Abstract

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**Thiamine and magnesium deficiencies: keys to disease.**

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**BACKGROUND:** Thiamine deficiency (TD) is accepted as the cause of beriberi because of its action in the metabolism of simple carbohydrates, mainly as the rate limiting cofactor for the dehydrogenases of pyruvate and alpha-ketoglutarate, both being critical to the action of the citric acid cycle. Transketolase, dependent on thiamine and magnesium, occurs twice in the oxidative pentose pathway, important in production of reducing equivalents. Thiamine is also a cofactor in the dehydrogenase complex in the degradation of the branched chain amino acids, leucine, isoleucine and valine.

**FINDINGS:** In spite of these well accepted facts, the overall clinical effects of TD are still poorly understood. Because of the discovery of 2-hydroxyacyl-CoA lyase (HACL1) as the first peroxisomal enzyme in mammals found to be dependent on thiamine pyrophosphate (TPP) and the ability of thiamine to bind with prion protein, these factors should improve our clinical approach to TD. HACL1 has two important roles in alpha oxidation, the degradation of phytanic acid and shortening of 2-hydroxy long-chain fatty acids so that they can be degraded further by beta oxidation. The downstream effects of a lack of efficiency in this enzyme would be expected to be critical in normal brain metabolism. Although TD has been shown experimentally to produce reversible damage to mitochondria and there are many other causes of mitochondrial dysfunction, finding TD as the potential biochemical lesion would help in differential diagnosis. Stresses imposed by infection, head injury or inoculation can initiate intermittent cerebellar ataxia in thiamine deficiency/dependency. Medication or vaccine reactions appear to be more easily initiated in the more intelligent individuals when asymptomatic marginal malnutrition exists. Erythrocyte transketolase testing has shown that thiamine deficiency is widespread. It is hypothesized that the massive consumption of empty calories, particularly those derived from carbohydrate and fat, results in a high calorie/thiamine ratio as a major cause of disease.

**CONCLUSIONS:** Because mild to moderate TD results in pseudo hypoxia in the limbic system and brainstem, emotional and stress reflexes of the autonomic nervous system are stimulated and exaggerated, producing symptoms often diagnosed as psychosomatic disease. If the biochemical lesion is recognized at this stage, the symptoms are easily reversible. If not, and the malnutrition continues, neurodegeneration follows and results in a variety of chronic brain diseases. Results from acceptance of the hypothesis could be tested by performing erythrocyte transketolase tests to pick out those with TD and supplementing the affected individuals with the appropriate dietary supplements.

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