

## Vitamin B<sub>12</sub> and folate depletion in the elderly Diagnosis, clinical correlates and causes

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Subclinical vitamin B<sub>12</sub> and folate deficiency is common in the elderly. The clinical significance remains unresolved. There is not a universally accepted set of laboratory criteria for diagnosis, however subclinical deficiency is important to diagnose since it is easy to treat. Currently available measures of vitamin concentrations are, except in pronounced deficiency, unreliable. Plasma tHcy and serum MMA are potentially more reliable markers of intracellular vitamin status.

The overall aim was to estimate the prevalence of B-vitamin deficiency and atrophic gastritis, to calculate health related reference intervals for plasma tHcy/serum MMA, to explore the dependence of glomerular filtration rate on these metabolites, and to study the effect of oral B-vitamin therapy both on biochemical and clinical outcome.

The thesis is based on a population-based study of 209 community-dwelling subjects, mean age 76 years. The study included a double-blind placebo controlled intervention with an oral daily combination of vitamin B<sub>12</sub> (0.5mg), folic acid (0.8mg) and B<sub>6</sub> (3mg) during four months.

Elevated plasma tHcy and serum MMA was found in 53% and 11%. Vitamin B<sub>12</sub> deficiency occurred in 7.2%, folate deficiency in 11%, atrophic gastritis in up to 14%. Health-related upper reference limits for the metabolites were higher than those commonly used. After adjustment for glomerular filtration rate also within its normal range, the fraction of subjects with elevated plasma tHcy diminished significantly. Plasma tHcy and serum MMA correlated inversely with movement and cognitive performance. Vitamin therapy significantly decreased plasma tHcy (32%) and serum MMA (14%) but failed to improve movement or cognitive performance. Atrophic gastritis did not cause reduced vitamin absorption.

In conclusion, elevated levels of plasma tHcy and serum MMA were common and more frequent than actual B-vitamin deficiency. The prevalence of "elevated" plasma tHcy may be overestimated unless adjusted for glomerular filtration rate. Atrophic gastritis was not uncommon and correlated to inferior B-vitamin status. Short-term oral B vitamin treatment normalized plasma tHcy and serum MMA levels also in subjects with atrophic gastritis, but did not affect movement or cognitive performance.

**Key words: aged, methylmalonic acid, homocysteine, vitamin B<sub>12</sub>, folic acid, renal function, cognition, movement, atrophic gastritis**

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