PE1463/BB

Kilmer McCully MD Email of 9 December 2013

Dear Members of the Scottish Parliament:

I am writing in support of Petition PE01463, concerning effective thyroid and adrenal testing, diagnosis and treatment. For many years my research team and I have been investigating homocysteine metabolism in normal cells and tissues and in age-related degenerative diseases, such as arteriosclerosis, cancer, dementia, and thyroid disorders. The results of these investigations support the purpose of the cited petition. The following information describes recent discoveries relating to homocysteine metabolism and thyroid disease:

Recent findings have demonstrated a close connection between the transport of thyroxine and retinol to cells for the synthesis of thioretinamide within target cells. This transport process is facilitated by transthyretin, a plasma protein formerly known as pre-albumin. As the name implies, plasma transthyretin is partially responsible for transport of thyroid hormone to cells. Within cells the retinol of transthyretin is oxidized by superoxide to retinoic acid, an active oxidized derivative of retinol (vitamin A). The enzyme cystathionine synthase catalyzes the synthesis of thioretinamide from homocysteine thiolactone and retinoic acid. The heme oxygenase function of the enzyme cystathionine synthase generates superoxide, which catalyzes oxidation of retinol to retinoic acid. Within cells, thioretinamide forms a complex with cobalamin (vitamin B12) to form thioretinaco. The process of adenosine triphosphate (ATP) synthesis from adenosine diphosphate (ADP) and phosphate is catalyzed by thioretinaco, ozone and oxygen to produce cellular energy, utilizing electrons from carbohydrates of the citric acid cycle to reduce oxygen to water. This process of cellular oxidative metabolism is regulated by thyroid hormone, specifically tri-iodothyronine, which is derived from thyroxine. The enzyme cystathionine synthase, which is responsible for biosynthesis of thioretinamide, is activated by the co-enzyme pyridoxal phosphate (vitamin B6). The activity of cystathionine synthase is regulated by allosteric interaction with adenosyl methionine, the co-enzyme responsible for transmethylation reactions in all cells and tissues. The synthesis of adenosyl methionine is dependent upon methionine and ATP, and methionine is derived from dietary protein or from methylation of homocysteine by methyl cobalamin, a derivative of vitamin B12. Methyl cobalamin is formed from methytetrahydrofolate and from methylenetetrahydrofolate, derivatives of vitamin B9. This new description of the biosynthesis of thioretinamide and its importance in oxidative metabolism is discussed in the review, Kilmer S. McCully, “Chemical Pathology of Homocysteine. V. Thioretinamide, Thioretinaco, and Cystathionine Synthase Function is Degenerative Diseases,” as published in Annals of Clinical and Laboratory Science, 2011;41:301-314, available online at http://www.annclinlabsci.org/.

A study of homocysteine metabolism in protein energy malnutrition, carried out in Chad, illustrates the important inter-connection between dietary vitamins, homocysteine accumulation, and vitamin deficiencies. In vegetarian populations with marginal dietary methionine consumption, the enzyme cystathionine synthase and the transsulfuration pathway are down-regulated to compensate for deficiency of dietary sulfur in the form of methionine by increased synthesis of methionine from homocysteine. The close connection of this regulation with thyroid hormone action is related to plasma transthyretin, which becomes diminished in protein energy malnutrition. The reciprocal relation of plasma transthyretin with plasma homocysteine was originally discovered by Professor Yves Ingenbleek, Professor of Nutrition at University Louis Pasteur, Strasbourg, France. These observations are of importance because of the elevation of plasma homocysteine as a factor in mortality from coronary heart disease, stroke, and arteriosclerosis in vegetarian populations.

A copy of the study of malnutrition in Chad, Yves Ingenbleek and Kilmer S. McCully, "Vegetarianism produces subclinical malnutrition, hyperhomocysteinemia and atherogenesis," as published in Nutrition, 2012;28:148-153, is available online at http://www.nutritionjrnl.com/. As you can see from this study, the consumption of folate (vitamin B9) and pyridoxal (vitamin B6) was adequate in the Chad population, while consumption of cobalamin (vitamin B12) was marginal because of deficiency of animal foods in the diet. Nevertheless, plasma homocysteine became elevated in this population through metabolic down-regulation of the transsulfuration pathway. An optimal diet contains adequate quantities of vitamins B6, B9, B12, vitamin A, vitamin C, and sulfur amino acids, as described in my book "The Heart Revolution," published by HarperCollins in 1999.

I have read the policy of the Scottish Parliament concerning publication of evidence in support of petitions and confirm that my present communication of evidence may be published in support of the cited petition.

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