

Risks of Copper and Iron Toxicity during Aging in Humans

Chemical Research in Toxicology
February 15, 2010; Vol. 23; No. 2; pp. 319–326

George J. Brewer

Departments of Human Genetics and Internal Medicine, University of Michigan
Medical School (this article has 89 references)

KEY POINTS FROM THIS ARTICLE:

- 1) Copper and iron are essential but also toxic metals.
- 2) Copper and iron toxicity are important in public health significance, yet are “virtually unknown to the general medical community and there is complete unawareness of the public.”
- 3) The subtle toxicity of copper and iron affects “almost all of us as we age.”
- 4) Copper and iron contribute to the production of excess damaging free radicals.
- 5) “Diseases of aging such as Alzheimer’s disease, other neurodegenerative diseases, arteriosclerosis, diabetes mellitus, and others may all be contributed to by excess copper and iron.”
- 6) In the general population, those in the highest fifth of copper intake, lose cognition at over three times the normal rate. **[Very Important]**
- 7) “Inorganic copper in drinking water and in supplements is handled differently than food copper and is therefore more toxic.”
- 8) “Trace amounts of copper in drinking water, less than one-tenth of that allowed in human drinking water by the Environmental Protection Agency, greatly enhanced an Alzheimer’s-like disease in an animal model.”
- 9) Humans use oxygen in the mitochondria to generate energy in the form of adenosine triphosphate (ATP). “Toxic byproducts of this metabolism are generated, called reactive oxygen species (ROS).”
- 10) “ROS can cause damage to most biological molecules, including DNA, protein, and lipids, resulting in damage to membranes and various cellular organelles.”
- 11) Copper and iron are essential for life, and especially for their roles in energy production. But both copper and iron have their toxic side that allows them to catalyze the generation of damaging reactive oxygen species (ROS).

- 12) Copper and iron are particularly damaging when they exist in their free state.
- 13) 85-95% of the copper in human blood is safely bound to a molecule called ceruloplasmin (Cp). The other 5-15% is loosely bound to albumin and this 5-15% is called free copper. It is this free copper that causes generation of the toxic ROS.
- 14) Those living on the high side of the 5-15 $\mu\text{g}/\text{dL}$ range may be suffering from subtle copper toxicity.
- 15) Organic food copper is bound to proteins and is processed by the liver, which does not allow excess release into the free copper pool in the blood.
- 16) Inorganic copper consumed in drinking water or mineral supplements bypasses the liver and contributes immediately to the free copper pool in the blood.
- 17) The higher the free iron, the greater the risks of developing the diseases of aging.
- 18) Evolution favors reproduction. In youth, high levels of copper and iron increase energy production, wound repair, compensate for blood loss, and therefore increase reproductive fitness. After about age 50 when reproduction is no longer a factor, high levels of copper and iron are toxic because they increase free radical production, enhancing the degenerative diseases of aging. "There is no natural selection against diseases of aging."
- 19) The levels of copper and iron considered normal for humans are acceptable during the reproductive years but are too high after age 50 and contribute to diseases of aging.
- 20) Rabbits fed diets to develop Alzheimer's disease would only do so if they also drank tap water; they did not develop Alzheimer's disease on the same diet if they drank only distilled water. The researchers determined that it was trace amounts of copper in the tap water that made the difference.
- 21) 0.12 ppm (parts per million) of copper added to distilled water trigger Alzheimer's plaques. "The Environmental Protection Agency (EPA) allows over 10 times (1.3 ppm) that much copper in human drinking water." **[Very Important]**
- 22) The inorganic copper in drinking water contributes directly to the free copper pool in the blood.
- 23) Free copper levels are elevated in the blood of AD patients compared to age-matched controls; the higher the free copper, the lower the cognitive ability.
- 24) The amino acid cysteine binds to copper and removes it from the brain. The ApoE protein has three alleles:

ApoE2, has 2 copper binding cysteines and is protective against Alzheimer's.
ApoE3, has 1 copper binding cysteine.
ApoE4, has no copper binding cysteines and increases the risk of Alzheimer's.

25) Homocysteine interacts with copper to produce increased oxidant stress, oxidizing low-density lipoprotein (LDL) that contributes to the development of AD.

26) Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis (Lou Gehrig's disease), and prion diseases such as Creutzfeldt-Jakob disease, are all diseases of neurodegeneration, all have misfolded proteins that form inclusion bodies that are a copper dependent mechanism.

27) People in the highest quintile of copper intake with a high fat diet, "lost cognition at a rate of 19 years in a six year period. In other words, they lost cognition at over three times the rate expected!" "These people were in the highest quintile of copper intake primarily because they took copper in their vitamin/mineral supplement pill. These data are frightening! Almost all vitamin/mineral supplements contain copper. Copper deficiency is extremely rare; therefore, almost no one needs copper supplements, yet tens of millions of people are taking copper supplements and in my view are running the risk of poisoning themselves with copper."

28) The interaction of copper and homocysteine generates oxidant stress and oxidize LDL, which is a component of the atherosclerotic plaque.

