Vitamin E, Atherosclerosis, Heat Shock Proteins: The Trojan Horse Hypothesis

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Letter to the Editor:

Multiple clinical trails have observed a lack of vitamin E supplementation benefit in cardiovascular disease, yet a clear explanation for the negative studies has not been forthcoming. We propose a novel pathophysiologic mechanism that offers a reason for the negative outcomes. The intention of the antioxidant trials was to protect the vasculature from oxidation and free radical formation, primary events leading to arterial wall injury and atherosclerosis. Our hypothesis is that vitamin E's reactive oxygen scavenging effect reduces heat shock protein 70 (Hsp 70), resulting in increased apoptosis. Hsp 70, a stress protein, is found in all living cells, providing protection of cellular elements from injury by refolding damaged proteins and reducing oxidation, inflammation, and apoptosis.[1] Indeed, vitamin E increases apoptosis in stressed cell culture systems in direct correlation with falls in Hsp 70 levels.[2] In fact, vitamin E supplementation has been proposed to augment cancer chemotherapies in order to increase apoptosis of malignant tumor cells.[3] Importantly, low serum Hsp 70 values have recently been observed to predict atherosclerosis progression in hypertensive subjects.[4] Finally, increased apoptosis of smooth muscle cells, and inflammatory cells in atherosclerotic lesions has been proposed to contribute to plaque instability.[5] So undoubtedly while oxidation plays a major role in cellular injury and atherosclerosis progression, vitamin E supplementation may have an unintended negative side effect of increasing apoptosis resulting in no vascular benefit. In this regard, Vitamin E plays the role of a Trojan horse, initially presenting itself to the cell as a friendly gift and then removing the major defensive guardians of the cell—heat shock proteins, resulting in cells vulnerable to stress.

References

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