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From the Desk of Dr. Stephen Sinatra

"Care," Cancer and Coenzyme Q_{10}

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LETTERS TO THE EDITOR

"Care," Cancer and Coenzyme Q10

I read, with great interest, the July 1998 article on the use of Pravastatin in postmenopausal women with a history of myocardial infarction, which revealed a significant reduction in a wide range of cardiovascular events for those with average cholesterol levels (1). These findings have been significant enough to encourage the use of Pravastatin for secondary prevention. However, I was alarmed by the number of women in the treatment group who developed breast cancer during the study period.

Although this phenomenon was attributed to chance by the researchers, we have to pause in our enthusiasm to ask ourselves a serious question: Could there possibly be any relationship between the HMG-CoA-reductase inhibitors and breast cancer? Does the fact that only one case of breast cancer was found in the placebo group and 12 cases developed in the experimental group represent a mere fluke in research, or do we owe it to our female patients to look further into the issue before it is dismissed? Although the research authors state "there is no known biologic basis for suspecting a causable link," I suggest that there very well may be. Some of the negative side effects already identified with HMG-CoA-reductase inhibitors are reduction of serum levels of Vitamin E, enhancing oxidizability (2) and interfering with the endogenous synthesis of the important nutrient/antioxidant CoEnzyme Q10 (Fig. 1).

Case study investigations that correlated a decrease in CoEnzyme Q10 levels during Lovastatin administration in humans (2,3) have been supported by subsequent double blind placebo controlled research that also clearly demonstrated scientific evidence of plasma CoQ10 lowering by HMG-CoA-reductase inhibitors (4). Because we know that HMG-CoA-reductase inhibitors are associated with lower plasma levels of CoQ10, a second question arises: Could there be any relationship between diminished CoQ10 and cancer?

In a Swedish study of 116 cancer patients, a definite relationship between low CoQ10 levels and the incidence of breast cancer was identified. In fact, researchers reported a 38.5% incidence of breast cancer for those women with plasma levels of CoQ10 levels below 0.6 μg/ml (0.6 to 0.8 is considered normal range) (5). The late Dr. Karl Folkers, a chemist who won every scientific award short of the Nobel Prize, spent his life investigating the chemistry of CoEnzyme Q10 (ubiquinone). He suggested that the impaired biosynthesis of CoQ10 involved abnormal pairing of DNA bases, which might suggest a rational basis for the molecular causes of cancer (6).

In addition, early animal research has demonstrated immune system decline in the presence of diminished levels of CoQ10 (7). We also know that Q10 levels decline as a factor of aging (8). The Pravastatin study, where the 12 cases were reported, included 576 postmenopausal women who may have already been so compromised.

The fact that we have evidence that cancer is correlated with lower Q10 levels and immune system dysfunction, and that HMG-Co-A Reductase inhibitors disturb the production of this essential nutrient and Vitamin E should be enough to warrant further investigation to identify any possible risks for postmenopausal women whose Q10 levels are already depleted with age. Further research could more clearly define assessment tools and treatment guidelines for use of the "statin" drugs, such as the possible coadministration of Q10. One of the key goals of further research would be to establish possible high risk groups when considering HMG-CoA-reductase inhibitors, such as postmenopausal women who are at known high risk for breast cancer.

We know that a woman's risk of breast cancer increases with positive family history, aging, high saturated fat diets, excessive use of alcohol or repeated exposure to environmental toxins such as pesticides or xenoestrogens. We need to investigate if HMG-CoA-reductase inhibitors, such as Pravastatin, may render these potentially high-risk subsets of women even more vulnerable to the possibility of breast cancer.

Certainly, the 46% risk reduction in coronary events is compelling evidence for the use of Pravastatin. But we cannot afford to ignore the 12 cases of breast cancer reported in the experimental group of menopausal women. This

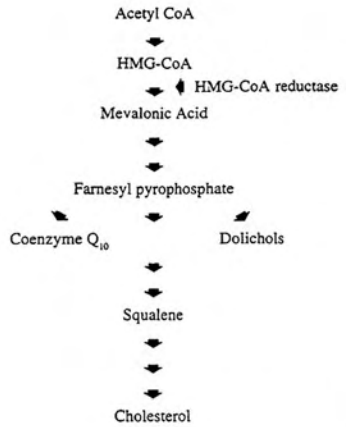

Figure 1. Biosynthetic Pathway of Cholesterol. The enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase is necessary for the conversion of HMG-CoA to mevalonic acid, an early step in biosynthesis of cholesterol. Because mevalonic acid is also a precursor of coenzyme Q_{10} via a branch of the cholesterol biosynthetic pathway, HMG-CoA reductase inhibitors could reduce serum concentrations of coenzyme Q_{10}. With Permission: Sinatra ST. CoEnzyme Q10: A Vital Therapeutic Nutrient for the Heart with Special Application in Congestive Heart Failure. Conn Medicine 1997;61(11):707–711.

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finding raises a red flag in my mind, suggesting the need for further research, especially for women at risk of breast cancer who are considered for or are already taking HMG-CoA-reductase inhibitors for cholesterol-lowering. We owe it to our patients to look further into this issue before we routinely prescribe what has the potential to be a dangerous medication for some women.

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