Iron—The Most Deadly Metal

Jym Moon, PhD

George Ohsawa Macrobiotic Foundation Chico, California Other books from the publisher include: *Acid and Alkaline; Basic Macrobiotic Cooking; Essential Ohsawa; Macrobiotics: An Invitation to Health and Happiness; Philosophy of Oriental Medicine; #7 Diet*; and *Zen Macrobiotics.* Contact the publisher at the address below for a complete list of available titles.

Cover design by Carl Campbell Text layout and design by Carl Ferré

First Edition 2008

© copyright 2008 by George Ohsawa Macrobiotic Foundation PO Box 3998, Chico, California 95927-3998 530-566-9765; fax 530-566-9768; gomf@earthlink.net

ISBN 978-0-918860-60-6

Foreword

For over seventy years, the North American public, as well as obdurate bureaucrats, have been enamored with the Popeye-the-Sailor myth, namely, that ingested iron can somehow overcome fatigue and confer strength. During the same time period, however, numerous scientists and medical practitioners have learned to fear rather than praise iron. It is now overwhelmingly apparent that iron loading is a serious risk factor for scores of diseases—an array of cardiovascular disorders; endocrine problems such as diabetes and impotence; neurological ills such as Alzheimer's and Parkinson's; arthritis and osteoporosis; cancers of lung, colon, liver, and skin; nearly all bacterial and fungal infections; and shortened lifespan.

Unfortunately, clever marketing and bureaucratic intransigence have trumped science. It is extremely difficult, if not impossible, for the consumer to select processed foods that have not been deliberately adulterated with troublesome quantities of iron. Finally, a professionally trained toxicologist, Dr. Jym Moon, has assumed the formidable task of dispelling the iron illusion for the public and for the inflexible bureaucrats. Dr. Moon's narrative style is highly appropriate for the intended readers. The book's arguments are strongly reinforced with numerous references to published works of leaders in the field. Thus Dr. Moon has been able to exclude the use of dubious anecdotal evidence.

Iron—The Most Deadly Metal is a timely, much needed addition for the working desks of leaders in health policy, wellness, and nutrition. Influential persons in such health advocacy groups as arthritis, cancer, diabetes, heart, and neurodegenerative disorders will want copies. The book also will be valuable for officials at all levels of the USDA, FDA, HHS, CDC, NIH, and related units.

Over the long run, scientists generally are optimistic that their work actually can dispel fallacious illusions. Hopefully, Dr. Moon's book will provide the spark that will catalyze the demolishment of the iron myth.

> – E.D. Weinberg, PhD Indiana University Bloomington, IN

Contents

Author's Note	3
Foreword	5
Chapter 1: A Failed Experiment	13
Iron Is an Essential Trace Element, but Not a Safe One	13
Human Iron Balance	14
Iron is a Cumulative Toxin	15
Iron Fortification of Food—A Failed Experiment	16
The Food and Nutrition Board	17
The Biochemical Basis of Iron Toxicity	19
Iron Excess Worsens Chronic Illnesses	19
Chapter 2: A Brief History	22
Introduction	22
1929: From Popeye to Geritol®	23
1941: Iron Adulteration of Food	24
1969: The FDA Increases Iron in Food	24
1970 – 2007: Beyond Geritol®	26
Hereditary Iron Overload	26
Transfusion Siderosis	27
Hemosiderosis Among the Bantus	28
1981: Iron Misregulation and Ischemic Heart Disease	28
1982: The Hemochromatosis Research Foundation	29
1984: Iron Can Redox Cycle in Biological Systems	29
1988: First International Conference on Hemochromatosis	30
1992: Iron Toxicology Becomes Firmly Established	30

1992–2007: Continuing Contributions to Iron Toxicology	30
References	33
References	55
Chapter 3: How Much Iron?	35
Level of Fortification	35
Labels are Misleading	36
Choose Your Poison	39
Heme Iron and Human Disease	39
Iron, Lung Cancer, and Vitamin C	40
Genetically Modified Iron-Accumulating Grains	40
Women of Childbearing Age	41
Acute Iron Poisoning	42
How Much Dietary Iron Do Most Adults Need?	43
Infant Iron Nutrition	43
How Much Iron Does an Infant Need?	44
Iron Withholding as a Defense Strategy	45
Lactoferrin and Xanthine Oxidase	46
Sweden Terminated Iron Fortification	47
References	48
Chapter 4: Maintaining Body Iron Balance	50
Iron Distribution in Humans	50
There is No Physiological Mechanism for Iron Excretion	52
Females of Childbearing Age	53
Iron Absorption and Storage	53
Hepcidin	54
Transferrin and Transferrin Receptors	55
Lactoferrin	56
Regulation of Cellular Iron Metabolism	57
How Can You Determine Your Iron Status?	57
What To Do For Abnormal Blood Iron	59
A Note on Zeolite	60
References	60

