

Alaska Community Action on Toxics

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## Diabetes: The Role of Persistent Toxic Chemicals in this Complex Disease

While diabetes is rarely considered to be an environmentally-induced disease, there is increasingly strong evidence that environmental exposure contributes to the incidence of both Type I and Type II diabetes. Type I diabetes, which usually has onset in childhood, is an autoimmune disease with loss of the pancreatic beta cells and secondary lack of insulin. Type II diabetes, which usually has adult onset, is associated with a cellular resistance to the actions of insulin (Zimmet et al., 2001).

A study of the U. S. Air Force personnel who were exposed to dioxin-contaminated Agent Orange on Vietnam during the war found a highly significant relationship between exposure to dioxin and onset and severity of diabetes in those individuals with the greatest exposure (Henrikson et al., 1997). This prompted a committee of the National Academy of Sciences' Institute of Medicine (IOM, 2000) to conclude that there was suggestive evidence of an association between dioxin exposure and diabetes.

Pesatori et al., 1998 and Bertazzi et al., 1998 found elevated diabetes in individuals exposed to dioxins at Seveso, Italy. A similar conclusion was drawn by Vena et al., 1998 from a study of phenoxyacid herbicides and chlorophenol production workers exposed to dioxins.

Cranmer et al., 2000 studied a population of individuals exposed to dioxin from a Superfund site, and demonstrated that plasma insulin concentrations were significantly higher in individuals with elevated dioxin levels. The scientists concluded that high serum dioxin levels are associated with insulin resistance.

Longnecker et al., 2001 studied 2,245 pregnant women, 44 of whom had diabetes. The mean serum PCB level in the women with diabetes (3.77 ppb) was 30% higher than the controls (2.79 ppb). The relationship of

PCB levels to the adjusted odds ratio (OR) for diabetes was linear. Taking PCB levels < 2.50 ppb to have an odds ratio of 1.0, the OR was 2.9 for PCB levels 2.50-3.75, 4.4 for PCB levels 3.75-5.00 and 5.1 for PCB levels greater than 5.0. All values were statistically significant, showing that increased exposure is associated clearly with increased risk.

Strong support for this relationship is also found in the Fierens et al., 2003 population-based study which showed that, after adjustment for age and other variables, that the total toxic equivalency factor (TEF) and 12-marker PCB concentrations were 62% and 39% higher, respectively than in controls. The ORs were 5.1 (95% confidence interval (CI) = 1.18-21.7) for dioxins, 13.3 (95% CI = 3.31-53.2) for coplanar PCBs and 7.6 (95% CI = 1.58-36.3) for 12 marker PCBs.

Vasiliu et al., 2006 investigated a Michigan cohort that had elevated exposure to polybrominated biphenyls (PBBs), and found a significant risk of diabetes with PCB concentrations (OR 2.33, 95% CI = 1.25-4.34), but not with PBB concentrations.

The strongest evidence for the relationship between PCB and other organochlorine exposure and diabetes has come from use of the US National Health and Examination Survey data. Lee et al., 2006 studied PCB 153, two dioxin congeners and three pesticide levels in relation to risk of diabetes in 2,016 adults. For PCB 153, the OR for individuals with serum levels in the greater than 90<sup>th</sup> percentile was 6.8 (95% CI = 3.0-15.5), and the p for trend was <0.001 with increasing concentration. Porta, 2006 stated: "Another striking finding in Lee and co-workers' study is that there was no association between obesity and diabetes in individuals with non-detectable levels of persistent organic pollutants. Obesity was a risk factor

for diabetes only if people had blood concentrations of these pollutants above a certain level. This finding might imply that virtually all the risk of diabetes conferred by obesity is attributable to persistent organic pollutants, and that obesity is only a vehicle for such chemicals. This possibility is shocking.

Rylander et al., 2005 also reported a significantly elevated risk of diabetes in relation to concentrations of PCB 153 in Swedish fisherman and their wives.

