

The Nutritional Relationships of Manganese

David L. Watts, Ph.D., F.A.C.E.P.¹

Introduction

Manganese is distributed in tissues throughout the body. The highest concentrations are found in the liver, thyroid, pituitary, pancreas, kidneys, and bone. The total manganese content of a 70 kg man is approximately 12-20 milligrams. A daily requirement for manganese has not been established; however, it appears that a minimum intake of 2.5 to 7 milligrams per day meets human needs.¹

Functions of Manganese

Manganese is located largely in the mitochondria. It activates numerous enzymes — such as hydrolases, transferases, kinases, and decarboxylases — and is a constituent of some enzymes. One of the most well known manganese metalloenzyme is pyruvate carboxylase, which catalyzes the conversion of pyruvate to oxaloacetate.² Other enzymes include arginase, which is involved in the conversion of the amino acid arginine to urea, and mitochondrial superoxide dismutase (SOD). The structure and function of the mitochondria are therefore particularly affected by manganese status. Manganese activates enzymes associated with fatty acid metabolism and protein synthesis,³ and is involved in neurological function.

Manganese Regulation

Manganese is apparently absorbed throughout the small intestine. Its absorption can be adversely affected by other elements such as calcium, phosphorus, and soy protein.⁴ Even though vegetarian sources are high in manganese, a vegetarian diet does not necessarily improve manganese status. This is due to the high phytate content, which inhibits manganese absorption. Although tea is rich in manganese, due to the tannin content the amount present is virtually unavailable. Meat,

which is actually a very low source, enhances the bioavailability of manganese from the diet. Human studies revealed a more positive balance of manganese in those subjects receiving a high protein diet compared to those on a low protein diet.⁵ The liver regulates manganese via excretion in the bile; however, if the liver excretory route is blocked or if overloading occurs, pancreatic excretion increases. Tissue manganese levels are directly related to availability in the diet. Alcohol increases the hepatic manganese level and apparently doubles its absorption.⁶

Hormonal Effects Upon Manganese

Manganese is required for normal thyroid function and is involved in the formation of thyroxine.⁷ Tissue mineral analysis (TMA) studies have revealed low manganese levels in hypothyroid patients. Due to the antagonistic effect of insulin, parathyroid hormone (PTH), and estrogen on thyroid function, absorption or utilization of manganese may be impaired when levels of these hormones are elevated.^{8,9}

The adrenal hormones are known to affect the tissue distribution of manganese as well as to alter its metabolism.¹⁰

Manganese Deficiency

Manganese deficiencies have been studied in animals, and the symptoms vary according to species and degree of deficiency. Many similarities exist among species, including skeletal abnormalities, postural defects, impaired growth, impaired reproductive function, and disturbances in lipid and carbohydrate metabolism.^{11,12} A common genetic condition caused by manganese deficiency produces a disturbance of the otolith in the inner ear during gestation.

Skeletal abnormalities include chondrodystrophy, or retarded bone growth with bowing. Perosis or "slipped tendon" is a widely recognized condition in chickens and ducks.¹³

1. Trace Elements, Inc., P.O. Box 514, Addison, Texas 75001.

Reproductive function in manganese deficient patients is characterized by defective ovulation, ovarian and testicular degeneration, and increased infant mortality.¹⁴

Manganese is involved in cholesterol synthesis; therefore, a deficiency can be related to a lack of this precursor for normal hormonal production. Manganese also shows a synergistic relationship with choline. A deficiency of either or both may lead to abnormal mitochondrial and cell membrane integrity.¹⁵ The liver mitochondria isolated from manganese deficient mice revealed abnormalities of the cristae and a lowered oxidation rate.¹⁶

Disturbances in carbohydrate metabolism is due to abnormal glycosyltransferase activity. Abnormality of the pancreas resulting in poor glucose utilization suggests that manganese may be involved with insulin formation or activity.¹⁷

Human manganese deficiency has been described in which manganese was inadvertently omitted from a purified diet. The symptoms included hypocholesterolemia, decreased triglycerides and phospholipids, weight loss, transient dermatitis, and intermittent nausea. The subject's hair colour changed from black to red.¹⁸ The purpose of the diet was to restrict vitamin K in order to study the prolongation of the prothrombin time and to correct it with vitamin K. However, when the manganese deficiency was discovered and replaced in the diet, the prothrombin time was corrected. Since prothrombin is a glycoprotein and manganese activates transferases, it is possible that manganese may be required for prothrombin synthesis.

Another study of manganese deficiency in a human volunteer has been reported.¹⁹ It was estimated that a 66% reduction of the body pool of manganese was reached. The subject developed a rash on the upper torso, groin, and thighs diagnosed as Malaria Crystallina or "prickly heat". Serum calcium and phosphorus decreased as well as alkaline phosphatase. Serum cholesterol and HDL also decreased.

Other abnormalities thought to be related to manganese deficiency have been reported. Epileptics were found to have lowered blood concentrations of manganese.²⁰ A deficiency of

manganese could be related to inborn errors of metabolism such as maple syrup disease and PKU.²¹ Sufferers of adult Down's syndrome who frequently develop secondary hip joint dislocations, and epiphysitis of the femoral head are suspected to have a deficiency of manganese. Other manganese related conditions include intrauterine malformations and osteoporosis.

