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DIETARY FAT INTERACTS WITH PCBs TO INDUCE CHANGES IN LIPID METABOLISM IN LDL RECEPTOR DEFICIENT MICE

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There is evidence that dietary fat can modify the cytotoxicity of polychlorinated biphenyls (PCBs), and that coplanar PCBs can induce inflammatory processes critical in the pathology of vascular diseases. To test the hypothesis that the interaction of PCBs with dietary fat and subsequent changes in lipid metabolism and gene induction is dependent on the type of dietary fat, LDL-R<sup>-/-</sup> mice were fed diets high either in olive oil or corn oil for 4 weeks. In addition, half of the animals from each group were injected with PCB 77. In contrast to the high olive oil diet, PCB treatment markedly increased staining for neutral lipids in aortic arches derived from mice fed the high corn oil diet. Compared to corn oil, VCAM-1 expression was non-detectable in the olive oil-fed mice but highly inducible in the presence of PCBs. Serum triglycerides were decreased in PCB-treated mice, independent of dietary fat. Oleic acid levels in olive oil-fed mice were unaffected in the serum by PCB treatment but increased in liver tissue. In contrast, PCB treatment markedly reduced serum linoleic acid levels in mice fed the high corn oil diet with little effect on liver levels of this fatty acid. Microarray analysis of liver mRNA revealed PCB-mediated up-regulation of genes involved in fatty acid uptake and catabolism (e.g., CD36 and carnitine-palmitoyl-CoA transferase) and down-regulation of genes involved in fatty acid synthesis (e.g., acetyl-CoA carboxylase) only in mice fed the high corn oil diet. Compared to olive oil, CYP1A1 was up-regulated by corn oil feeding alone. PCB treatment markedly increased CYP1A1 gene expression in all mice. These data suggest that dietary fat can modify changes in lipid metabolism induced by PCBs and that dietary oils rich in linoleic acid, such as corn oil, can amplify compromised gene expression during PCB cytotoxicity. This may have implications in understanding the interaction of nutrients with environmental contaminants on the pathology of diseases such as atherosclerosis. (Supported by grants from NIEHS/NIH (P42 ES 07380), the KY Agr. Exp. Station and AHA).