ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

January, 1993 Volume 2, No. 1

MANGANESE — Beware of Marginal Deficiencies

Over the course of modern medical history, very few reports of severe manganese deficiency have been recorded. Analysis of a variety of human tissues from numerous age groups has not indicated much variance for manganese (ppm/gm tissue) with life stage. Some scientists suggest that this consistency of manganese tissue concentration indicates adequate dietary intake coupled with strong homeostatic control. Others claim that this is a result of our inability to devise practical methods to assess manganese status. For example, it now appears that mitochondrial superoxide dismutase activity is a function of dietary manganese intake, but its usefulness in routine testing of nutritional status is limited by the cost of such testing.

Signs of manganese deficiency are poor reproductive performance, growth retardation, congenital malformation of offspring, abnormal formation of bones and cartilage, and impaired glucose tolerance.

Other conditions associated with a marginal manganese deficiency include ataxia, atherosclerosis, dizziness, hearing loss, hypercholesterolemia, muscle weakness, pancreatic damage, and tinnitus.

Manganese plays key roles as an activator of numerous enzymes, as well as being an element of the metalloenzymes, pyruvate kinase, and superoxide dismutase. As an enzymatic component or activator, manganese plays essential roles in protein, carbohydrate and fat metabolism; skeletal development; blood formation; sex hormone production; thyroxin production; milk and urea formation.

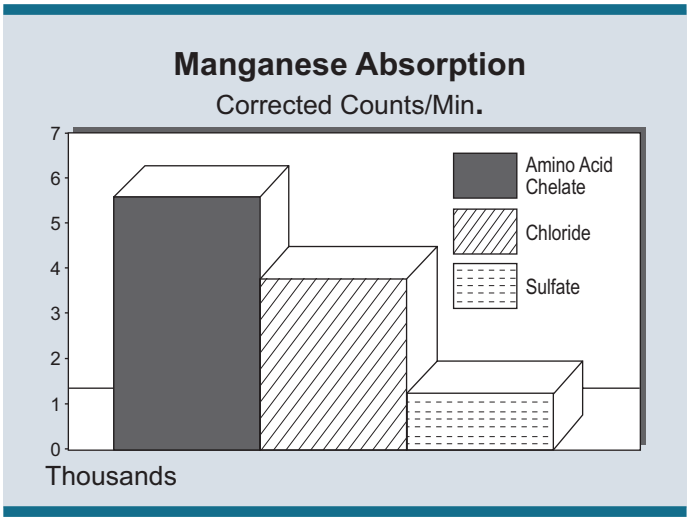
Although no US RDA has been established for manganese, the National Research Council has estimated that a safe and adequate daily dietary intake of manganese for adults should range between 2.0 and 5.0 mg per day.

Manganese Intake

Absorption/Retention/Tissue Concentration

Even though the National Research Council recommends dietary intake of up to 5 mg of manganese, the "Total Diet Study" conducted in the United States between 1982 and 1986 indicated the mean daily intake of manganese was only 2.7 mg for adult men and 2.2 mg for adult women. This problem of potential deficiency is even more accentuated when one realizes that most dietary manganese sources are very poorly absorbed – only in the range of 3 to 4% absorption. Of the absorbed portion, only that which is protein bound is actually carried into the blood.

Animal research has shown that manganese amino acid chelate is absorbed significantly better than inorganic forms, such as sulfates and chlorides.[1] As the chart on the



cover illustrates, up to 40% more manganese from manganese amino acid chelate is absorbed than from the chloride and over 300% more than from the sulfate. Furthermore, the absorption of Albion's amino acid chelate is not decreased by the typical dietary factors that hinder inorganic manganese forms. Factors like phosphorus, iron, fiber, and calcium supplements are all known to decrease the absorption of inorganic manganese supplements, but not the Albion manganese amino acid chelate.

In addition to having greater bioavailability, more of Albion's manganese amino acid chelate is retained for use in the body. Tissue retention studies have found manganese amino acid chelate to be retained 61% higher than the non-chelated manganese forms.[2] In isotope studies, in which tissue deposition of manganese from Albion's manganese amino acid chelate was compared to $MnCl_2$, the increase from the chelate averaged 82% more than the chloride. These comparisons are shown in Table 1[3].

