Recent clinical and laboratory findings have attracted much interest in homocysteine (Hcy) because the latter is relevant to numerous medical conditions. Elevated plasma level of Hcy (eHcy) is a recognized independent risk factor for cardiovascular disorders [1,2], causing atherosclerosis and myocardial infarction. Additionally, eHcy has been observed in a number of neurological disorders including stroke [3], dementia, Alzheimer’s disease (AD) [4], Parkinson’s disease (PD) [5], and amyotrophic lateral sclerosis (ALS) [6].

Hcy is an intermediate metabolite of the essential amino acid methionine involving DNA metabolism via methylation. Hcy can be converted into either methionine or cystathione by the enzymes methionine synthase, which requires B12 as a cofactor to remethylate Hcy to methionine, or cystathione-β-synthase, which controls transulfuration of Hcy to cystathione and requires B6 as a cofactor; and methyltetrahydrofolate reductase (MTHFR), which requires folate for reaction. In physiologic conditions, Hcy is converted to methionine which is activated by ATP to form S-adenosylmethionine (SAM) and serves as a universal methyl donor. The transfer of SAM's methyl group to an acceptor molecule generates S-adenosylhomocysteine (SAH) and accelerates motor neuronal death [25,26]. Clinical studies have documented that eHcy causes vascular endothelial cells dysfunction leading to hypercoagulation, atherosclerosis and stroke [3], which may, in turn, play a role in the pathogenesis of neurodegenerative disorders [8]. Notably, those neurologic disorders commonly occur in late adult life, which may suggest possible cumulative effects, such as Hcy, from environments with possible genetic predispositions. Importantly, eHcy level is related with various physiologic and pathologic conditions including old age [3], male sex, cigarette smoking [27], chronic renal insufficiency, high blood pressure, elevated cholesterol level, and lack of exercise [28].

Currently there is no cure for neurodegenerative disorders. The best approach in clinical practice is primarily prevention through modification of acquired risk factors. As eHcy may play a role in promoting early onset of various neurologic disorders, exacerbating the symptoms, and accelerating neurodegeneration, eHcy may become a therapeutic target in tertiary management although evidence of Hcy as a definite risk factor for the development of neurodegenerative disorders is still lacking. Nevertheless, information that eHcy may be causally relevant to neurologic disorders could have important clinical implications, because administration of vitamin B-complex with folate to reduce eHcy is inexpensive, potentially effective, and devoid of adverse effects, therefore, having an exceptionally favorable benefit/risk ratio [2,29,30]. However, the efficacy in prevention of neurologic disorders remains to be elucidated and in debate [21]. Well-designed prospective randomized placebo-controlled clinical trials are warranted to evaluate the efficacy of administration of vitamin B-complex with co-factors.
folate to patients with eHcy in preventing the onset, or mitigating the severity, of neurologic disorders.

References