Contents	9
Chapter 5: The 2001 DRIs: Iron Hazard Identification	62
Pitifully Inadequate	62
The Debate	63
The Panel on Micronutrients	64
Iron Hazard Identification	64
Missing Information	65
Why Did the 2001 DRIs Not Discuss Iron Neurotoxicity?	66
Examples of Iron Accumulation in Neurodegenerative Diseases	68
High Iron Levels and Neurodegeneration	69
Iron Chelation Therapy	69
Conclusions	70
References	70
Chapter 6: Carcinogenicity of Iron Compounds	81
Introduction	81
Carcinogenicity of Iron in the 2001 DRIs	82
Iron is a Carcinogen	83
Follow the Evidence	83
Testing the Hypothesis	84
Inhalation Toxicology	86
Iron Dextran	87
Iron Gluconate	88
Iron Dextran in Developing Countries	89
Inhaled Iron	89
Asbestos Carcinogenicity	90
Iron in Cigarette Smoke and Fly Ash	93
Iron and Scrotal Cancer	94
Increased Liver Iron: Hepatocellular Carcinoma	95
Dietary Iron Overload	96
Iron is a Co-carcinogen with Hepatitis B and C Viral Infections	97
Hepatic Iron Overload and Alcoholic Liver Disease	99
Iron Overload and Aflatoxins	101
High Iron Stores Sensitize to Ionizing Radiation	101
Iron Increases the Damaging Effects of Ionizing Radiation	102
Caged-Iron Chelators in Sunscreens and Cosmetics	103

Lactoferrin or Ovotransferrin in Sunscreens and Cosmetics	104
Increased Iron Stores are Associated with Breast Cancer	104
Epidemiology Regarding Iron and Breast Cancer	
HHE Gene Mutations and Breast Cancer	106
Oxidative Stress and Breast Cancer	107
Increased Levels of Serum Ferritin in Breast Cancer	107
High Ferritin Concentrations and Recurrence of Breast Cancer	108
Elevated Iron in Benign Breast Tissue	109
Abnormal Ferritin-Bearing Lymphocytes	109
Iron and Estrogens	109
Iron and Colon Cancer	111
Patients with Colorectal Cancer	111
Iron Deficiency Anemia is Common in Colon Cancer	112
Heme Iron and Colon Cancer	113
Experimental Studies	116
Cancer Cells Require More Iron than Normal Cells	117
Transferrin Receptors	118
Applications of Increased Transferrin Receptors	119
Lactoferrin	119
Cancer-Associated Anemia	120
Conclusions	121
References	121
Chapter 7: Additional Iron-Deposition Diseases	147
Introduction	147
Hereditary Hemochromatosis	148
Cardiovascular Diseases	148
Iron Deposits in Atherosclerotic Lesions	149
Iron is Directly Cardiotoxic	150
Epidemiology	151
Books and Articles	153
Ferritin Light Chain	153
Excess Iron is Characteristic of Type 2 Diabetes	153
Iron Overload in Laboratory Animals Results in Diabetes	154

Contents	11
Type 2 Diabetes in HHC and Thalassemia	154
Elevated Serum Ferritin in Type 2 Diabetes	154
Iron and Arthritis	155
Iron Overload Causes Osteoporosis	156
Stroke and Traumatic Brain Injury	156
Elevated Serum Ferritin is a Risk Factor for Stroke	156
Increased Body Iron Burden in Traumatic Brain Injury	157
What is the Role of Iron in Hearing Loss?	158
Iron/Aminoglycoside Complex Causes Hearing Loss	159
Superficial Siderosis of the Brain Results in Hearing Loss	159
Iron, the Kidneys, and Chronic Kidney Disease	160
Iron/Aminoglycoside Complex Induces Kidney Damage	160
Iron Excess in Chronic Kidney Disease	160
Iron in Ocular Pathology	161
Thalassemia: Osteoporosis and Heart Disease	161
Iron Effects on the Pituitary Gland and Reproductive Organs	162
Iron Deposited in the Pituitary Gland	162
Sperm Damage Due to Iron Overload: B-Thalassaemia	162
Sperm Damage Due to Iron Overload: Animal Studies	163
Iron and Porphyria Cutanea Tarda (PCT)	163
Iron and Sudden Infant Death Syndrome	164
A Note of Caution to Endurance Athletes	165
References	166
Chapter 8: The Best Defense	172
Introduction	172
The Chemical Nature of Dietary Iron	172
Iron in Unfortified Foods is Chelated	172
Heme iron	172
Organic Iron	172
Inorganic iron	172
Dietary Antioxidants that Prevent Iron Overabsorption	175
Lactoferrin, Ovotransferrin, and Phytate	175
Lactoferrin	176
Phytate	178

