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Moderate hyperhomocysteinemia and immune activation.

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Moderate hyperhomocysteinemia is associated with an increased risk of atherosclerosis, thrombosis and neurodegenerative diseases. Homocysteine accumulation in the blood can be due to many underlying causes, which may interact with each other, e.g. genetic disposition and B-vitamin status. The role of the sulfur-containing amino acid homocysteine in the pathogenesis of diseases remains unclear, even if many studies suggest a causal relationship between homocysteine-mediated processes like oxidative stress, NO-inactivation and endothelial deficiency and atherogenesis. Proposed mechanisms of action of homocysteine are discussed, and the question is addressed, whether effects that are attributed to homocysteine, are not rather the consequence of folate and vitamin B12-deficiency. **Deficiency of vitamin B12 in parallel with moderate hyperhomocysteinemia is often found in patients with *enhanced activation of the cellular immune system*, like Alzheimer's disease, rheumatoid arthritis and also vascular diseases.** In patients with these diseases an association between homocysteine metabolism, oxidative stress and immune activation exists. On the one hand **proliferation of immunocompetent cells having an enhanced demand for B-vitamins leads to the accumulation of homocysteine**. On the other hand macrophages stimulated by TH1-type cytokine interferon-gamma form reactive oxygen species (ROS), which oxidize antioxidants, lipoproteins and oxidation-sensitive B-vitamins. Thereby Th1-type immune response could contribute importantly to the development of hyperhomocysteinemia, and may also be a major determinant of disease progression.

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