Vitamin E: the enigmatic one!

William S. Blaner, *Editorial Board*!

Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY 10032

Vitamin E was first identified more than 90 years ago by Evans and Bishop as an essential dietary factor that is required by rats to maintain normal reproduction (1). Unlike the other three fat-soluble vitamins that have very specific molecular targets and actions, vitamin E lacks specific pathways or specific molecular targets that account for its requirement from the diet. Considerable research had been focused on identifying specific molecular targets and actions for vitamin E (2). For instance, as it became clear that vitamins A and D act through cognate nuclear hormone receptors to regulate vitamin-responsive gene expression, investigators sought, without success, to identify similar activities for vitamin E. These investigations simply led back to the same understanding of vitamin E obtained from studies carried out between the 1930s and the 1980s, that vitamin E acts as a fat-soluble antioxidant. Vitamin E serves as a peroxyl radical scavenger that protects polyunsaturated fatty acids in membranes and lipoproteins from oxidative damage (3). Given that many dietary substances, as well as many substances synthesized within the body, have potent antioxidant properties, what selective pressures drove evolution to require humans and other higher animals to acquire vitamin E from the diet? Is this simply due to the physical properties and/or redox chemistry of vitamin E or is there something about vitamin E that we still do not understand?

This issue of the *Journal of Lipid Research* contains the second installment of the JLR’s Thematic Review Series on fat-soluble vitamins. The biology of vitamin E and its role in human cardiovascular disease will be considered in the two reviews that comprise this edition of the Thematic Review Series on fat-soluble vitamins.

**THE VITAMIN E THEMATIC REVIEWS**

Vitamin E is a collective term that refers to all tocol and tocotrienol derivatives that exhibit the antioxidant activity of α-tocopherol (2, 4). These antioxidants include four tocopherols and four tocotrienols that share the chromanol ring structure but which differ by the number of methyl moieties present on the chromanol ring (2, 4). The trimethylated species constitute α-tocopherol and α-tocotrienol; the dimethylated ones, the β- and γ-forms of tocoferol and tocotrienol; and the monomethylated one, δ-tocopherol and δ-tocotrienol (2, 4). However, not all vitamin E forms are processed equally by the body. Regardless of the composition of vitamin E intake obtained from the diet, α-tocopherol is selectively enriched in human tissues (2, 4). This selectivity for α-tocopherol is largely conferred by two hepatic activities, an α-tocopherol transport protein and a catalyzing cytochrome P450 system that preferentially degrades the other dietary forms of vitamin E (5). The review by Traber (6) entitled “Mechanism for the prevention of Vitamin E excess” will consider recent advances in understanding the regulatory mechanisms that are responsible for modulating vitamin E levels in the body. This article will focus primarily on metabolic events that take place in the liver, because this is the tissue most responsible for regulating vitamin E homeostasis in the body. Central to this will be consideration of how dietary vitamin E is taken up into the liver in chylomicron remnants and processed by the liver so that α-tocopherol is selectively resorbed into the circulation in nascent very low density lipoprotein.

In humans, a number of disorders requiring administration of α-tocopherol to prevent vitamin E deficiency have been identified. These predominantly arise due to genetic abnormalities or fat malabsorption syndromes and clearly define the essential nature of dietary vitamin E intake (2). Because the basic research literature has provided credible mechanisms by which vitamin E could protect against chronic disease development, a relatively large number of intervention studies involving pharmacologic amounts of vitamin E have been carried out to assess the validity of this notion. In addition, numerous epidemiologic studies focused on identifying benefits of vitamin E intake in preventing chronic diseases have also been reported; however, the findings from these studies have been controversial with regards to the potential health benefits of vitamin E for preventing chronic diseases, especially cardiovascular disease and cancer. Clearly, vitamin E must be obtained from the diet to prevent signs of deficiency but it remains
to be established whether doses of vitamin E beyond those that can be obtained in the diet afford additional health benefits to humans. The second review from Vardi, Levy, and Levy (7) entitled “Vitamin E in the prevention of cardiovascular disease: the importance of proper patient selection” provides a review of the literature regarding vitamin E and its benefits in primary and secondary prevention of cardiovascular disease morbidity and mortality. Based on their review of the literature, these authors conclude that vitamin E does not protect against the development of cardiovascular disease when administered indiscriminately to unselected populations. However, Vardi, Levy, and Levy go on to conclude that vitamin E is cardio-protective in certain subgroups that are experiencing high levels of oxidative stress, including individuals on hemodialysis or diabetic patients harboring the Hp 2-2 haptoglobin genotype.

REFERENCES