Other Dietary Antioxidants	179
Vitamin E	179
Polyphenols	179
Quercetin	180
Vitamin C	181
De-Ironing	181
Antioxidant Enzymes	182
Glutathione Peroxidase / Selenium	182
Superoxide Dismutase (SOD)	183
Sulfur-containing Antioxidants	183
Final Remarks	183
References	184
Bibliography	187
Index	231

Chapter 1

A Failed Experiment

Iron Is an Essential Trace Element, but Not a Safe One

Iron is an essential trace element with many important functions in human physiology. In North America hundreds of thousands of people, predominantly women during menstruation, suffer from "iron deficiency anemia". Although not usually fatal, iron deficiency anemia is reputed to be one of the leading causes of sickness and debility among North American pre-menopausal women.

Iron was one of the first essential trace metals discovered. It has long been known that iron is a critical element for carrying oxygen in the blood. It is the central metal in the oxygen carrying heme complex. Oxygen attaches to heme iron and is transported in this form to various body tissues where it is released to support oxidative metabolism. For this reason, a lack of heme iron results in depressed tissue oxygenation, causing the condition of "iron deficiency anemia."

Because iron deficiency anemia is so common in the target population (menstruating women), public health officials have promoted the addition of iron to many of the most commonly consumed foods, i.e., nutrition supplements, flour, breads, pastas, and breakfast cereals. Despite this practice, iron deficiency anemia remains prevalent in the people who are supposed to be helped by the fortification programs.

In addition to its important function in carrying oxygen, iron

is a critical element in numerous enzymes, where it promotes normal metabolism. Iron is also important in the iron-sulfur clusters that facilitate transport of electrons in mitochondria. However, iron deficiency is not known to affect levels of iron-sulfur clusters or enzymes, unless the deficiency is very severe.

Although essential to life, iron is a very toxic metal. Most people are familiar with the highly publicized toxic metals such as lead, mercury, cadmium, manganese, aluminum, and arsenic. However few people know that iron is responsible for a great deal more sickness and death than all of these other toxic metals combined! We have been mesmerized into thinking that iron is somehow different from other metals, simply because it is essential.

Human Iron Balance

The Recommended Dietary Allowance (RDA) for iron for women from 19 years to 50 years is 18 mg/day; for pregnant women it is 27 mg/day, and during lactation, 10 mg/day. The RDA for all other adults is 8 mg/day. The Tolerable Upper Intake Level (UL) for dietary iron is 45 mg/day.

According to the Food and Nutrition Board, one half of ingested iron comes from fortified foods, although this may be an underestimate. Some cereals contain 24 mg iron per 1-cup serving. Most all grain products have varying amounts of iron added—this means virtually all flour, all pastas, all bread, all cereals. Iron supplements commonly sold over the counter contain from 15 mg to around 60 mg iron according to the label-recommended daily intake. It is easy to see how perhaps millions of people in North America are daily consuming more than the UL for iron.

Why are companies allowed to fortify foods with more than the Dietary Reference Intakes (DRIs) in a single serving? What controls are in effect to regulate the amount of iron delivered in food or supplements? Do companies that fortify foods also analyze the food after fortification to determine if the proper amount of iron has been added? Studies of iron balance in humans have demonstrated that we ordinarily absorb around 15% of the iron that we consume. A person consuming a daily diet containing approximately 15 mg of iron will absorb 1-2 mg. Similarly, approximately 1-2 mg of iron are excreted each day. Children are reported to absorb less iron than adults—around 10%. Pregnant women absorb more—around 17%.

Although only a small percentage of the iron that we consume is absorbed, many factors affect iron absorption. For instance, heme iron is very efficiently absorbed. High heme iron consumption has been correlated with the development of breast cancer. Also, iron absorption can be increased considerably when it is held in the iron 2+ form as it is in the supplements that have combined iron with vitamin C. Iron/vitamin C supplements containing far more than the daily UL for iron are freely sold in spite of their clear danger to human health. Vitron-C[®], for instance, contains around 60 mg iron in a single pill as the recommended daily intake. These supplements are very likely the most dangerous "nutritional" supplements ever conceived. Beware!

