LETTER FROM THE EDITOR

Hepatotoxicity is often a concern when prescribing certain drugs, as serious drug reactions can occur with potentially devastating consequences. While vigilance in this regard is warranted, concern about possible liver injury should be tempered by the latest drug safety information, which is growing thanks to ongoing research and registries such as the US Acute Liver Failure Study Group. As the understanding of drug-induced liver injury becomes more complete, researchers are starting to see that some concerns about drug-induced liver toxicity may be out of proportion to the real risk. Indeed, some of the drugs that have previously prompted concern may actually be hepatoprotective.

As James H. Lewis elegantly explains in this month's Advances in Hepatology column on page 333, the cellular mechanisms that cause drug-induced injury are balanced by mechanisms that protect hepatocytes from drug-induced injury. Called the adaptive response or drug tolerance, this phenomenon allows some drugs to be continued safely in patients who show low-level elevations in liver enzymes such as alanine aminotransferase. Specifically, if the patient's total serum bilirubin level is less than twice the upper limit of normal and the patient does not show any symptoms of liver injury, then elevations in liver enzyme levels up to 8 times the upper limit of normal may be tolerated, provided patients are adequately monitored, as these liver-enzyme elevations are unlikely to cause permanent hepatic injury. From a clinical standpoint, this means that beneficial medications can be continued in patients who show minor elevations in liver-enzyme levels in the absence of symptoms or other indicators of liver injury.

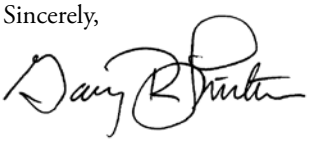
While the cellular mechanisms underlying drug tolerance have not yet been fully elucidated, some protective cytokines and chemokines have been identified—including interleukin-6 and interleukin-10—and researchers are also looking into the genetic basis of the adaptive response. Hopefully, future studies will reveal which specific genotypes are associated with an elevated risk of drug-induced liver injury. Given this information, clinicians could then test for these genotypes before prescribing a drug, potentially distinguishing between patients who are likely to develop irreversible liver injury and those in whom liver enzyme elevations are probably inconsequential.

Interestingly, recent research suggests that statins may actually be hepatoprotective, despite earlier concerns about liver injury with these drugs. When statins were first marketed, their labeling required frequent liver enzyme monitoring, and some clinicians remain cautious when prescribing these drugs in patients who are at risk of liver injury. However, recent research suggests that statins may actually reduce the risk of hepatocellular carcinoma (HCC) in some patients. As is discussed in the literature review on page 318, a study published in the *Journal of Clinical Oncology* reported that statin use is associated with a reduced risk of HCC among hepatitis B virus (HBV)-infected patients (2012;30:623-630). Further, the literature review commentary by Myron J. Tong on page 320 mentions another study that yielded similar findings; this latter study assessed patients with diabetes rather than HBV-infected patients, but it also found an association between statin use and reduction in HCC risk. While we do not yet have enough evidence to support the prescription of statins solely for the purpose of cancer prevention, these results are intriguing and will hopefully be explored further in future studies.

Moving on to the current issue of *Gastroenterology & Hepatology*, I invite readers to take a look at this month's 3 feature articles; they address hepatitis C virus infection in patients with nonalcoholic steatohepatitis, serum antibodies to *Clostridium difficile* toxin B in patients with inflammatory bowel disease (IBD), and adverse metabolic sequelae following restorative proctocolectomy with an ileal pouch. In addition, this month's other columns discuss the management of arthritis in patients with IBD, recent research on pneumatic dilatation versus laparoscopic Heller myotomy for treatment of achalasia, and inappropriate uses of colonoscopy.

Finally, I would like to welcome you to stop by our booth at this year's Digestive Disease Week meeting in San Diego, where you can pick up copies of the journal as well as various supplements. I hope to see you there!

Sincerely,



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