Featured Investigator: May, Dr. James M.

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Keywords: research | vitamin C | diabetic endothelium

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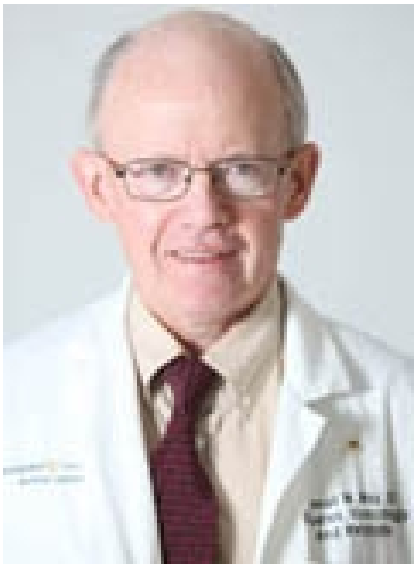

James M. May, M.D. »

Professor, Medicine and Molecular Physiology and Biophysics
Director, Endocrinology and Diabetes Fellowship Program
Section Chief, Endocrinology, Nashville Veterans Hospital

Specialty: Vitamin C Function in the Diabetic Endothelium

Description: James M. May's research has been in the area of diabetes for the last 35 years, initially on mechanisms of glucose transport, and for the last 15 years on antioxidant function in atherosclerosis and diabetes. His laboratory uses murine models of type 1 diabetes to understand the damage of oxidative stress related to high glucoses (glucotoxicity) to the endothelial cells that line all blood vessels. Vitamin C is being studied as a potential therapeutic intervention. This Vitamin is beneficial to the endothelium because it scavenges reactive oxygen and nitrogen molecules that would otherwise damage the cells. Perhaps more important, Vitamin C is required as a co-factor by several enzymes that function to hydroxylate collagen, cholesterol, carnitine, the transcription factor HIF-1α, and many neurotransmitters. Recent results from this laboratory have shown that it tightens the endothelial barrier to the transit of large molecules such as albumin from the blood vessel to the interstitial space. By doing this, Vitamin C could decrease tissue edema that is a problem with high glucoses. The effect of Vitamin C to improve endothelial barrier function was first shown in cultured human umbilical vein endothelial cells, but now has been extended to primary culture cells from human dermis and the blood-brain barrier. The mechanism of the effect has not been fully elucidated, but appears in part to relate to the ability of Vitamin C to spare tetrahydrobiopterin, a crucial co-factor for endothelial nitric oxide synthase. In so doing, Vitamin C increases the generation of nitric oxide, which can both help to dilate vessels, but also to tighten the endothelial barrier. Studies in mice also suggest that Vitamin C can decrease trans-endothelial leakage caused by both Vitamin C deficiency and by high glucoses due to diabetes. Activation of the receptor for advanced glycation end products (RAGE) by high glucose is one of the major damaging actions of glucose, and Vitamin C prevents increases in endothelial permeability due to RAGE agonists. Studies are now focused on novel mouse models of Vitamin C deficiency and excess to test effects of diabetes and to determine whether Vitamin C excess or repletion can decrease systemic damage to the endothelium by high glucose.