Iron is a Cumulative Toxin

The inability to excrete iron is the primary problem—we can excrete only around 1.2 mg per day no matter how much we absorb. Once iron has been absorbed in excess of the body's need, it is very difficult to remove it. Much of the excess will be stored in the liver in ferritin. When ferritin is saturated, hemosiderin is released into the liver and can lead to all of the damaging effects of iron to liver cells.

The iron that we consume that is in excess of the amount we absorb is carried through the intestines and excreted in the feces. This iron can be very dangerous since it can exist in free form and generate oxygen radicals resulting in intestinal damage and colon cancer. Colon cancer has been induced in laboratory animals given large excesses of iron. Certain food factors can prevent this kind of damage—in particular phyates that are abundant in plant food.

Iron Fortification of Food

Iron is currently added to most all grain products, including many found in Natural Food stores. In the 1990s, the U.S. Food and Nutrition Board, Institute of Medicine, considered the controversy over iron fortification of food. A number of nutritionists desired to increase the amount of iron added to grain products because "iron-deficiency anemia" was still prevalent in spite of the iron fortification program that had been initiated in the early 1940s.

It was clear even then that the iron-fortification program had failed. The purpose of iron fortification was to eliminate or at least control "iron deficiency anemia" which was prevalent among premenopausal women. Unfortunately, the addition of iron to food was unsuccessful. "Iron deficiency anemia" was still endemic among pre-menopausal women in 1990. Instead of acknowledging that the food iron-fortification program had failed, some members of the Food and Nutrition Board desired to increase the amount of iron added to food.

The simple fact is that "iron deficiency anemia" is not a nutritional deficiency disease. There are dozens of very diverse factors that can cause the conditions generally referred to as "iron deficiency anemia". Chronic "iron deficiency anemia," no matter what its origin may be, is a medical problem, not a nutritional problem.

Several iron toxicologists expressed their opinions to the Food and Nutrition Board that iron should be treated like all other metals that accumulate with age in the human body. These specialists suggested that we should minimize iron intake, except under conditions that require additional iron. Otherwise iron can do serious damage to any and every tissue of the human body. The comments of several of these experts are given here:

 Randall B. Lauffer, PhD, Harvard Medical School warned the Food and Nutrition Board that his investigations indicated that iron excess may be a primary cause of coronary artery disease. Dr. Lauffer is editor of the first book on iron toxicology, *Iron and Human Disease* (CRC Press, 1992).

- 2. Dr. J.L. Sullivan, MD, Department of Pathology, University of Florida College of Medicine, provided direct evidence of iron deposits in heart tissue, and showed that stored iron levels are a better predictor of heart disease than is blood cholesterol.
- 3. E.D. Weinberg, PhD, Indiana University warned that there is an association between iron and hepatocellular carcinoma. He pointed out that iron has been demonstrated to be carcinogenic in laboratory animals, and is known to cause hepatocellular carcinoma in humans.
- 4. Dr. William Crosby, Director of Hematology at the Chapman Cancer Center in Joplin, Missouri, argued that the Delaney Amendment of 1958 specifically forbids the addition of any substance to food that induces cancer in animals. He suggested that food fortification with iron should be terminated because iron has been shown to cause cancer in both laboratory animals and humans.
- 5. Baruch S. Blumberg, MD, PhD, Nobel Laureate in Medicine, has spent many years studying the relationship between the hepatitis B virus and liver iron. He warned that high liver iron stores feed the hepatitis B virus, and that this may explain the high incidence of liver cancer found among people infected with the hepatitis B virus.

The Food and Nutrition Board

Since "iron-deficiency anemia" among pre-menopausal women has not been controlled by the food fortification program, and since fatal illnesses due to iron overload are well documented, it seems unreasonable to continue the iron fortification of food. However, the Food and Nutrition Board basically ignored information regarding iron's toxicity, and all grains marketed in North America continue to be "fortified" with iron.

The Food and Nutrition Board, Institute of Medicine, is directly responsible for the food fortification program, and has issued two major statements regarding iron fortification of food.

- Iron Deficiency Anemia: Recommended Guidelines for the Prevention, Detection, and Management Among U.S. Children and Women of Childbearing Age. Committee on the Prevention, Detection, and Management of Iron Deficiency Anemia Among U.S. Children and Women of Childbearing Age. Robert Earl and Catherine E. Woteki, Editors. National Academy Press, Washington, D.C., 1993.
- Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. National Academy Press, Washington, D.C., 2001.