Straus and Saltman reported an interesting case of manganese deficiency in a well-known professional basketball player who suffered from frequent broken bones with slow healing and joint instability. They found no detectable manganese in his serum, which was attributed to his very limited vegetarian diet. Supplementation over several months resulted in improved bone healing that allowed his return to professional athletics. They also reported similar findings in orthopedic patients with impaired bone healing.²²

Since manganese is involved in the biosynthesis of mucopolysaccharides, a deficiency may play a role in cartilaginous and collagen disorders, such as Osgood Schlatters, Perthes disease, and lupus. Hydralazine, a drug once used extensively in the treatment of hypertension, can produce a syndrome identical to lupus erythematosus. Patients with drug-induced and non-drug induced lupus have been reported to benefit from manganese administration.²³ Since manganese is required for the conversion of ammonium ions to urea, a deficiency may lead to a ammonium toxicity.

Excessive intake of those nutrients that are considered antagonistic to manganese may contribute to a deficiency. Figures 1 and 2 show the vitamins and minerals that are antagonistic to manganese.

A deficiency of the synergistic factors may also lead to poor manganese status. Nutrients considered synergistic include the minerals potassium, zinc, magnesium, iron, phosphorus, and the vitamins A, E, B₁, B₃, B₅, and B₆.

Manganese Toxicity

Reports of manganese toxicity due to oral intake are relatively rare. Manganese toxicity is usually caused by chronic exposure of workers in iron and steel factories, manganese ore mining, welding, chemical

plants, dry cell battery, and fuel oil industry. The first reports of manganese toxicity were made by Couper in 1837.²⁴ He described a condition similar to paralysis agitans in pyrolusite mill workers. Greater attention to manganese toxicity developed in the 1930's and 40's following several reports of similar conditions in miners.

Symptoms of manganese toxicity have been described in three grades. Mild toxicity produces manganese psychosis and includes the following symptoms: asthenia, anorexia, insomnia, muscular pains, mental excitement, hallucinations, unaccountable laughter, impaired memory, and compulsive actions. Moderate toxicity symptoms include speech disorders, clumsy movements, abnormal gait, poor balance, hyperreflexia in the lower limbs, and fine tremors. Severe signs include, rigidity, spasmodic laughter, and mask-like face-all similar to symptoms of Parkinson's disease.²⁵ The mechanism of manganese neurotoxicity appears to be due to neuronal degeneration in various areas of the brain and abnormalities of neurotransmitters.

Factors that may increase the susceptibility to manganese toxicity include iron deficiency, alcoholism, chronic infections, and decreased excretion.

Reduction in manganese toxicity, other than reduced exposure, may be aided by supplementing the antagonistic nutrients shown in figures 1 and 2. Excessive manganese levels may also contribute to a deficiency or may increase the requirement of those nutrients.

Manganese and Tissue Mineral Analysis (TMA)

In review, the following changes in hair manganese concentration in various disease states have been reported. Lowered levels have been found in Down's syndrome, epilepsy, and schizophrenia. Elevated levels have been associated with multiple sclerosis, learning disabilities; and Parkinson's disease.^{26 27}

Manganese deficiency appears to be as prevalent as iron deficiency. In TMA testing, Trace Elements has commonly found low manganese levels in the hair of patients with hypoglycemia, hypothyroidism, adrenal insufficiency, and diabetes.

Within the past few years we are finding

a greater incidence of elevated manganese with no apparent associated symptomatology. Since many of these findings are in individuals living in densely populated cities such as New York and Boston, it is speculated that the source may be from the burning of fuel oils. As mentioned previously, manganese compounds are substituting for lead as an anti-knock additive in unleaded gasoline. Excess manganese is also often seen in conjunction with iron toxicity. In this case the manganese is not a toxin per se, but is a secondary elevation due to excess iron retention. In this case the elevation may be due to the body's attempt to decrease the effects of iron toxicity by increasing manganese retention, or the excess iron may be displacing manganese from storage tissues.

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Figure 1

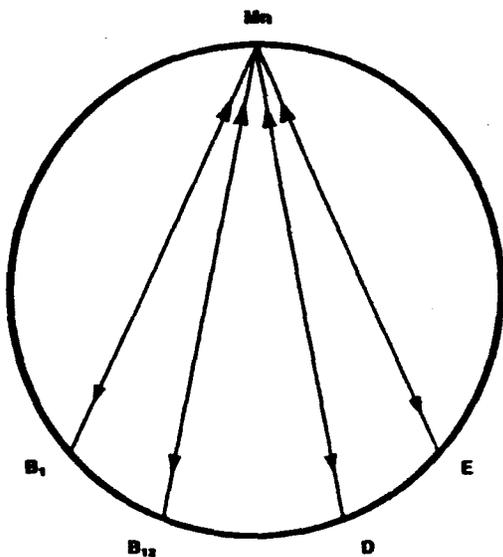


Figure 2

