


Plasma concentrations of total homocysteine predict mortality risk^{1,2}

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In this issue of the Journal, investigators from Norway, who are well known throughout the world for their contributions to the field of blood homocysteine, have added another important finding (1). In a prospective study of 2127 men and 2639 women aged 65–67 y in 1992–1993 from Hordaland County, Norway, 162 men and 97 women died during a median 4.1 y of follow-up. The association between mortality and plasma total homocysteine (tHcy), distributed by quintiles with use of those with a concentration <9.0 μmol/L as the referent group, was highly significant for both nonvascular and cardiovascular causes of death. An increase in tHcy of 5 μmol/L was associated with a 49% increase in all-cause mortality, a 50% increase in cardiovascular mortality, a 26% increase in cancer mortality, and a 104% increase in non-cancer, noncardiovascular mortality. Thus, plasma tHcy was a strong predictor of both cardiovascular and noncardiovascular mortality. The strongest association was between tHcy and non-cancer, noncardiovascular mortality. The present observation confirms the prognostic value of elevated plasma tHcy for total mortality reported in Israel (2) and the United States (3, 4). Consequently, as Vollset et al (1) suggested, in addition to investigations of the mechanisms of the relation between tHcy and atherosclerosis and thrombosis, future studies should focus on tHcy and pathologies other than vascular diseases.

The association between elevated concentrations of plasma tHcy and mortality emphasizes the desirability of conducting widespread screening of plasma tHcy concentrations in middle-aged and elderly persons to help identify potential candidates for treatment. Because folic acid is the cornerstone in the treatment of elevated tHcy concentrations, it is likely that an inexpensive and usually well-tolerated vitamin therapy could prevent many deaths (5). However, pharmacologic doses of folic acid increased tHcy in

≈20% of subjects in a study of 304 men and women (6). Although the significance of this paradoxical tHcy response needs further study, repeated testing may be necessary to determine the effects of folic acid supplementation on tHcy. The questions of potential therapy raised by the above observations may be partly answered when the results of ongoing, secondary-prevention clinical trials are known (7), yet data from these observations suggest that primary prevention trials should also be considered. 

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