1. *Garcia Aranda, JA, Wapnir, RA, Lifshitz, F. "In Vivo Intestinal Absorption of Manganese in the Rat," J Nutr, 113:2601-7, 1983.*
2. *Lee, DY, Johnson, PE. "Manganese Absorption and Excretion in Rats Fed Soy Protein and Casein Diets," Proc Biol Med, 190:211-216, 1989.*
3. *Ashmead, HD. "Comparative Intestinal Absorption and Subsequent Metabolism of Metal Amino Acid Chelates and Inorganic Metal Salts," in Subramanian KS, et al., eds., Biological Trace Element Research (Washington DC: ADA) 306, 1991.*

Table 1

Mean ^{54}Manganese Levels in Tissue (cc/m/gm)

Tissue	Albion Mn A A Chelate	$MnCl_2$	% Increase
Heart	107	36	197
Liver	106	52	104
Kidney	97	80	21
Spleen	397	190	109
Lung	56	54	4
Small Intestine	141	89	58
Muscle	28	22	27
Bone	266	112	138

Manganese and Thyroid Activity

Several clinical studies have shown a direct relationship between manganese status and thyroid activity. It has been shown that the Thyroid Stimulating Hormone (TSH) causes an increase in adenylate cyclase activity, which in turn, stimulates intracellular cyclic-AMP. It is the cyclic-AMP which then mediates the effect of the TSH within the cells and controls the release of the thyroid hormones (T-3 and T-4). A study involving TSH regulation of adenylate cyclase showed that basal adenylate cyclase activity was increased in the presence of manganese.[1] Aihara, et al., found there was a positive correlation between erythrocyte manganese concentrations and T-4 and T-3 levels.[2] The higher erythrocyte manganese concentrations were associated with higher plasma hormone levels. Nishida, et al., found evidence that TSH increases manganese transport to the thyroid gland.[3] Further evidence of the involvement of manganese in thyroid regulation comes from Cui and Dannies.[4] Their study concluded that Thyrotropin Releasing Hormone (TRH) stimulated the entry of manganese into the cells of the anterior pituitary, the site for TSH syntheses and release. Although the exact mechanism of action of manganese in thyroid function is not completely understood, current research indicates that it is a key player in the regulation of proper thyroid function.

Hypofunction of the thyroid results in a decrease in the activity of all tissues and glands, as well as a lower metabolic rate (rate of energy production). Individuals with lower thyroid activity have been seen to have a higher body fate composition and elevated cholesterol levels.

1. *Clark, OH and Gerend, PL. "Thyrotropin Regulation of Adenylate Cyclase Activity in Human Thyroid Neoplasms," Surgery, 97:539-45, 1985.*
2. *Aihara, K, et al., "Zinc Copper, Manganese, and Selenium Metabolism in Thyroid Disease," AM J Clin Nutr. 40:26-35, 1984.*

3. *Nishida, M, et al., "Alterations in Manganese and Iodide Contents in Human Thyroid Tumors: A Correlation Between the Contents of Essential Trace Minerals and the States of Malignancy," Clinica Chimica Acta, 187:181-88, 1990.*
4. *Cui, ZJ and Dannies, PS. "Thyrotropin Releasing Hormone Mediated Mn2+ Entry in Perifused Anterior Pituitary Cells," Biochemical Journal. 283:507-13, 1992.*

Manganese Metalosate®

Study Associates it With Decreases in Body Fat and Increases in Lean Muscle Mass

A Thyroid Effect?

Published research has reported that manganese supplementation in a manganese deficient diet has reduced fat deposition in the tissues.[1] Recent unpublished studies have shown that a patented dipeptide-like amino acid chelate of manganese from Albion may have beneficial effects on pituitary and thyroid activity. The thyroid gland, through the action of the thyroid hormones, has a significant effect on basal metabolic rate and the partitioning of energy through burning fat. As noted above, manganese plays a key role in thyroid hormone activity.

A recent study in laboratory animals demonstrated that manganese from Albion's manganese amino acid chelate accumulated at higher concentrations in the hypothalamus, pituitary, and thyroid glands than the inorganic manganese (see Table 2).[2] It is interesting to note that the tissue concentration of manganese changed in accordance to the flow of the overall thyroid axis – from hypothalamus to pituitary to thyroid gland.

