

## Dioxins and Endometriosis: Cohort Study of Women in West Virginia

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### Introduction

Kanawha Valley of West Virginia has a history of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin contamination (dioxin, TCDD). The bulk of the dioxin found in this area appears to be derived from the production of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and the disposal of associated wastes. The 2,4,5-T was produced between 1948 and 1969 in the Kanawha Valley; during the years of production, the waste containing high concentrations of dioxin was deposited in several waste sites throughout the Kanawha Valley. More than thirty years after production of 2,4,5-T was stopped, the USEPA has found that dioxin still resides in the soils, sediments, groundwater, and river water in portions of the Kanawha Valley. High levels of the toxic dioxin have been detected in the Kanawha River and at outfall locations on the river. Dioxin has been also identified in other water bodies downstream, including hundreds of miles of the Ohio River.

The women in this endometriosis/dioxin health study reside in the Kanawha/Ohio River Valley area of West Virginia and comprise a potential cluster (cohort) of individuals who have been exposed to dioxins (dioxin and dioxin-like chemicals) at background levels higher than those seen in other areas of the United States. The emissions from an unique constellation of chemical industries appear to have led to high levels of environmental dioxin contaminants. In addition, this area has a high incidence of endometriosis. Previous animal studies, both in

nonhuman primates and rodents, have demonstrated a correlation between dioxin exposure and endometriosis<sup>1-6</sup>. Human epidemiology studies have suggested an association but have not demonstrated a statistically significant correlation, possibly due to limitations in study design such as insufficient numbers, measurement of only TCDD rather than total equivalents to TCDD (TEQs), and/or lack of surgical ascertainment of endometriosis. The present study is addressing these issues. Thus, we have the unusual congruence of identified emission sources and high background levels of dioxins and a potentially related elevation of endometriosis.

Endometriosis is a condition suffered by women in which the endometrial tissue, that usually lines the uterus, migrates to other areas. Most commonly it is found in the abdomen, bladder, ovaries or bowel. Patients with endometriosis experience pelvic pain, irregular bleeding, infertility and other problems. Immune suppression has been associated with severe endometriosis<sup>7</sup>. This debilitating condition is a poorly understood disease. In the United States, this condition affects millions of women in their reproductive years and is showing up more frequently in very young women. Endometriosis will seriously impact future fertility and health care utilization. Data suggest that the rate of endometriosis in the Kanawha and Ohio River valleys is higher than is seen in other regions of the United States.

## **Objective**

This study addresses the hypothesis that dioxin is associated with the observed increase in endometriosis in the developed world. The study will evaluate a potential link between human dioxin exposure and the incidence of endometriosis in a potentially highly exposed population in West Virginia. The combination of the high incidence of endometriosis and the high levels of dioxins in the environment in West Virginia makes this population unique, increasing our ability to detect an association, if it exists.

## **Methods**

The subjects in the present study comprise a cohort of women who may have been exposed to dioxins at background levels higher in West Virginia than those seen in other areas of the country. In addition, the rate of endometriosis has been increasing and the age of onset has been decreasing in the Kanawha Valley of West Virginia.

Physicians at Marshall University Medical Center (Huntington, WVA) are the primary care providers for the women patients (control and test groups) and

have developed the trusting relationships needed to conduct the present study. Importantly, there will be a sufficient number of subjects in this study to demonstrate a statistically significant correlation between dioxin and endometriosis. A detailed medical history will be obtained from all study participants. In addition, an environmental exposure questionnaire will be administered to all participants.

Test groups consist of patients undergoing diagnostic laparoscopy for endometriosis, or patients that have previously been diagnosed as having endometriosis and who are undergoing hysterectomy or other related surgery such as laser treatment for endometriosis. Control groups consisting of the same number of patients will be age-matched (25-45) to the test groups. Two control groups will be identified and samples of blood and will be collected: the first group will consist of symptomatic individuals undergoing diagnostic laparoscopy with negative findings, and the second group will be comprised of an asymptomatic group of female patients undergoing elective laparoscopy and laparotomy for other reasons, such as cholecystectomy and confirmed to be free of endometriosis.

Exposure of patients (test and control groups) will be evaluated by determining total equivalent (TEQ) dioxins which includes dioxin congeners and dioxin-like chemicals including PCBs. The samples of blood and adipose tissue from these patients will be evaluated for the total TEQ using the CALUX<sup>®</sup> bioassay<sup>8-11</sup>. A selected number of positive samples then will be analyzed for specific dioxin congeners.

The environmental and medical history surveys will be compiled into a database and statistically analyzed to determine if a correlation exists between exposure to dioxins and endometriosis.

## Results and Conclusions

The present cohort study explores the association of dioxin and endometriosis in a highly exposed population of women in West Virginia. The study design has been carefully planned as described above. Surgical ascertainment of endometriosis is essential to avoid misdiagnosis. This cohort study includes women with and without endometriosis coupled with adequate exposure determination. All of these factors in the study design are critical in providing clear evidence for the role of dioxins in the increased incidence of endometriosis, if this association exists.

This cohort study of women is at the beginning stages of its implementation. Women are being selected as participants (control and test group

alike) and are completing environmental and medical histories. All necessary consent forms are being reviewed and signed by the subjects. At this time, a few of the participants have completed the preliminary processes and have undergone surgical procedures and tissue samplings.

This study will evaluate a potential link between human dioxin exposure and the incidence of endometriosis. It will provide epidemiological data regarding environmental dioxin exposure; establish population group data on tissue dioxin levels that are linked to an environmental database; determine the levels of dioxins in human fat; and correlate levels of dioxins in blood with those in fat tissue in humans.

#### **Acknowledgements and Disclaimer**

The authors thank Samuel L. Rotenberg for addressing the needs of USEPA Region 3; Ken Ellison for his support in securing West Virginia state funds; Sandy White for her technical and data support; and Mary Lou Ballweg, Sherry Rier, and Kevin Osteen for their helpful comments during the review process.

This work is being funded in part by a cooperative agreement (CR-831516010) with USEPA under the RARE Program and West Virginia Department of Environmental Protection.

This abstract does not reflect USEPA policy.

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