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Response Letter to Lawrence Solomon

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To the Editor: We appreciate Dr. Solomon's interest in our recent study of vitamin B12 and peripheral nerve function. We agree that B12 deficiency is only one risk factor for poor peripheral nerve function, and many older adults with “normal” B12 levels may have subclinical B12 deficiency, as shown according to methylmalonic acid (MMA) levels, and have poor peripheral nerve function. Because diabetes mellitus accounts for only approximately 40% of prevalent cases of peripheral neuropathy and half of incident cases,¹ additional risk factors need to be identified in individuals without diabetes mellitus. Clinicians are often unable to determine a reasonable cause of neuropathy in older adults. We recognize that older adults with “normal” serum B12 levels (>260 pmol/L) can still have high MMA levels. A recent review showed that homocysteine and MMA levels may be high for serum B12 levels up to 400 pmol/L.² Therefore, the cut point of 260 pmol/L may be inadequate for determining associations with poor peripheral nerve function. More importantly, the clinical deficient cutpoint of 148 pmol/L may need to be reexamined because many older adults with “clinically normal” B12 levels may have nerve deficits caused by low B12 availability. Thus, clinicians may believe that, because their patients' serum B12 level is “clinically normal,” poor B12 is not causing the symptoms of peripheral neuropathy and B12 replacement is not needed.

Unfortunately, MMA or homocysteine levels are not available for those with B12 levels greater than 260 pmol/L to determine those with “functional B12 deficiency.” In our study, in those with low serum B12 (<260 pmol/L), no significant difference existed in MMA levels between older adults with (358.9 ± 252.1 nmol/L) and without diabetes mellitus (323.5 ± 213 nmol/L) ($P = .20$). The analysis that Dr. Solomon has performed is important to determine that “functional B12 deficiency” is probably present in a substantial proportion of older adults, particularly in older adults with diabetes mellitus. The use of metformin, which impairs absorption of B12 found naturally in food (animal products), accentuates this relationship in older adults with diabetes mellitus.^{3,4} The role of “functional B12 deficiency” and the threshold of vitamin B12 levels affecting peripheral nerve function in older adults is a critical future direction of our work.

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