



## **Copper: The Missing Link?**

**By Hans R. Larsen MSc ChE**

Ever since I discovered that the average afibber (myself included) has a dietary copper intake about one fifth of that of our benchmark (Fran's) diet I have become increasingly intrigued by the possibility that copper and the ratio of zinc:copper in the diet (zinc inhibits the absorption of copper) could be a key factor in lone atrial fibrillation. I would like to propose a new hypothesis for your scrutiny and comments.

In my book (pages 137-138) I discussed the possibility that oxidative stress could play a major role in LAF. Here is the relevant quote (see the book for references):

"Mapping of fibrillating atria has shown that ectopic (premature) beats and fibrillation itself originate in clearly discernible agglomerations of individual heart cells that are beating to their own rhythm rather than to the rhythm generated in the SA (sino-atrial) node. It is thought that these agglomerations are actually inflamed heart tissue and that atrial fibrillation originates here and is sustained by scar tissue (fibrosis) generated by previous inflammations[9,10,16,17,55]. It is also clear that the junctions between the left atrium and the pulmonary veins are the most common locations for these "rogue", inflamed cell agglomerations.

What, apart from size, is different between the left and right atrium, or for that matter, between the junctions of the left atrium and the pulmonary veins and the junctions of the right atrium and the venae cavae?

In a nutshell, oxygen concentration (partial pressure) and shear stress. The blood returning to the right atrium is relatively low in oxygen content and flows fairly sedately through the venae cavae into the heart. The blood flowing from the lungs to the left atrium, on the other hand, is highly oxygenated and flows more forcefully through the pulmonary veins thus generating a significant amount of shear stress, especially at the junctions with the left atrium.

The combination of a high oxygen pressure and shear stress is a potent breeding ground for reactive oxygen species (ROS). The superoxide anion, singlet oxygen, nitrogen dioxide (peroxynitrite) and hydroxyl radicals are all members of the ROS family. They share the dubious distinction of being able to cause inflammation and inflict considerable damage in tissues, cells and individual DNA strands.

One would expect vigorous exercise to markedly increase oxygen concentration and shear stress and thus promote the formation of ROS. Indeed, there is evidence that orienteering, marathon running, and cross-country skiing are associated with an increased incidence of arrhythmias and asthma[57-59]. Finnish researchers found that middle-aged, elite orienteers had a 5 times higher incidence of

lone atrial fibrillation than did the general population[57]. Breathing air polluted with nitrogen dioxide has also been found to increase the incidence of inflammation and arrhythmias[60-62]. Other forms of air pollution (particulate matter) has been linked to the formation (in the lungs) of inflammatory cytokines that are released into the blood circulation[63].

Under normal circumstances any ROS attacking the heart lining or adjacent lung tissue would quickly be rendered harmless by the body's own antioxidants or by antioxidants obtained through the diet. However, if antioxidant defenses are inadequate, the immune system is compromised, or if the autonomic nervous system is highly dysfunctional or stressed, it is likely that the ROS could get the upper hand and initiate an inflammatory response and subsequent arrhythmia. Researchers at the Cleveland Clinic and the Ohio State University have found that AF patients show signs of extensive oxidative injury to their myofibrillar creatine kinase (MM-CK). MM-CK is involved in the control of the contraction of individual heart cells (myocytes). The researchers also determined that the oxidative damage was caused by peroxynitrite, a highly potent free radical. They conclude that peroxynitrite-induced oxidative stress can damage individual heart cells to such an extent that their normal function is disrupted and atrial fibrillation results[64]."

Although dietary antioxidants such as vitamin C, gamma-tocopherol (vitamin E) and lycopene may help prevent oxidative damage there is no question in my mind that the body's own naturally produced antioxidants superoxide dismutase and glutathione peroxidase would be far more effective in preventing oxidative damage than would the dietary antioxidants.

Superoxide dismutase comes in two varieties: one containing copper and zinc and one containing manganese. For the purposes of this discussion I'll leave out the manganese-based version and concentrate on the Cu/Zn superoxide dismutase. Glutathione peroxidase contains selenium (Se) and is vital in defusing the hydroperoxide formed when superoxide dismutase breaks down superoxide to oxygen and hydroperoxide. In other words the two antioxidants work together and need an adequate supply of Cu, Zn and Se in order to be produced by the body.

The free radicals, superoxide and peroxynitrite have both been shown to cause damage to heart tissue leading to fibrosis, a well-known player in the LAF drama. Peroxynitrite is formed through a reaction between superoxide and nitric oxide and experiments have shown that peroxynitrite formation is completely suppressed in the presence of adequate amounts of superoxide dismutase. HOWEVER, adequate amounts of superoxide dismutase cannot be produced unless the body receives an adequate and balanced intake of copper and zinc.