Table 2

^{54}Manganese Radioactive Study

Manganese Amino Acid Chelate Versus Manganese Chloride

Post treatment results expressed as cc/min/mg/tissue				
	$MnCl_2$		Mn Amino Acid Chelate	
	1 Hour	2 Hours	1 Hour	2 Hours
Hypothalamus	25	25	50	25
Pituitary	100	100	125	150
Thyroid	0	12	25	50

As noted above, manganese deficiency appears to be linked to excess body fat in animals. With this in minds, Dr. David Atherton (U.K.) and Dr. Alain Bourdonnais (France) conducted a series of animal trials to test the effects of Albion's Manganese Metalosate® on body composition.[3] Manganese Metalosate® is an amino acid chelate of manganese produced by Albion Laboratories, Inc. that contains 10% elemental manganese. In five separate trials reported at an international conference by Drs. Atherton and Bourdonnais, the addition of Manganese Metalosate® to the diets of animals resulted in significant improvements in body composition, including higher lean muscle mass with lower body fat composition (6.5% increases in mass with a 6.0% loss in body fat). In other studies, Albion's manganese amino acid chelate was compared to manganese gluconate. It was found that there was 4% less fat in the animals that received Albion's Manganese Metalosates® compared to the manganese gluconate group and 8% less fat than the control group that received no supplemental manganese.[4]

Manganese appears to be a nutrient which is essential to control fat deposition in the muscle. Other research has demonstrated that both liver and bone fat are reduced with manganese supplements.[5] A manganese deficient diet has resulted in excessive fat deposition in pigs.[6,7] This may have been due in part to the essential role that manganese plays in the metabolism of fatty acids. In diets which are deficient in manganese, fatty acids are not synthesized from body tissue fat.[8] When fatty acid synthesis is impaired, dietary fat is stored as body fat rather than being used for energy.[9] In fact, a clinical sign of a manganese deficiency in pigs is increased fat deposition.[10]

1. *Underwood, EJ: "Trace Elements in Human and Animal Nutrition," (NY Academic Press) 181, 1977.*
2. *Ashmead, H and Graff, DJ: "Experiments Done on the Effect of Manganese on the T.R.A. Hormone and the Pituitary Gland,"*

Unpublished, 1987.
3. *Atherton, D. and Bourdonnais, A. "Manganese Metalosate®, and Effective Way of Improving Carcass Quality in Pigs," Albion Nutritional Seminar, February 1992.*
4. *Atherton, D: "A Nutritional Approach to Maximizing Carcass Leanness," in Ashmead, H.D. ed., The Roles of Amino Acid Chelates in Animal Nutrition. (Ridge Park: Noyes) 269, 1993.*
5. *Amdur, M.O., et al., "The Lipotropic Action of Manganese," J Biol Chem. 164:783, 1964.*
6. *Plumlee, M, et al., "The Effects of a Manganese Deficiency on the Growth, Development, and Reproduction of Swine," J Ani Sc. 14:996, 1954.*
7. *Plumlee, M, et al., "The Effects of a manganese Deficiency upon the Growth, Development, and Reproduction of Swine," J Ani Sci. 15:352, 1956.*
8. *Cotzias, G: "Manganese," in Comar, C and Bronner, F. Mineral Metabolism and Advanced Treatise. (New York, Academic Press), V2:411, 1962.*
9. *Guthrie, H: Introductory Nutrition (St. Louis, Times Mirror, Mosby College Publishing), 118, 1986.*
10. *Teague, H, et al. Nutrient Requirements of Swine (Washington, D.C., National Academy of Sciences) 1979.*

Manganese & Carbohydrate Metabolism

While animal studies suggest a human application, it should be emphasized that to date, no human clinical studies involving manganese amino acid chelate and fat deposition have been conducted. In a United States government publication, An Evaluation of Research in the United States on Human Nutrition, it was reported that there are certain dietary factors that cause some people to convert carbohydrates to fat at increased rates, instead of utilizing these carbohydrates for energy. Perhaps one of these factors is the amount of biologically available manganese in the diet.

It is known that in man, manganese activates the serum fat-clearing factor, lipoprotein lipase as well as operating as a co-factor in the synthesis of long-chain fatty acids. Furthermore, manganese activates several conversion reactions of the glycolytic pathway as well as the Krebs cycle in glucose oxidation. Both are essential for carbohydrate metabolism in man.[1]

A number of animal studies and human clinical responses have indicated a role for manganese in human carbohydrate metabolism.

1. *Williams, SR: Nutrition and Diet Therapy (St. Louis, C.V. Mosby College) 156, 1977.*

Albion Human Nutrition
100 Maple Park Blvd., Suite 110
St. Clair Shores, Michigan 48081 USA
[P] 586•774•9055 | [TF] 800•222•0733
[F] 586•774•8838
[e] info@AlbionMinerals.com