percent of lung volume) among those with a higher amount of potentially recruitable lung, but these volumes included 183±482 and 135±434 ml of gas, respectively, and only 14±32 and 11±35 g of tissue, respectively, accounting for 1±3 percent and 1±2 percent of the total lung tissue.

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Hepatitis B Virus with Primary Resistance to Adefovir

TO THE EDITOR: Schildgen et al. (April 27 issue)\(^1\) describe the results of tenovifor treatment in three patients infected with adefovir-resistant variant hepatitis B virus (HBV) that had a valine at position 233 of the reverse-transcriptase domain instead of isoleucine (rtI233V). We recently published the results of two trials in which entecavir demonstrated superiority over lamivudine in patients with chronic hepatitis B that was positive for antibody against hepatitis B e antigen (HBeAg)\(^2\) and in patients with HBeAg-negative chronic hepatitis B.\(^3\)

Four of the patients with HBeAg-positive chronic hepatitis B and four of those with HBeAg-
negative chronic hepatitis B were infected with a strain that had the rtI233V mutation and received entecavir therapy. After 48 weeks, all six patients with paired liver-biopsy specimens that could be evaluated had histologic improvement, and two of the four HBeAg-positive patients had seroconversion.

Seven of the eight patients had undetectable viral loads (<300 copies of HBV DNA per milliliter) by week 36, and the mean decrease from baseline was 6.75 log (on a base-10 scale) copies per milliliter in the HBeAg-positive group and 5.11 log copies per milliliter in the HBeAg-negative group (Fig. 1). We tested the in vitro susceptibility to entecavir of one HBV isolate with the rtI233V (and V191I) mutation from our viral archive and found a median effective concentration of 1.4 nM, as compared with 4 nM for wild-type virus.

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THE AUTHORS REPLY: Chang and Lai describe eight patients infected with an HBV variant carrying the novel rtI233V mutation we recently identified in three German patients. It causes primary resistance to adefovir, and it was also recently described in one Australian patient in whom adefovir therapy failed.1

Chang and Lai report that their patients were very efficiently treated with entecavir. We greatly appreciate their rapid comments for two reasons. First, their data, in agreement with ours, indicate that the rtI233V mutation occurs in approximately 2 percent of all patients with chronic hepatitis B (8 of 434 patients). Thus, our finding was not an isolated observation. It remains surprising that the mutation was not detected in earlier studies of adefovir.2,3

Second, the observations by Chang and Lai show entecavir to be a highly efficient therapy option for patients with the rtI233V mutation who have no response to adefovir, since tenofovir, which is what we used in our study, is still not licensed for HBV therapy. Since the receipt of lamivudine therapy for more than 12 weeks was an exclusion criterion in their studies, it is very likely that their patients were sensitive to lamivudine. Thus, it remains unknown how useful entecavir would be in patients with lamivudine-resistant rtI233V mutations. In our study, two patients with a response to tenofovir were resistant to lamivudine.

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