



The UK Superfund Research Center supports biomedical and environmental science research to improve health by preventing exposures to environmental pollutants and promoting healthful lifestyles.

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Superfund Chemicals, Nutrition, and Endothelial Dysfunction

Atherosclerosis, a chronic inflammatory disease, is still the number one cause of death in the United States. Numerous risk factors for the development of atherosclerosis have been identified, including obesity and hypertriglyceridemia. Superfund chemicals, and especially persistent organic pollutants such as PAHs and PCBs, also have been shown to increase the risk and incidence of cardiovascular diseases. Most of all, we have evidence that both selected PCBs and fatty acids can induce endothelial cell dysfunction and inflammation, critical events in the early pathology of atherosclerosis. On the other hand, healthful nutrition can protect against environmental insults. Our data suggest that diet, nutrition, and lifestyle changes can modify pathologies of chronic diseases, as well as diseases associated with environmental toxic insults.

Little is known about mechanisms and regulation of cellular uptake, trafficking and initiation of proinflammatory pathways by both PCBs and fatty acids. Membrane lipid rafts such as caveolae are particularly abundant in endothelial cells, where they are believed to play a major role in the regulation of endothelial vesicular trafficking. Thus, we hypothesize that caveolae are critical in the cellular uptake of lipophilic environmental contaminants such as PCBs. Caveolae have also been implicated in the regulation of cell signal transduction. We further hypothesize that PCBs interact with caveolae and trigger distinct proatherogenic signaling pathways, leading to endothelial cell dysfunction. We also hypothesize that these signaling pathways can be down-regulated by antioxidant nutrients and related bioactive compounds, including polyphenols such as flavonoids.

These hypotheses are tested *in vitro* as well as *in vivo* by studying the interactions of PCBs with dietary compounds such as fatty acids and antioxidant nutrients. We explore mechanisms of nutrient-mediated changes of PCB toxicity, and the outcomes of these studies are geared to provide meaningful nutritional recommendations and therapeutic interventions for exposed populations.

Take Home Message:

Exposure to PCBs and other pollutants may lead to chronic inflammation and heart disease, but eating diets high in antioxidant and anti-inflammatory bioactive nutrients such as those found in fruits and vegetables may buffer the body against toxic insult.