

## Timing of DDT Exposure and Breast Cancer Before Age 50

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The insecticide dichlorodiphenyltrichloroethane (DDT) was introduced in 1945 and is still used for malaria control where needed. The United States banned DDT in 1972, as have other countries, because DDT disrupts wildlife reproduction. DDT is no longer detectable in the majority of human samples in the United States, although a common DDT metabolite, dichlorodiphenyldichloroethene (DDE), is still found in most human serum specimens.

Previous breast cancer studies have measured DDE as a surrogate of lifetime DDT exposure, usually in specimens obtained decades after DDT had been banned. This design may have obscured true past exposure due to variation in exposure intervals and elimination rates; these prior studies have been largely negative. Previous studies also did not consider timing of exposure.

We tested the hypothesis that DDT is a stronger breast cancer risk factor for women who are exposed during childhood and adolescence, when undifferentiated cells are most vulnerable. We measured DDT and DDE in blood samples drawn during active DDT use.

We measured serum levels of DDT and DDE during the early postpartum in 131 age-matched case-control pairs in a prospective, nested case-control study in the Child Health and Development Studies, a pregnancy cohort based on the Kaiser-Permanente Health Plan, near Oakland, California. Women entered the study while pregnant, between 1959-1967, before DDT was banned. The average time between serum sampling and breast cancer (before age 50), was 16 years. DDT and DDE were detected in all subjects. Median DDT was 11.64 ng/ml and median DDE was 46.31 ng/ml. We estimated DDT associations with breast cancer in conditional logistic regression models adjusted for age at first pregnancy, age at menarche, parity, race, DDE, total cholesterol and total triglycerides. We found that risk of breast cancer increased with increasing concentrations of serum DDT for women exposed in childhood or adolescence. The odds ratio (OR) for the second versus the first tertile of DDT was 3.9, 95% Confidence Interval (95% CI)= 1.4, 10.9. The OR increased to 10.4, 95% CI= 2.5, 43.2 for the third tertile of DDT exposure versus the first. This trend over quartiles was significant ( $p < 0.001$ ). The DDT association with breast cancer was significantly stronger for women exposed to DDT before age 15 than for women exposed after age 15 ( $p < 0.02$ ). Similar results were obtained with lipid-adjusted DDT and DDE.

Our findings are consistent with prior studies of radiation effects on breast cancer (for atomic bomb and for therapeutic radiation) where increased risk of breast cancer was reported primarily for women exposed in childhood or adolescence. Our study provides further support for the hypothesis that environmental risk factors have maximum effects on early breast cancer when exposure occurs prior to reproductive maturation.

