which a drug is prescribed somehow lessens its effect. Although this statement may have been made tongue-in-cheek, we do not believe that it is an unreasonable policy to promote when the outcome can only increase patient safety. We therefore stand by our recommendation that when the patient is an individual whose job performance has the potential to adversely affect others, it is reasonable to make sure he/she is not impaired before returning to work.

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Why Vitamin D Status Should Be Checked in Patients With Nonalcoholic Fatty Liver Disease

To the Editor: In an excellent clinical vignette in the January 2012 issue of *Mayo Clinic Proceedings*, Nelsen et al[1] discussed the diagnosis and management of patients with nonalcoholic fatty liver disease (NAFLD). We suggest that in patients with this hepatic manifestation of the metabolic syndrome, vitamin D status should also be considered.

In addition to its traditional calcium-related effects on the skeleton, vitamin D deficiency has now been recognized to exert nonskeletal adverse effects on several other organ systems. Hypovitaminosis D is highly prevalent in the United States and around the world. In particular, it reaches a peak of 75% in patients with metabolic syndrome.[2] In this setting, it has been found that patients with biopsy-proven NAFLD had a significantly higher prevalence of hypovitaminosis D (defined as a serum vitamin D concentration of ≤37.5 nmol/L) and markedly lower 25-hydroxyvitamin D (25[OH]D) levels (the best estimates of overall vitamin D status level) than matched controls.[3] The 25(OH)D concentrations were lower in individuals with nonalcoholic steatohepatitis than in those with simple steatosis and inversely associated with the severity of liver histology among NAFLD patients, after adjustment for a broad spectrum of potential confounders. Interestingly, a strong independent association between low 25(OH)D levels and NAFLD has also been found in a population of adults without signs of severe liver damage.[4] This association was independent of diabetes, dyslipidemia, and insulin resistance.

Although the cross-sectional design of these studies[3,4] does not allow establishment of a causative nature of the associations between hypovitaminosis D and NAFLD, the linear inverse correlation between serum 25(OH)D levels and the degree of NAFLD suggests that vitamin D may exert a dose-dependent effect of fat accumulation in hepatocytes. Several mechanisms may explain a causal role of vitamin D deficiency in the development of NAFLD and nonalcoholic steatohepatitis. In fact, vitamin D is capable of reducing free fatty acid–induced insulin resistance both in peripheral tissues and in hepatocytes.[4] Moreover, vitamin D exerts an immunomodulatory action by suppressing fibroblast proliferation and collagen production,[5] which may be particularly important in the evolution to cirrhosis.

Therefore, although intervention trials are warranted to evaluate whether vitamin D supplementation may be a means to prevent and/or treat patients with NAFLD, we believe that vitamin D status should be checked in individuals with liver steatosis.

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In reply: Vitamin D and its relationship to nonalcoholic fatty liver disease (NAFLD) has become of recent interest as studies have linked low serum 25(OH)D levels with NAFLD. The potential therapeutic role of vitamin D supplementation in NAFLD is an intriguing concept given its