

A PILOT CASE CONTROL STUDY OF BREAST CANCER AND DDT/DDE SERUM LEVELS IN WOMEN LIVING IN THE NORTH OF VIETNAM

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ABSTRACT: There has been a positive association reported between elevated tissue organochlorines (DDT/DDE, PCBs, dioxins) and breast cancer in some previous case-control studies. Several studies on dioxin-exposed workers suggest an association between dioxin exposure and breast cancer. We previously reported levels of organochlorines such as DDT and its metabolite DDE to be high in women living throughout Vietnam. Also, dioxins, dibenzofurans and PCBs were found to be very low in northern Vietnamese and higher in southerners. We report here a small pilot DDT/DDE and breast cancer case-control study conducted in northern Vietnam during 1994, with twenty-one cases and twenty-one controls. We found no statistically significant association between DDE, DDT, total DDT or PCB serum levels and an increased risk of breast cancer. We plan to repeat this study in the south of Vietnam where dioxin, PCB, and DDT/DDE levels are all elevated.

INTRODUCTION: The incidence of breast cancer among American and Canadian women has been steadily increasing for the past thirty years⁽¹⁾. Currently, no definitive explanation for this occurrence exists. It has been suggested that environmental factors, including diet, play an important role. This hypothesis is based on several migrant-studies from low to high incidence areas, for example, Japanese women who have migrated to North America from low incidence areas. It has been shown that within three generations, there is an equalization in breast cancer incidence rates between the daughters of Japanese immigrant women and Caucasian (European-American) women. Several prior breast-cancer related studies have reported associations between DDE and breast cancer⁽²⁻⁴⁾. PCDD/Fs, with similar chemical and toxicological properties to PCBs, are potent promoters of cancer in *in vivo* and *in vitro* studies. These compounds also appear to initiate cancer in humans as well as in laboratory animals.⁽⁵⁻¹⁰⁾ The published literature does not yet provide a clear relationship between chemical exposure from organochlorines and breast cancer.

We designed this study to add to previous studies which have shown an association of DDE, PCBs and beta-HCH to breast cancer in American and Finnish women.⁽²⁻⁴⁾ Breast cancer has been hypothesized by some to be related to total organochlorine body burden. PCB, dioxin, and dibenzofuran levels in the blood of Vietnamese women living in the south

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are usually similar to that of American women as compared to the north of Vietnam, where levels are considerably lower.⁽¹¹⁻¹⁴⁾ There is a low incidence of breast cancers in Vietnam and other Southeast Asian countries compared with western industrialized nations.⁽¹⁵⁾ It has previously been found that DDT and beta-HCH levels in women throughout Vietnam are high.^(16,17) Vietnam offers the possibility of studying the effects of DDT, DDE and beta-HCH to breast cancer separate from and also with PCBs and dioxins.

METHODS. We conducted a pilot, hospital-based, case-control study in one area of north Vietnam, in Hanoi and nearby rural localities. Breast cancer cases and controls (twenty-one subjects in each cohort) were interviewed concerning known breast cancer risk factors; their residence, migration histories, occupational exposures, and their dietary habits with particular reference to the intake of meat, milk and fish.

The study cases were obtained from the first twentyone histologically-confirmed cancer cases detected consecutively at the Oncology hospital in Hanoi during the study period in 1994. Only Vietnamese women born in north Vietnam, with no other prior diagnoses of cancer, were eligible for this study. The controls were selected from women undergoing breast surgical biopsy for suspicion of breast cancer who, upon review of the pathological documentation, were found to be free of breast tumors. These controls were individually matched to the breast cancer cases by place of residence (city of Hanoi or elsewhere) and by age at diagnosis (\pm one year).

Containers used for the blood were free of organochlorines. Cells and serum were separated and frozen in different containers. Specimens were kept frozen until analyzed for PCBs and DDT/DDE at Mt. Sinai Medical School. The protocol for determining DDE and PCBs has been described previously.^(18,19)

For evaluation of breast cancer risk associations, the data were analyzed using conditional logistic regressions. To assess the increase in breast cancer associated with different levels of organochlorine residues, we classified the subjects in tertiles using the frequency distribution of all subjects combined. The effects of potential confounding variables, such as age at menarche, number of full-term pregnancies, lifetime months of lactation, and weight adjusted by height (Quartet indexes) were evaluated but none of these variables altered the regression coefficients in any appreciable way so that the results are reported unadjusted (except matching criteria).

