Investigation of biomarker responses to depletion/repletion with vitamin B$_{12}$

C. F. Hughes$^1$, M. Ward$^1$, L. Hoey$^1$, A. Molloy$^2$, K. Pentieva$^1$, J. M. Scott$^2$, F. Tracey$^3$ and H. McNulty$^1$

$^1$Northern Ireland Centre for Food and Health, University of Ulster, Coleraine BT52 1SA, UK, $^2$Trinity College, School of Biochemistry and Immunology, Dublin, Ireland, and $^3$Causeway Hospital, Coleraine BT52 IHS, UK

Despite dietary intakes well above current recommendations, low biomarker status of vitamin B$_{12}$ is a common problem in older adults, largely as a result of malabsorption of food-bound vitamin B$_{12}$. This arises mainly from atrophic gastritis which leads to reduced gastric acid production (hypochlorhydria). Hydrochloric acid is essential for the absorption of food-bound vitamin B$_{12}$, and thus vitamin B$_{12}$ absorption is reduced in states of hypochlorhydria, although in theory free vitamin B$_{12}$ (from supplements or fortified) should still be absorbed. Gastric acid suppressant medications, such as proton pump inhibitors (PPI) drugs induce hypochlorhydria and therefore a state similar to atrophic gastritis. The aim of the present study is to investigate the effect of hypochlorhydria on absorption of food-bound vitamin B$_{12}$ and to determine whether low-dose supplemental vitamin B$_{12}$ would overcome any vitamin B$_{12}$ malabsorption. Forty-one healthy males, aged 18–45, participated in a vitamin B$_{12}$ depletion/repletion trial. During the depletion phase (week 0–6) all subjects were administered with a PPI (omeprazole, 20 mg/d); after which they were randomised (by vitamin B$_{12}$ status as measured by serum holo-transcobalamin; holoTC; the metabolically active fraction of total circulating vitamin B$_{12}$) into one of the two treatment groups to receive; omeprazole (20 mg/d) plus supplemental vitamin B$_{12}$ (10 mg/d) or omeprazole (20 mg/d) plus placebo for the repletion phase of the study (week 7–12).

Contrary to expectations, no significant change in vitamin B$_{12}$ status (as assessed by either total vitamin B$_{12}$ or holoTC) was observed during the depletion phase of the study. During the repletion phase of the study, an increase in vitamin B$_{12}$ status was observed in the treatment group, but this was significant ($P = 0.006$) only using the biomarker holoTC, with the response for total vitamin B$_{12}$ failing to reach significance. In conclusion, these results supports the emerging view that holoTC (compared with the traditional biomarker of status, serum total vitamin B$_{12}$) is a more sensitive biomarker in detecting small changes in vitamin B$_{12}$ intake. Although the acute administration of PPI drugs did not significantly suppress vitamin B$_{12}$, repletion with 10 µg/d of supplemental vitamin B$_{12}$ was sufficient to significantly increase biomarker status within just 4 weeks. The consequence of long-term PPI therapy on vitamin B$_{12}$ status is still to be determined.

Fig. 1. Serum total B12 and holoTC responses to vitamin B$_{12}$ depletion/repletion were compared by repeated measures ANOVA on log transformed data.