TWO CASE REPORTS: I. DIOXIN LEVELS IN BLOOD OF TWO PAPER MILL WORKERS WITH NON-HODGKIN'S LYMPHOMA. II. ELEVATION OF DIOXINS IN BLOOD, LIVER AND FAT IN AN AMERICAN VETERAN WHO DIED OF SOFT TISSUE SARCOMA

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Objective: Non-Hodgkin's lymphoma (NHL) and soft-tissue sarcoma (STS) have been associated with exposure to phenoxyherbicides or phenoxyacetic acids and chlorophenols with contaminating dioxins and dibenzofurans.[1-5] We present two case studies; the first is of two patients with non-Hodgkin's lymphoma and the second is a patient with soft-tissue sarcoma. The two NHL patients, seen in consultation, were both long term employees of a paper and pulp mill in the U.S. Whole blood samples were taken and levels of PCDD/F and PCBs determined. The patient in the second case report was referred to one of us (AS) because of possible occupational exposure to Agent Orange during military service. This possible exposure occurred, surprisingly, in Germany, not Vietnam. This patient was diagnosed with soft-tissue sarcoma and eventually died of this disease. Polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) were measured in a whole blood sample, obtained several months prior to his death, and autopsy specimens of fat and liver tissue, obtained several months after the whole blood sample, to determine whether elevated dioxin levels were present following potential exposure. Also of interest was partitioning between b'ood, fat, and liver tissue in a person with wasting disease, cancer.

Methods: Pooled blood and tissue samples were collected in chemically cleaned glass containers, frozen immediately and kept frozen at -20° C until dioxin analysis was performed. The analytic methods used by the dioxin laboratories[6,7] have been previously reported and will not be repeated here. Dioxin analyses were performed by Stanley and Boggess for the first case study (Fig. I) and Päpke and associates for the second (Fig. II).

Results: Figure I compares PCDD, PCDF, and PCB toxic equivalents in the two NHL patients to U.S. general population levels.[8,9,10] Patients 1 and 2 had been under vigorous treatment, both had chemotherapy, and Patient 2 also had been treated with blood transfusions and a bone marrow transplant prior to our obtaining blood samples. Patient 1, who had elevated dioxin levels, worked in the paper mill for over 38 years prior to blood sample collection. Blood samples obtained from Patient 1 showed some elevations in the levels of 2,3,7,8-TCDD, Penta-CDD, Hexa-CDD, and PCDF, but 2,3,7,8-TCDF was not elevated. He also had an elevated PCB

TEq level when compared with the general population. Patient 2, had been working in the paper mill for over 12 years, but no elevation of PCDD, PCDF, or PCB was found. Figure 2 presents PCDD, and PCDF toxic equivalents for the patient with soft-tissue sarcoma. This patient presented a history involving handling of "Agent Orange" during his military service in Germany to his oncologist and consulting physician. However, besides elevated TCDD (which would be expected from Agent Orange exposure), we note elevated levels of PnCDD, HxCDD, PnCDF, and HxCDF in his whole blood, fat, and liver. This pattern of high elevation of chlorinated dioxins is consistent with dioxin exposure from another source since the herbicide 2,4,5-T of Agent Orange is characteristically contaminated with 2,3,7,8-TCDD.