Everett et al., 2007 independently analyzed similar data to that used by Lee et al., 2006 in determining diabetes risk for exposure levels of PCB 126 in 2,090 persons. PCB 126 levels >83.8 pg/g showed an OR for diabetes of 3.68 (95% CI=2.09-6.49) as compared to PCB 126 levels < 31.2 pg/g. The results of Lee et al., 2006 and Everett et al., 2007 are of particular interest because PCB 153 is not active at the dioxin receptor, whereas PCB 126 is. Therefore it may be that both dioxin-like and non-dioxin-like PCBs increase risk of diabetes.

In a follow-up study, Lee et al., 2007 found that the relationship with diabetes was much greater for the sum of four dioxin-like PCB congeners than it was for the sum of three dioxins, the sum of three furans, the sum of five non-dioxin-like congeners or the sum of four organochlorine pesticides.

Our research team, Codru et al., 2007, has recently reported that in a Native American population that is not particularly highly exposed to PCBs and pesticides, there is a significant relationship between tertiles of PCBs, hexachlorobenzene and DDE and risk of diabetes, identified either on the basis of having been diagnosed by a physician or by having a fasting blood glucose level of 125 mg/ml or higher. For total PCBs, the chance that an individual would have diabetes if their PCB levels were in the top tertile was 3.9 fold greater than that for individuals whose PCBs levels were in the bottom tertile after adjustment for gender, age, body mass index and smoking. For the two pesticides, the risks were even more elevated. However for mirex, a different organochlorine pesticide, there was no significant elevation in risk of diabetes with exposure. When individual PCB congeners were studied, the risk associated with PCB 74 (a congener most associated with consumption of contaminated fish) was 4.9 fold for the highest to lowest tertile.

Animal studies are consistent with the evidence that PCB and dioxin exposure increases risk of diabetes. Nishizume et al., 1995 showed that rats given Kanechlor-400 (a Japanese equivalent to Aroclor) showed depressed insulin sensitivity which increased with the duration of PCB exposure, as well as disturbed glucose and lipid metabolism and elevated serum lipids. Stahl, 1995 reported that dioxin alters enzyme activity related to glucose metabolism in rat liver cells. Several older studies have demonstrated morphological changes in the structure of the pancreatic beta cells upon PCB exposure (Kimbrough et al., 1972; Wassermann et al., 1975). Boll et al., 1998 demonstrated that gluconeogenic enzymes in rat liver are altered upon PCB exposure.

### CONCLUSION

Diabetes is a serious, life-threatening disease that is increasing in frequency. It is usually ascribed to obesity and inactivity, along with genetic susceptibility. However, the growing body of evidence strongly indicates that exposure to persistent organic pollutants is important, and indeed may be a **very** important factor, in elevating risk for diabetes.

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Alaska Community Action on Toxics (ACAT) is a statewide environmental health and justice organization established in 1997. Our mission is to assure justice by advocating for environmental and community health. *We believe that everyone has the right to clean air, clean water, and toxic-free food.*

We help communities implement effective strategies to limit their exposure to toxic substances and to protect and restore the ecosystems that sustain them and their way of life.

We work to eliminate the production and release of harmful chemicals by industry and military sources, ensure the public's right to know, achieve policies based on the precautionary principle, and support the rights of Indigenous peoples.

### **The Collaborative on Health and the Environment - Alaska**

The Collaborative on Health and the Environment (CHE) is a national non-partisan partnership of individuals and organizations concerned with the role of the environment in human and ecosystem health. CHE seeks to raise the level of scientific and public dialogue about the role of environmental contaminants and other environmental factors in many of the common diseases, disorders, and conditions of our time. CHE promotes interdisciplinary discussions, sharing of scientific evidence, outreach and education, and an agenda to bring about systemic change in improving environmental public health. Underlying all of CHE's activities is a commitment to strong, uncompromised science. We believe that the truth emerges through discussion and that civility among CHE partners is a condition of honest dialogue and learning. Visit us at: [www.healthandenvironment.org](http://www.healthandenvironment.org).



CHE-Alaska formed as a regional group in December 2005 following the Alaska Conference on Health and the Environment. We invite participation from health care professionals, researchers, health-affected and patient groups, students, advocacy organizations, and any individual concerned about protecting the health of current and future generations from environmental harm. Visit us at: [www.akaction.org](http://www.akaction.org).



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