The consequences of a copper deficiency were discussed in the October 2003 issue of *The AFIB Report*. Here are the relevant paragraphs:

"Copper deficiency is widespread in the western world. A daily intake of between 0.65 and 1.02 mg (based on analyses of actual food consumed) has been found to lead to deficiency symptoms and it is estimated that approximately one third of the populations of Belgium, Canada, the UK, and the United States have daily intakes in this range[1]. A copper deficiency has been linked to osteoporosis, high cholesterol levels, hypertension, cardiac rhythm abnormalities, increased tendency to blood clotting (thrombosis), an increase in the oxidative stress on the heart tissue and the development of fibrosis[1,2,3,4,5].

Of particular interest to afibbers is the finding of an association between a copper deficiency and fibrosis of the heart muscle (a suspected important player in afib), cardiac arrhythmias, and in particular, a tendency to experience an increased level of premature ventricular complexes (PVCs)[1,6,7]. While PVCs have not been linked directly to the initiation of atrial fibrillation it is possible that they could be involved indirectly. PVCs do cause anxiety, particularly when they come in runs and may also disturb the mechanical, if not electrical, balance of the heart. Both could lead to increased anxiety and thus provoke an afib episode.

A copper deficiency also reduces the level of superoxide dismutase (copper-zinc superoxide dismutase)[1,4,5,8,9,10]. Superoxide dismutase is one of the body's most effective antioxidants and is particularly adept at neutralizing the superoxide radical, a potent free radical generator and initiator of oxidative stress. It is likely that the superoxide radical would be particularly plentiful in the blood entering the left atrium through the pulmonary veins and thus could be involved in the etiology of afib episode initiation[11].

Blood (erythrocyte) levels of superoxide dismutase can be increased by copper supplementation, but commensurate high intakes of zinc or ascorbic acid (vitamin C) reduce the effectiveness of the supplementation[12,13].

Several experiments have shown that the frequency of PVCs can be markedly reduced by supplementation with copper. As early as 1979 it was observed that daily supplementation with as little as 4 mg of elemental copper (from copper gluconate) completely eliminated PVCs in less than 2 weeks in three individuals suffering from PVCs[6]. Again it was pointed out that a high zinc intake would be detrimental because it interferes with copper absorption.

The average copper intake among the 65 afibbers participating in the 2001 diet survey was 1.3 mg/day. However, this is a value calculated from the USDA nutrition database. According to research yet to be published calculated values are at least 52% higher than the values obtained by actually analyzing meals consumed[2]. So the calculated 1.3 mg/day would actually correspond to an analyzed value of about 0.86 mg/day. This is well within the deficient range; considerably below the official "Adequate and Safe Intake" of 1.5 to 3.0 mg/day, and even below the recently established RDA of 0.9 mg/day (many scientists feel that this value is way too low)[3].

So not only could many afibbers be deficient in copper, but it would also seem that the average Zn:Cu ratio in the afibbers diet is undesirably high at 7.8:1 compared to 3.1:1 in the benchmark diet (Fran's diet) and the RDA of 6:1. Many researchers consider the Zn:Cu ratio in human milk to be ideal[2]. This ratio is 3:1, very close to the benchmark diet, but substantially lower than the RDA and the average ratio found in the afibbers diet survey. Considering that many men take zinc supplements for prostate health without a commensurate intake in copper would further push the Zn:Cu ratio in an undesirable direction.

Nuts, legumes, and dark chocolate are excellent dietary sources of copper and chelated copper and copper gluconate are effective supplements[14,15,16]. Copper intakes up to 10 mg/day are considered safe, but intakes of 6 mg and more may produce stomach upsets[2].

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What I am now proposing is that a copper deficiency and an elevated Zn:Cu ratio could result in suboptimal levels of superoxide dismutase which in turn could result in an increased level of PVCs and – perhaps – an increased frequency of afib episodes.

I believe it is quite possible that copper may prove to be as important as magnesium for afibbers and probably even more important for those of us with a high level of PVCs. I have been experimenting a bit recently with copper and zinc supplementation and for the time being (I may cut back a bit later) have settled on 5 mg chelated copper (Albion Process) at lunch (no zinc or vitamin C at this time) and 25 mg of zinc citrate at dinner (with 500 mg of vitamin C). My two most recent Holter monitor recordings showed a total of 2600 PVCs over a 23-hour period or 113 PVCs per hour. I am now down to 10 per hour or less and expect to eliminate them completely within the next week or so. I should point out that hair analyses carried out in 1993 and 1998 (my afib career began in late 1989) showed my copper levels to be well below normal.

Whether elimination of PVCs will influence afib episode frequency remains to be seen. I'll keep you posted on that. In the meantime it sure feels good not to miss what seemed to be every second heart beat.

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