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Abstract

Pathologies ranging from diabetes, and hypertension to cardiovascular risks such as hypercholesterolemia and obesity all exemplify a common dysfunction found in endothelium. Endothelial dysfunction is due to the presence of oxidative stress, determined as increased reactive oxygen species from cytosolic NADPH oxidases or inefficient antioxidant defense mechanisms. Vascular diseases are linked to oxidative stress within mitochondria, which modifies mitochondrial DNA, and therefore, may impair transcription of proteins from the mitochondrial genome. Lesions in mitochondrial DNA decrease the mitochondria's bioenergetic function and increase superoxide production as electrons are leaked from the electron transport chain. Inefficient mitochondrial bioenergetic activity can lead to decreased concentrations of ATP, a product necessary for the function of endothelial vasodilation due to the use of several protein kinases in the production of NO. Based on the above observations, we hypothesized that oxidative injury to mitochondrial DNA and the consequential impairment in bioenergetic capacity impairs endothelial function in the metabolic syndrome, i.e., obesity, insulin resistance, hypertension. Pathologies linked to an increased presence of ROS from mitochondrial dysfunction display endothelial dysfunction. Mitochondrial dysfunction inhibits the physiological production of ATP, a molecule essential in the production of adequate amounts of NO. With insufficient supplies of NO, endothelial vasodilation may be severely impaired, leading to various pathologies and cardiomyopathies.