CHAPTER 3

Manganese

The high copper level of many schizophrenics can be reduced by dietary intake of zinc and manganese. Manganese is similar to zinc in the way it increases urinary copper excretion; a combination of zinc and manganese is more effective than either alone. High-copper schizophrenics are improved by the zinc-manganese combination in Ziman drops or tablets.

Manganese is one of the essential trace metals, a necessary dietary constituent obtained from nuts, seeds, and whole-grain cereals. It is necessary for bone growth and development, reproduction, lipid metabolism and the moderation of nervous irritability. Manganese is also important in the building and breakdown cycles of protein and nucleic acid (the chief carrier of genetic information). As an activator of such enzymes as arginase (required for the formation of urea) and some peptidases (which cause the hydrolysis of proteins in the intestine), manganese may also contribute to a mother's love and instinctive maternal protection of her child. (Through certain enzymes, manganese affects the glandular secretions underlying maternal instinct.) Manganese is important in the formation of thyroxin, the principle of the thyroid gland.

Required Intake

Every day a healthy person excretes approximately 4 mg of manganese, this amount is then needed in the diet for replacement of the lost manganese.

Adequate intake is required for the lipid and glucose metabolism and oxidative phosphorylation (among other Intrinsic biochemical processes). On normal lipid metabolism manganese has a beneficial effect, particularly in cases of atherosclerosis.

Manganese Deficiency

Analysis of hair samples has indicated the manganese deficiency may be common among older males. Manganese deficiency may be a cause of atherosclerosis, although no studies have clearly demonstrated a true deficiency of this trace metal in man. Similarly, manganese deficiency is suspected in diabetes. A study by L. G. Kosenko in 1964 implicated manganese deficiency *after* an examination of 122 diabetics from fifteen to eighty-one years of age. Dr. Kosenko found that the manganese content of whole ashed blood was approximately half that of normal control subjects. In 1968 G. J. Everrson and R. E. Shrader reported that manganese deficiency can impair the glucose metabolism so as to lower glucose tolerance (the ability to remove excess sugar from the blood). The deficiency may produce abnormalities in the pancreatic secretion of insulin, the agent which utilizes excess sugar. Thus, a diabetic condition may result.

The enzymes which manganese activates are also necessary for the utilization of vitamin C, choline and other B vitamins (biotin and thiamin). Without the ability to use choline or deanol properly, the body underproduces, acetylcholine, a neurotransmitter in the brain. In a body deficient in acetylcholine and properly utilized B vitamins, various conditions may result, among them myasthenia gravis (grave loss of muscle strength). This condition may respond to manganese if doses are given at each meal, in addition to a high-protein diet, vitamin E and all the B vitamins. All these nutrients aid in the transmission of impulses between nerve and muscle.

Poisoning

Manganese overloading or poisoning has been reported only in industries where manganese-containing dust may be inhaled. In mining operations in Chile and in the dry battery industry, where workers are exposed to manganese oxide dust, cases of manganese poisoning have been recorded. Symptoms are similar to those of Parkinsonism and include

tremor, muscular rigidity, irritability and impotency. Symptoms of chronic manganese poisoning in these industries may also resemble those of schizophrenia. A drug used in treating Parkinson's disease, I-dopa (dihydroxyphenylalanine) has been found useful in treating manganese overload.

Metabolism

Manganese metabolism is somewhat similar to that of iron. Manganese is absorbed slowly from the small intestine, and the unneeded portion excreted. The absorbed portion is transported through the blood by the protein transmanganin; the manganese quickly leaves the bloodstream and is stored mainly in the kidney. Some is excreted in the urine, most into the bile.

Manganese and Schizophrenia

Manganese chloride was first tested and found effective in treating schizophrenia by Dr. Reiter of Denmark. This finding was confirmed in 1929 by Dr. W. M. English, superintendent of a hospital in Brockville, Ontario. A later study by Hoskins, however, found manganese dioxide ineffective and since then, little attention has focused on the possibility of its therapeutic effects. The finding of high copper levels in the schizophrenia has also been ignored by the medical establishment. Furthermore, there is little dispute over the biochemical fact that zinc and manganese may replace copper and so reduce high copper levels. In evaluating the relative merits of the trace metals, then, we might categorize manganese as one of the "desirables" and copper as one of the "undesirables." This applies particularly to the schizophrenic.

In oral doses, manganese is never harmful, although in patients older than forty it has occasionally elevated blood pressure. The elevated pressure returns to normal when zinc alone is used.

Soil Depletion

Manganese is removed from the soil by current farming and food-processing practices. Soil erosion, leaching and soil exhaustion deplete the amount of manganese available to vegetables. Even normally manganese-rich foods are subject to wife variations. This depletion of the soil may be unsuspected since the foliage of plants may be lush without manganese. This is typified by the growth of lettuce. If lime is applied to solid clay, leafy vegetables grown in the more alkaline soil that is produced will contain much less manganese - simply because of the application of the lime. This finding points up the real need for scientific farming wherein the fertilizer will contain all of the trace elements in which the soil is deficient.

