**Using ZIP Code and GIS Studies to Assess Disease Risk**

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In several recent articles in *EHP*, investigators have attempted to link proximity to hazardous waste sites, as measured by geographic information systems (GIS) or ZIP codes, with increased incidences of various diseases. An implicit assumption in these studies is that proximity is a surrogate for exposure. However, numerous studies have demonstrated that the presence of chemicals in an individual’s environment does not necessarily translate into a dose. For example, Stehr-Green et al. (1988) found that Serum PCB [polychlorinated biphenyl] levels in persons at highest risk of nonoccupationally related exposures ... at 10 sites were within background ranges, even though environmental contamination levels as high as 2.5 parts per billion (ppb) in monitoring well water samples and 330,000 ppb in soil samples were measured.

In a recent study, Fitzgerald et al. (2007) investigated the impact of living near a known source of PCBs on the body burdens of local residents and concluded that

Consequently, it is erroneous to conclude that simply living in geographic proximity to a potential source is synonymous with an exposure, much less a dose, which is the critical determinant of risk.

The pitfalls of relying on spatial location as a surrogate for exposure and potential disease risk is illustrated by the study of Kouznetsova et al. (2007), which using ZIP codes reported an increased rate of hospitalization for diabetes and residential proximity to PCBs as a consequence of living near the Hudson River. The authors described this study as hypothesis generating, but nevertheless concluded that it provided “additional support for a relationship between exposure to environmental contaminants, especially POPs, and risk of diabetes.” We do not understand how a hypothesis-generating study (with no ability to account for a single known risk factor for diabetes) would offer support for an association between a chemical and a disease.

The hypothesis that PCB exposure might be etiologically involved in diabetes risk is not supported by the numerous mortality studies of PCB-exposed workers, none of which were mentioned by Kouznetsova et al. (2007). Table 1 summarizes diabetes mortality in all PCB-exposed occupational cohorts in which such data were reported. These data show no evidence that even prolonged occupational exposure to PCBs, with resulting accumulations approximately 100 times greater than background exposure, poses an increased risk of diabetes. It is reasonable to presume that if PCBs were etiologically implicated as a risk factor for diabetes, there would be increased mortality from diabetes in these cohorts. Because there is not, a more biologically plausible explanation for the findings of increased incidence of diabetes associated with environmental exposure to PCBs is that the accumulation and/or excretion of PCBs is a consequence of diabetes-related metabolic perturbations, not that diabetes is caused by PCBs.

The authors consult for the General Electric Company on matters pertaining to PCBs.

**Table 1. Mortality from diabetes in PCB-exposed occupational cohorts.**

| Study            | Mortality results for diabetes | Cohort size           |
|------------------|-------------------------------|-----------------------|
| Prince et al. 2006a | Total SMR = 0.88; 95% CI, 0.5–1.43 | 2,572 most heavily exposed M and F capacitor workers |
| Prince et al. 2006b | Total SMR = 0.88; 95% CI, 0.7–1.12 | 14,458 M and F capacitor workers |
| Rudor et al. 2006 | Lowest tertile SMR = 0.42; 95% CI, 0.1–1.5 | 3,569 M and F capacitor workers |
| Kimbrough et al. 2003 | Hourly workers | 7,075 M and F capacitor workers |
| Loomis et al. 1997 | SMR = 0.56; 95% CI, 0.49–0.64 | 138,905 M electrical utility workers |

Abbreviations: CI, confidence interval; F, female; M, male; SMR, standardized mortality ratio.

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**ZIP Code and GIS Studies: Kouznetsova et al. Respond**

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There is strong evidence that exposure to persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs), is associated with an increased risk of diabetes, and that evidence does not come only from studies of residential proximity to waste sites. In our studies in an adult Native-American population, individuals in the top tertile of serum PCBs showed a 3.9-fold [95% confidence interval (CI), 1.5–10.6] elevated risk of diabetes after adjustment for age, body mass index, smoking, sex, and serum lipid levels (Codru et al. 2007). Diabetes was defined as either taking prescription antidiabetes medication or having a fasting glucose level of > 125 mg/dL. In another study, Lee et al. (2006), using NHANES (National Health and Nutrition Examination Survey) data, found a dose-dependent relationship between prevalence of diabetes and serum concentrations of six different organochlorine compounds.
compounds, including one PCB. Other studies reporting this relationship are cited in our recent article (Codru et al. 2007).

The occupational studies listed by Golden and Schell do not demonstrate a relationship with diabetes. However, absence of evidence does not mean evidence of absence. Most occupational studies have poor exposure assessment and short follow-up periods, and are compromised by the healthy-worker effect.

Studies such as ours (Kouznetsova et al. 2007) do, of course, have limitations, in that we do not have personal information of exposure to individuals beyond their ZIP code of residence. But they also have strengths, especially in the very large numbers of hospitalizations and the uniformity of the data-collection system in New York. We recognize the limitations, which we discussed extensively in our article. Although it is difficult to control for all confounders in investigations such as this, they are hypothesis generating and should lead to studies where exposure can be better assessed. This we have done. Our parallel study (Codru et al. 2007), in which we assessed exposure by measuring serum PCBs and fasting glucose, provided extremely strong support for the conclusion of Kouznetsova et al. (2007): that simply living near a PCB-contaminated site (in this case the Hudson River) poses a risk of both exposure and disease.

We have also reported an elevated rate of hospitalization for cardiovascular disease and heart attacks among individuals living in ZIP codes containing waste sites contaminated with POPs, especially along the Hudson River (Sergeev and Carpenter 2005). Also, in another study with excellent exposure assessment, we demonstrated that elevated exposure to PCBs leads to elevated levels of serum lipids and heart disease in a human population (Goncharov et al. 2007).

Golden and Schell actually have two arguments, each fallacious. First, they discount our evidence that residential proximity to hazardous waste sites leads to disease, arguing that some others have not demonstrated elevated serum PCB levels. The above observations show that this is not so. Golden and Schell’s last sentence basically accepts the evidence that “increased incidence of diabetes [is] associated with environmental exposure to PCBs,” but then they argue that this relationship is a consequence of diabetes-related metabolic perturbations. You really cannot have it both ways. We have demonstrated that residence near the Hudson River (where average income is higher and there is less smoking, more exercise, and better diet than in the rest of New York State) is associated with increased rates of hospitalization for not only diabetes and heart disease but also hypertension (Huang et al. 2006), stroke (Shcherbatykh et al. 2005), and chronic respiratory disease (Kudyakov et al. 2004). These associations cannot be explained away by “diabetes-related metabolic perturbations.”

The mechanisms responsible for the relationship between PCB exposure and these multiple chronic diseases are not certain, but it is likely that they result from secondary to posttranscriptional gene regulation. The studies of Adeeko et al. (2002) and Vezina et al. (2004) demonstrate that a very large number of diverse genes show altered expression upon exposure to POPs. There is still a lot that we do not know, but it is very clear that these chemicals are dangerous compounds and that exposure to them is associated with an elevated risk of a variety of chronic human diseases.

The authors declare they have no competing financial interests.

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