RESULTS. Table 1 illustrates selected characteristics of the case and control study subjects. Our previous data of DDT, DDE, PCBs and beta-HCH in human milk from Vietnam and the U.S.⁽¹⁶⁾ is presented in Table 2. The milk samples from Vietnam showed consistently elevated levels of DDT, DDE, and beta-HCH, in all geographic locations sampled, north or south. Table 3 reviews our previously reported data on human blood from Vietnam and the US.^(11,13,20) Presented in Table 4 are the organochlorine levels measured in the entire north Vietnam study group (cases and controls) classified by geographic area of residence, urban vs. rural (Hanoi). The values suggest higher levels of the compounds in urban as opposed to rural area individuals. DDE was consistently higher in both compared with the US.⁽²¹⁾ Table 5 shows the mean and standard deviation in organochlorine levels for cases and controls. The levels of DDE and DDT are 12.17 and 2.33 ng/mL for the cases and 16.67 and 2.38 ng/mL for the controls, respectively.

CONCLUSIONS: The purpose of this pilot study was to test the hypothesis that elevated levels of DDT/DDE may be associated with breast cancer. Initial review of the data from this

small pilot study does not seem to support the hypothesis that organochlorine exposure is an important etiologic factor for breast cancer in this population. The possible role of dioxins and dibenzofurans as cofactors, promoters or possibly inhibitors of breast cancer will be studied in a similar pilot study in the south of Vietnam where PCB and PCDD/F body burdens are much higher in comparison to the north. The relatively small sample size also works against possible positive statistical associations.

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TABLE 1. SELECTED CHARACTERISTICS OF STUDY SUBJECTS (MEAN & SD), 1994

	Cancer Patients N = 21	Controls N = 21
Age (Years)	42.3 +/- 6.9	42.3 +/- 7.0
Age at Menarche	16.9 +/- 2.2	16.2 +/- 2.5
Age at 1st pregnancy*	26.1 +/- 5.0	26.1 +/- 4.0
Number of Children	3.2 +/- 1.7	2.5 +/- 1.5
Lifetime Lactation (months)*	49.9 +/- 26.0	42.7 +/- 18.9
Maximum Weight (Kg)	50.22 +/- 5.0	51.4 +/- 5.9

* N=18.

**TABLE 2. SELECTED ORGANOCHLORINE PESTICIDES AND PCBs
IN HUMAN MILK (ppb/Lipid)**

Substance	South Vietnam (N = 22)	North Vietnam (N = 2)	USA (N = 7)
Beta-HCH	344	836	20
PCB as Clophen A60	334	154	378
p.p. DDE	10955	11480	541
p.p DDT	5760	3770	23

TABLE 3. DIOXINS AND DIBENZOFURANS IN HUMAN BLOOD (ppt,Lipid)

	South Vietnam* (N=483)	North Vietnam* (N = 82)	USA** (N.= 44)
Total Dioxins (PCDDs)	759	185.8	1019
Total Dibenzofurans (PCDFs)	94.4	101.1	67
Total PCDD/Fs	853.4	286.9	1086
Total TEQs	31.3	15.3	26.7

* Reference 15

** Reference 21

TABLE 4. LEVELS OF DDT, DDE, TOTAL DDT AND DDE
IN THE BLOOD SERUM FROM NORTH VIETNAMESE WOMEN

Compound	Rural N = 30	Urban N = 8
DDE	9.24 +/- 10.18	24.84 +/- 12.97
DDT	1.38 +/- 1.27	4.61 +/- 2.92
Total DDT	11.68 +/- 12.11	32.30 +/- 17.16

TABLE 5. SERUM LEVELS OF ORGANOCHLORINES BY CASE-CONTROL
STATUS, 1994 (Mean +/- Standard Deviation)

	Cancer Patients N = 21	Controls N = 21
DDE (ng/mL)	12.17 +/- 11.08	16.67 +/- 18.98
DDT (ng/mL)	2.33 +/- 2.10	2.38 +/- 2.65
Total DDT (ng/mL) (DDT + DDE)	14.50 +/- 13.98	19.05 +/- 23.55