TABLE 3.1 Selected foodstuffs with appreciable amounts of manganese *Mg per 100gm edible parts*

TABLE 3.1

Selected foodstuffs with appreciable amounts of manganese

MG *per 100* gm *edible parts*

	Cereals		
Corn germ	10	Oats	3.0
Wheat bran	14	Corn flakes	0.04
Rice bran	26	White bread	0.25
Oat bran	10	Rice Krispies	1.0
Corn	1.0	Oatmeal	0.03-3.0
Wheat	5.0	Buckwheat	1.3
Rice	2.0		
	Nuts		
Walnuts	15	Pecans	1.5
Peanuts	1.9	Chestnuts	3.7
	Spices		
Cloves	30.0	Ginger	17.6
Cardamom	27.0		
	Fruits		
Strawberries	0.33	Prunes	0.08
Raspberries	0.12	Pineapple	0.1-3.0
Bananas	0.2-0.8	Cherries	0.03-0.78
Blueberries	0.15-1.9	Watermelon	0.03
Apples	0.20		
	Vegetables		

Lettuce	0.7-0.80	Onions	0.52-1.0
Spinach	0.2-15.0	Green beans	0.2-2.0
Peas	0.11	Dandelion greens	0.30
Lima beans	0.5-1.0	Carrots	0.06-0.6
Parsley	0.90-8.5		
	Proteins		
Meat	0.03	White	0.01
Whole egg	0.05	Sea fish	0.02
Shrimp	0.04	Fresh-water fish	0.06
Liver	0.12-0.53	Yolk	0.10
Clams	0.25	Snails	1.6
	Miscellaneous		
Yeast	0.53-0.90	Macaroni	0.5
Spaghetti	0.54	Coffee beans	2.0
Tea leaves	5.71	Egg noodles	0.78

Sources: D. Schlettwein-Gsell and S. IMommsen-Straub., *International Journal* of *Vitamin and Nutrition Research* 41 :268, 1971, and A. Gormican, *Journal* of *the American Dietetic Association* 56:397, 1970

Leafy vegetables and grains constitute our main sources of dietary manganese. The more alkaline the soil, the less manganese there will be in the leaves. This accounts for the variable range of manganese content. Liming of the soil increases foliage but decreases the manganese content. The germ or bran of the grain contains most manganese, but this is lost in the milling process. Note the drastic losses of manganese in corn: corn germ (10), corn (1) and corn flakes (0.04). Similarly drastic losses in manganese occur in the processing of wheat. Except for the organ meats (such as liver) protein is not a good source of manganese. Fish is low except for shellfish such as clams and snails. The daily requirement of man for manganese is about 4 mg

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Manganese and the Brain

Manganese stimulates adenylate cyclase activity in brain and other tissues of the body as demonstrated in numerous experiments. In one study the striate cortex of rats was tested as a focus of manganese-catalyzed enzyme activity in this region of the brain. This study has great importance because cyclic-AMP plays a regulatory role in the action of several brain neurotransmitters. Thus, it was concluded that manganese has an important role in brain function.

In other studies, schizophrenic patients developed tardive dyskinesika, a Parkinson-like disease while on large doses of anti-schizophrenic medicines such as phenothiazine and butyrophenones and the newer drugs as well. Hair analysis done on patients who had ingested these drugs daily for several years revealed a manganese deficiency according to Dr. R. Kunin. High doses of a manganese chelate produced improvement in fourteen out of fifteen cases tested. Normally, high manganese concentrations are found in human basal ganglia where the ion is believed somehow to stimulate acetylcholine storage or activity. Manganese, acetylcholine and ATP are stored together as a complex in test tube experiments.

Our present knowledge of manganese function in human and animal brains cannot explain why a deficiency or intoxication of manganese results in Parkinson-like diseases.

Manganese and Blood Clotting

Manganese deficiency affects both man and animals. For example, it reduces

the blood clotting response to extra vitamin K in chickens. One human patient with low clotting protein levels did not become normal until manganese supplements were given in addition to vitamin K. Manganese catalyzes the aggregation of human platelets in vitro. The Manganese ion has an essential role in blood clotting and functions somewhere in the chain prior to direct vitamin K action.

Manganese and the Reproductive Function

Manganese-deficient female rats and chickens have defective ovulation and their offspring increased mortality. Deficient male rats and rabbits have a

loss of libido, lack of semen and seminal tubule degeneration. The site of manganese action in the reproductive system is as yet unknown.

Manganese and Other Nutrients

The absorption of iron and manganese is inversely related. High iron in the diet inhibits manganese absorption, and, conversely, high manganese intake reduced iron absorption in several animal species, including man. This relationship also holds for calcium and zinc.

Calcium affects absorption and retention of manganese. In birds, high dietary levels of calcium phosphate aggravates manganese deficiency. In addition, manganese tested in the test tube at levels of 0,5 to 4.0 milli-molor concentration inhibits calcium-dependent histamine release. The inhibitory effect, however, is reversed by increased ion concentration. We know that both histadelic and histapenic patients do better if they have a daily source of zinc and manganese.

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