Abstract

Vitam Horm. 1991;46:165-228.

Pantothenic acid in health and disease.

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BACKGROUND: In summary, the vitamin pantothenic acid is an integral part of the acylation carriers, CoA and acyl carrier protein (ACP). The vitamin is readily available from diverse dietary sources, a fact which is underscored by the difficulty encountered in attempting to induce pantothenate deficiency. Although pantothenic acid deficiency has not been linked with any particular disease, deficiency of the vitamin results in generalized malaise clinically.

DISCUSSION: In view of the fact that pantothenate is required for the synthesis of CoA, it is surprising that tissue CoA levels are not altered in pantothenate deficiency. This suggests that the cell is equipped to conserve its pantothenate content, possibly by a recycling mechanism for utilizing pantothenate obtained from degradation of pantothenate-containing molecules. Although the steps involved in the conversion of pantothenate to CoA have been characterized, much remains to be done to understand the regulation of CoA synthesis. In particular, in view of what is known about the in vitro regulation of pantothenate kinase, it is surprising that the enzyme is active in vivo, since factors that are known to inhibit the enzyme are present in excess of the concentrations known to inhibit the enzyme. Thus, other physiological regulatory factors (which are largely unknown) must counteract the effects of these inhibitors, since the pantothenate-to-CoA conversion is operative in vivo. Another step in the biosynthetic pathway that may be rate limiting is the conversion of 4'-phosphopantetheine (4'-PP) to dephospho-CoA, a step catalyzed by 4'-phosphopantetheine adenylyl-transferase. In mammalian systems, this step may occur in the mitochondria or in the cytosol. The teleological significance of these two pathways remains to be established, particularly since mitochondria are capable of transporting CoA from the cytosol. Altered homeostasis of CoA has been observed in diverse disease states including starvation, diabetes, alcoholism, Reye syndrome (RS), medium-chain acyl CoA dehydrogenase deficiency, vitamin B12 deficiency, and certain tumors. Hormones, such as glucocorticoids, insulin, and glucagon, as well as drugs, such as clofibrate, also affect tissue CoA levels. It is not known whether the abnormal metabolism observed in these conditions is the result of altered CoA metabolism or whether CoA levels change in response to hormonal or nonhormonal perturbations brought about in these conditions.

CONCLUSION: In other words, a cause-effect relation remains to be elucidated. It is also not known whether the altered CoA metabolism (be it cause or result of abnormal metabolism) can be implicated in the manifestations of a disease.

PMID: 1746161