development of PBC is influenced by genetic variance of the vitamin D receptor (VDR) gene.\textsuperscript{4} Moreover, 1,25-dihydroxyvitamin D, the bioactive form of vitamin D, inhibits Th1-mediated immune response.\textsuperscript{5} This suggests that reduced activity of VDR-dependent signalling pathways caused by the VDR polymorphism might skew the immune response to the Th1 pathway, contributing to the development of PBC.

On the other hand, it is well known that vitamin D has direct effects on muscle strength modulated by specific VDRs present in human muscle tissue.\textsuperscript{6} The binding of vitamin D to its nuclear receptor in muscle tissue may lead to \textit{de novo} protein synthesis,\textsuperscript{7} a benefit that appears to precede the effect of vitamin D on bone. Interestingly, a meta-analysis of randomized controlled trials\textsuperscript{8} found that supplemental vitamin D in a dose greater than 700 IU/day significantly reduced the risk of falling among older individuals.

Therefore, studies of vitamin D supplementation for fall prevention in individuals with PBC are urgently needed. In the meantime, we suggest that all PBC patients should maintain adequate levels of vitamin D.

L. Mascitelli  
Comando Brigata Alpina “Julia”, Medical Service  
Udine 33100, Italy  
e-mail: lumasci@libero.it

F. Pezzetta  
Cardiology Service Ospedale di Tolmezzo  
Tolmezzo 33028, Italy

M.R. Goldstein  
Fountain Medical Court Bonita Springs FL 34135, USA

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Response: Primary biliary cirrhosis is associated with falls and significant fall related injury

Sir,

We would like to thank the author of the letter regarding our recent paper in \textit{QJM}\textsuperscript{1} where we identified an increased prevalence of falls in those with the autoimmune liver disease primary biliary cirrhosis (PBC). The author raises some very interesting and important points.

The full extent of the biochemical and physiological role of vitamin D is not yet fully understood. It is well known that it plays an essential role in bone metabolism and calcium homeostasis, but it also appears to play a role in immunity, muscle strength, fatigue and falls.\textsuperscript{2,3} Metabolism of calcium and vitamin D is almost always normal in PBC and the process of 25-hydroxylation is maintained.\textsuperscript{4,5} Although vitamin D deficiency is the second most common fat-soluble vitamin deficiency in PBC, it is uncommon and absorption from the gut is not affected until there is severe cholestasis.\textsuperscript{6,7} The majority of those in our study had early stages of liver disease and none of our participants had evidence of cholestasis.

There is much debate about whether vitamin D supplementation reduces falls in the elderly with many conflicting results.\textsuperscript{8,9} However, it appears that those who do benefit from supplementation do so regardless of their serum vitamin D status.\textsuperscript{9} With this in mind, it may therefore be that it is the biological activity which is more relevant than actual serum levels; the emerging research concerning vitamin D receptor polymorphisms in PBC is very interesting and may be relevant here.\textsuperscript{10}

We agree with the respondent that vitamin D supplementation may be necessary in PBC to improve muscle weakness, falls and even fatigue just as it...
does so in the general and elderly population. However, we feel that including vitamin D status in a regression model may be misleading as the absence of an independent association would not mean that supplementation is not worthwhile. What is more important is to conduct a prospective trial evaluating the clinical and personal effects of vitamin D supplementation.

J. Frith
J.L. Newton
UK National Institute for Health Research,
Biomedical Research Centre in Ageing-Liver Theme,
Newcastle University, Newcastle UK
e-mail: james.frith@ncl.ac.uk

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