Conclusions: In the first case study, both TCDD and PCB levels were elevated in patient 1, a paper mill worker with NHL. Although elevated TCDD is characteristic of exposure to chlorine bleaching of paper pulp, PCB elevation is not usually characteristic of paper and pulp effluent. Therefore, this patient may have been exposed to PCBs from some other source, such as consumption of contaminated fish, or PCBs might have been used at his worksite. However, 2,3,7,8-TCDF was not elevated in this patient although 2,3,7,8-TCDD and 2,3,7,8-TCDF are characteristically present in paper and pulp mill effluent when chlorine bleaching has been used. The elevated levels of PCDD/F and PCBs and total TEq found in the NHL patient 1 are consistent with and support the association of exposure of dioxins and dioxin like chemicals to NHL, whether or not the exposure occurred at the worksite. In NHL patient 2, the levels of PCDD/Fs and PCBs are lower than the general population group. Thus no direct association between the NHL and dioxins can be established; it is not clear what the effect of cancer therapy on this patient's blood dioxin levels might have been. In the second case study, the veteran with STS, we would expect to see only 2,3,7,8-TCDD elevation if the exposure was to Agent Orange alone. However in this case, there is an elevation of other PCDD/Fs as well as TCDD. When compared with general population levels of 3.4 ppt, TCDD in this patient is elevated at 19 ppt in blood, 16 ppt in fat, and 13 ppt in liver tissue, all on a lipid basis. However in this case, there is also elevation of other PCDD/Fs in this patient who ultimately died of soft-tissue sarcoma from an unknown source.

In summary, the sources of dibenzodioxin, dibenzofuran, and coplanar PCB elevation in the two (of three) cases are not entirely clear. However, an association of NHL and STS to the elevation of dioxins and related chemicals, PCDD/F and PCBs was found in two of these three cancer patients.

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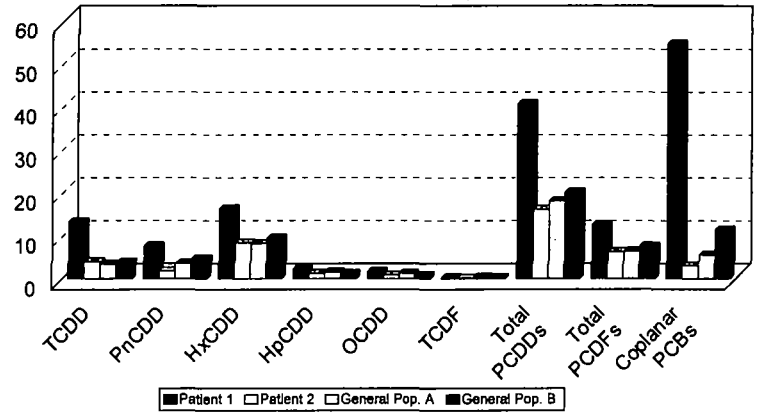
Figure I: PCDD, PCDF, AND PCB DIOXIN TOXIC EQUIVALENTS (TEq) IN TWO NON-HODGKIN'S LYMPHOMA PATIENTS AND THE GENERAL U.S. POPULATION

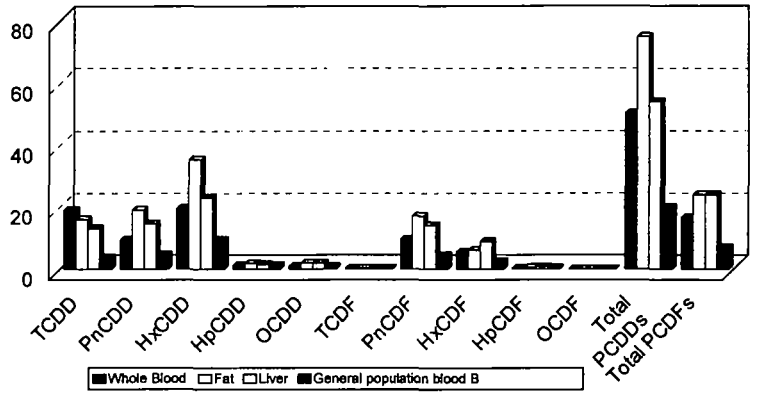
(in parts per trillion, lipid)



General population A has sample size of 6 individual from Missouri Blood Bank. General population B has sample size of 44 individuals for TCDD, and 50 individuals for other congeners (from Michigan adult male residents).

Figure II: PCDD AND PCDF TEq IN WHOLE BLOOD, FAT, AND LIVER OF A PATIENT WITH SOFT-TISSUE SARCOMA COMPARED TO THE GENERAL U.S. POPULATION

(in parts per trillion, lipid)



General population blood B has sample size of 44 individual for TCDD, and 50 individual for all other congeners (from Michigan adult male residents).