The most dangerous feature of iron is that it is attracted to, and deposits in, damaged tissue.

In the *Dietary Reference Intakes* (DRIs 2001), the Food and Nutrition Board acknowledged an increased risk for hepatocellular carcinoma in individuals with hereditary hemochromatosis, and reviewed some of the evidence linking iron excess to coronary artery disease. However, there is no mention of the involvement of iron in neuron degeneration caused by iron deposited in the brain. The information linking iron deposits in the brain to Parkinson's, Alzheimer's, and other neurological diseases is compelling. How could the people responsible for the welfare of our entire population have ignored this information?

The Food and Nutrition Board made the following statement in a "Risk Characterization" paragraph stating that the possible cardiovascular and hepatic hazards make it "prudent to recommend that men and postmenopausal women avoid iron supplements and highly fortified foods." However, there was still no mention of the neurological risks. Also, since most all grains continue to be fortified with varying amounts of iron, the Food and Nutrition Board didn't offer any way for people to avoid these "highly fortified foods," nor has there been any attempt to inform people that they may be harmed by these foods.

The Biochemical Basis of Iron Toxicity

Under healthy circumstances, iron is tightly bound to organic components. This binding is referred to as chelation. Chelation prevents iron from redox cycling. Hemoglobin and myoglobin are the most abundant mammalian hemoprotiens, but there are also cytochromes and enzymes that utilize iron. In addition iron is present in iron-sulfur clusters that are important in electron transfer reactions.

However, when present in excess, iron poses a threat to cells and tissues. Iron exists as ferrous iron, Fe(II), or ferric iron, Fe(III). Free iron can be oxidized from ferrous iron to ferric iron, and reduced from ferric iron to ferrous iron. This is known as redox cycling. When iron redox cycles, oxygen radicals are generated. The resulting superoxide and hydroxyl radicals damage cell structures.

Iron Excess Worsens Chronic Illness

Iron can accumulate in free form in any body tissue under conditions of iron overload. That is why iron excess causes such a wide variety of illnesses.

The most dangerous feature of iron is that it is attracted to, and deposits in, damaged tissue. Thus, the neurofibrillary tangles of Alzheimer's, the substantia nigra of Parkinson's, the atherosclerotic plaques of coronary artery disease, the inflamed joints of arthritis, the pancreatic islet cells of adult-onset diabetics all display increased levels of free iron. There is no way to tell whether the iron initiates the disease or if the diseased tissue attracts the iron which then exacerbates the condition. But either way, free iron in any body tissue is dangerous.

As stated earlier, nearly every individual in North America displays some manifestation of iron poisoning with advancing age. Here is a brief list-these and other diseases will be discussed at length in the following chapters.

• Neurological Degeneration: Parkinson's & Alzheimer's

- Accumulation of iron in brain tissue either causes, or contributes to, neurological diseases such as Parkinsonism and Alzheimer's disease.
- Cancer: Iron is a powerful carcinogen.
 - Excess iron is a well-documented cause of hepatocellular carcinoma.
 - o Elevated levels of iron predispose to breast cancer.
 - Animals fed iron excesses develop colon cancer, believed to be the result of free radical generation by unabsorbed iron.

• Heart Disease:

- Excess iron accumulates in the heart and arteries.
- Free iron as found in heart and arteries may provoke arterial damage.

• Diabetes:

- In hereditary hemochromatosis, excess iron accumulates in the pancreas where it disrupts insulin secretion and causes adult-onset diabetes.
- Iron deposits are found in pancreatic islet cells in people with adult-onset diabetes.
- Joint Inflammation/Arthritis: Iron is found in free form in arthritic joints.
- **Osteoporosis:** People with transfusion siderosis develop osteoporosis at a very young age; iron accumulation in bone causes osteopenia and osteoporosis.
- **Pituitary Function:** People with hereditary iron overload may have "hypogonadotrophic hypogonadism"—infertility due to iron accumulation in the pituitary gland.
- **Sperm Damage:** Iron overload diseases are uniformly associated with sperm damage.
- Sexual dysfunction:
 - o Hypogonadotrophic hypogonadism & infertility.
 - Sperm and egg DNA damage.
- Eye diseases: age related macular degeneration (AMD).
- Kidney damage: hypertension.

- Hearing Loss.
- Cerebrovascular accidents: stroke.