Environmental Organochlorine Exposure and Risk of Breast Cancer

Polychlorinated biphenyls (PCB's) and dichlorodiphenyl-trichloroethane (DDT) are persistent organic pollutants in the Great Lakes and other aquatic ecosystems. Currently in North America, human exposure to these compounds occurs primarily through the ingestion of contaminated fish, meat and dairy products. Many of these compounds have anti-estrogenic activity, stimulating estrogen receptors in both animal and human tissue. Yet others of these compounds have anti-estrogenic capacity. This estrogenic effect of xenobiotics in wildlife include an altered male:female sex ratio among California gulls exposed to DDT.

The large variations in international breast cancer rates, and the sustained rise in incidence in most countries, have prompted research into possible etiological factors for this disease. Among known risk factors for breast cancer are those related to the duration of breast exposure to physiologic estrogen (early age at menarche, late menopause); prolonged lactation, which interrupts this exposure, is protective. Thus, there is interest in whether “environmental estrogens” may contribute to the development of breast cancer. This newsletter reviews ten recent papers which have addressed DDE, PCB or other organochlorine exposure and breast cancer risk in women.

The first study, by Wolff, et al. at Mount Sinai, was a nested case-control study which examined the relationship between serum DDE (the stable metabolite of DDT) and PCB levels and breast cancer. The study was conducted within a large cohort study, the New York University Women’s Health Study. Between 1985 and 1991, 14,290 women were enrolled in the cohort, had screening mammography, and blood drawn and frozen. From among 1805 white, 230 black, and 62 Asian women identified as having developed breast cancer during the follow-up period (through 1990), random samples of fifty from each racial/ethnic group were selected as the cases. Matched controls were identified from the cohort. Serum DDE and PCB concentrations were determined in cases and controls. Results: Mean differences in DDE and PCB serum concentrations did not differ between cases and controls, for the racial/ethnic groups combined. Serum levels of both agents tended to be higher among black patients compared to white controls, and slightly lower among white cases compared to Asian controls. PCB levels were somewhat lower in white cases, compared to white controls. Adjusting for known risk factors did not alter the result. The authors note several limitations of the study, including a relatively small sample size (which would decrease the likelihood of identifying a small relative risk, if it exists) and inability to control for lactation history. They also note that the DDE levels measured in this group of northern Californian women were much higher than those reported by Wolf, et al., and raise the possibility of a “leveling-off” effect at higher exposure levels. They note that any alterations in DDE and PCB serum levels associated with the cancer itself would be avoided by the prospective design of this study. The authors conclude that the current data do not support an association between DDE and breast cancer risk. They recommend that future research should address the possibility of a “leveling-off” effect at high exposure levels, and the effects that lactation and estrogen/progesterone receptor status have on the relationship between organochlorine exposure and breast cancer risk.

A hospital-based case-control study was conducted by Lopez-Carrillo, et al. to examine the relationship between DDT exposure and breast cancer in Mexico, where DDT is still used for malaria control. The study took place at three referral hospitals in Mexico City, from 1994 to 1996. Cases were women at three referral hospitals, between 1994-1996, with a new diagnosis of histologically confirmed breast cancer. There were 141 cases, with age-matched controls, who underwent interviews regarding reproductive, lactation, diet and occupational histories, evaluation of Body Mass Index, and blood sampling for DDE and p,p'-DDT determinations. Results: The mean DDE levels were not significantly different between cases and controls. There were also no differences between the cases and controls regarding p,p'-DDT levels. OR’s for the higher tertiles of DDE levels versus the lowest tertile was low (0.97, 95% C.I. 0.38-2.42), thus indicating that there was no dose-response relationship between DDE levels and breast cancer risk. The authors note that in contrast to other case-control studies, they were able to control for multiple known

(Continued on page 2)
variables associated with breast cancer risk. They conclude that their data do not support an association between DDT exposure and breast cancer, but that the possibility of an etiologic role at higher DDT concentrations is not excluded.

European investigators (van’t Veer, et al.) conducted a multi-centered case-control study to examine the relationship between DDE levels in adipose tissue and the presence of breast cancer in women in Germany, the Netherlands, Northern Ireland, Switzerland, and Spain. They found a statistically significant association between DDE levels and breast cancer risk; however, there was no increased risk with levels of mirex above the limit of detection. In addition, there was no evidence of an increased risk with higher levels of DDE or PCB'S and breast cancer risk. The authors conclude that their data do not support a relationship between DDT or PCB'S and risk.

Finally, a recent nested case-control study by Hoyer, et al., reports on the experience of Danish women enrolled in the Copenhagen Women's Health study (CCHS). These were 7712 women who enrolled in the study in 1976 and provided a blood sample at that time. Cases were women who developed breast cancer from the beginning of the study until 1993 and were identified using the Danish Cancer Registry, two age-matched controls per case were identified from the CCHS cohort. The serum levels of DDE and PCB were analyzed for 28 PCB congeners, and 18 organochlorine pesticides or metabolites (mirex, dieldrin, aldrin, endrin, \( \gamma \)-chlordane, \( \delta \)-chlordane, heptachlor, heptachlor epoxide, oxychlordane, transnonachlor, \( \gamma \)-HCH, \( \delta \)-HCH, PCB, and five DDT-related compounds). The results show that the association between body-mass index and plasma DDE; cholesterol-adjusted. Results: Both DDE and PCB concentration rose with age. There was a positive association between body-mass index and plasma DDE; however, there were no associations between body-mass index and current alcohol use strengthened the inverse response relationship seen (OR 2.42, 95% C.I. 0.98 -4.32). There was a slight risk with increasing concentrations of \( \delta \)-HCH. The risk from these two agents were strengthened when excluding cases diagnosed within five years of serum sampling. There was no association seen for DDT isomers, PCB congeners, or other organochlorine contaminants. The authors note that there is no experimental evidence for estrogenicity of dieldrin; they suggest that their results regarding \( \delta \)-HCH require replication and further evidence of biological plausibility. They note that their data do not support a relationship between DDT or PCB'S and risk.

Conclusion: The observation of risk for breast cancer from dieldrin and beta-HCH in a single study is interesting and requires confirmation. The weight of current epidemiologic evidence cast doubt is sufficient to support an association between DDT or PCB exposure and the development of breast cancer in women. One possibility is that DDT and some PCB congeners do not increase the risk of breast cancer. Another possibility is that, if such an association exists, it may be a weak one, and the cited negative studies had insufficient power.

REFERENCES: