death or transplantation.[2] Larger prospective studies of lamivudine and other antiviral therapies in liver transplantation would help answer these questions.

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