

Research Brief 161: PCB77 Promotes Obesity-associated Atherosclerosis

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Background:

Polychlorinated biphenyls (PCBs) are industrial chemicals that bioaccumulate in the ecosystem. PCBs are highly lipophilic and accumulate markedly in fatty tissues, so obesity could increase the body burden of PCBs. Although adipocytes (fat cells) are likely to be frequently exposed to PCBs, the specific effects of PCBs on adipocyte function have not been defined. Moreover, the relationship between increased PCB body burden with obesity and the development of obesity-associated diseases is unknown.

Dr. Lisa Cassis (University of Kentucky SBRP) and her research team are investigating the impacts of PCB exposures on the development of obesity and the mechanisms that link obesity to cardiovascular disease. Studying PCB77, a "dioxin-like" coplanar arylhydrocarbon receptor (AhR) ligand, they are working to:

- Define the concentration-dependent effects of PCB77 on the development of obesity.
- Examine the effects of PCB77 on adipocyte production of pro- and anti-inflammatory factors.
- Investigate the effects of adipocyte-sequestered PCB77 on alterations in serum lipids and development of atherosclerosis.

Advances:

Dr. Cassis' team conducted both *in vitro* and *in vivo* studies in rodents. In the first series of experiments, they examined the concentration-dependent impacts of exposures to PCB77 or dioxin (tetrachlorodibenzo-p-dioxin, TCDD) on rates of preadipocyte differentiation to mature adipocytes. They found that low concentrations of PCB77 and TCDD **increase** adipocyte differentiation, resulting in an increase in body weight, adipose mass and adipocyte area. Higher concentrations **inhibit** adipocyte differentiation.

Effects of PCB77 were abolished by the AhR antagonist, α -naphthoflavone (α -NF). The research team also showed that PCB153, which has a low affinity for interaction with AhR, did not impact adipocyte differentiation. These findings suggest that PCB77 and TCDD effects on adipocyte differentiation and body weight are AhR-mediated.

Dr. Bernhard Hennig, also an SBRP-funded researcher at UK, previously demonstrated that PCB77 promotes inflammation in endothelial cells.

Obesity is associated with an elevation in the systemic concentrations of adipokines (cell-to-cell signaling proteins) that have been linked to obesity-related diseases including coronary artery disease. Dr. Cassis conducted a study to determine if PCB77 impacts adipokine secretion from adipocytes. Such an effect would influence not only obesity, but also obesity-associated atherosclerosis. The researchers found that PCB77 promotes the expression and secretion of a variety of proinflammatory adipokines, and decreases the expression of an anti-inflammatory adipokine (adiponectin). To our knowledge, this is the first report demonstrating that PCBs can promote the production of these factors from adipocytes.

Dr. Cassis' research also revealed that exposure to low doses of PCB77 results in a marked increase in serum cholesterol concentrations, with predominant increases in very-low-density lipoprotein (VLDL) or "bad" cholesterol. In addition, the elevations in VLDL-cholesterol by PCB77 were associated with increased atherosclerosis. To the researcher's knowledge, this is the first study that has directly examined the effects of PCB exposure on experimental atherosclerosis.

Significance:

Though production of PCBs was banned in 1977 in the United States, PCBs are persistent, and biomagnified, in the environment. On-going sources of potential human exposures include fish consumption, soil, groundwater and drinking water. At the same time, the prevalence of obesity in both adults and children continues to increase at an alarming rate.

Dr. Cassis' groundbreaking research reveals that even low level exposure PCBs may contribute to the development of obesity and obesity-associated atherosclerosis. This discovery of the inter-relationships between PCBs, obesity, and obesity-related diseases could inform public health policy and practice.

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To learn more about this research, please refer to the following sources:

Arsenescu, V., R.I. Arsenescu, V. King, Hollie Swanson, and Lisa A. Cassis. 2008. Polychlorinated Biphenyl-77 Induces Adipocyte Differentiation and Proinflammatory Adipokines and Promotes Obesity and Atherosclerosis. *Environmental Health Perspectives*. 116:761–768.
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