29) Abnormal copper metabolism increases diabetes and is involved in the etiology of diabetic neuropathy.

30) Increased copper has also been linked to Parkinson's disease, autism, Tourette's syndrome, age related macular degeneration and cancer.

31) Zinc is an anti-inflammatory and antioxidant agent. Supplemental zinc of 15 mg or more significantly protects against advanced prostate cancer.

32) Increased iron levels play a major role in producing atherosclerosis.

33) Menstruating women have reduced iron load as a result of blood loss and have strong protection against atherosclerosis compared to men. Post-menopausal women lose this protective effect. Blood donors have less atherosclerotic disease.

34) The interaction of iron and cholesterol promote oxidative damage, causing both atherosclerosis and neurodegeneration.

35) The constant production of toxic free radicals, particularly reactive oxygen species, slowly produces mitochondrial damage. The slow loss of mitochondria and their energy production is associated with aging and may be the major cause of aging; greater levels of free iron and free copper accelerate the production of toxic radicals.

36) "The toxicity of free copper and free iron extends to the very basic process of aging itself."

37) To Minimize Copper and Iron Toxicity:

- Avoid taking supplements containing copper and iron. "Most multivitamin/multimineral pills have copper, and this copper is potentially dangerous." "Scan the label on your supplement bottle, and stop taking it if it contains copper." "Copper deficiency is extremely rare, and almost no one needs copper." Those with the highest quintile of copper intake lose cognition at over 3 times the normal rate, and "got there for the most part by taking copper supplements."
- "Men rarely need iron supplements unless they have chronic blood loss. But some menstruating girls and women, particularly if menstrual flow is heavy, may become iron deficient."
- "Both copper and iron are much more bioavailable from meat than from vegetable foods. That means that these metals are much more easily absorbed from meat sources. Liver and shellfish are particularly high in copper content. Red meat is particularly high in bioavailable iron. But copper and iron are readily bioavailable from all meat foods."
- "Those who averaged 2/3 of an ounce of red meat/day had 30% less mortality than those who averaged 5 ounces of red meat/day. Processed meats also increased mortality. Mortality was 20% higher in those who averaged 2 ounces of processed meat per day (an average of one hot dog/day), compared to those who ate almost 15% that much. It is possible that the reduction in mortality seen in the study is at least partially due to the reduction of copper and iron intake."
- "Avoid drinking water with elevated copper content, one has to measure the copper in their drinking water."

38) "80% of homes in the U.S. have copper water pipes. Whether toxic amounts of copper leaches from the copper pipes depends mostly on the acidity of the water. The more acidic the water, the more copper leaches from the pipes. If the plumbing system is used as the electrical ground for the house (which is legal in many places, but should not be), more copper can leach from the pipes."

39) There are various laboratories where copper in the water can be measured. It is best to measure both the first draw water in the morning and water after allowing the tap to run for five minutes. Because stagnant water may contain more copper, it is good to know if this is the case so that it can be avoided if necessary.

40) "We recommend the drinking water contain no more than about 0.01 ppm. (The EPA allows 1.3 ppm!)"

- 41) "If the drinking water contains too much copper, a reverse osmosis device can be installed on the tap used for drinking and cooking water. Alternatively, distilled water, which contains no copper, can be purchased for drinking and cooking."
- 42) "Bottled waters, which many people now drink, are an unknown for copper content, and at this point cannot be used to avoid copper in drinking water."
- 43) The intervention step required to further lower free copper is to take oral zinc supplements; zinc will lower free copper levels. It does so by strongly limiting copper absorption. "The minimal dose of zinc to do this is about 40 mg twice a day." "The zinc dose must be separated from food and beverages other than water by at least 1 h before and 2 h after." The best is zinc acetate and zinc gluconate.
- 44) "Lowering free copper levels is beneficial in fibrotic, inflammatory, and autoimmune disease processes."
- 45) "The intervention for lowering free iron is blood donation or removal of a significant amount of blood on a regular basis. Men and menopausal women could donate 500 mL of blood every 2 months (or have that much removed if they are not suitable blood donors), until their percent transferrin saturation is in the 15-25 range."
- 46) "If one is going to intervene by taking zinc to lower free copper and or donate blood to lower free iron, it is important to monitor free copper and/or free iron levels."
- 47) "It appears very likely that copper and iron toxicity are occurring in a large proportion of our population."
- 48) "Both copper and iron toxicity are likely contributing to Alzheimer's disease."
- 49) "There is a major epidemic of AD in the industrialized world, and this disease did not exist until 100 years ago. It still is rare in India and Africa."
- 50) "The process of loss of cognition during aging may be greatly speeded up by increased free copper exposure, and the very process of aging itself, if due to a lifetime of oxidant stress, is likely increased by higher levels of free copper and free iron since the toxicities of these two metals is through the production of oxidant stress."
- 51) Lower the risks of free copper and iron by "throwing away supplements containing these metals, by lowering meat intake, and by avoiding drinking water with elevated levels of copper."
- 52) Rigorous methods of lowering free copper and free iron exposure include taking zinc to lower copper and using blood donation to lower iron.