FACTORS RELATED TO DIOXIN AND FURAN BODY LEVELS AMONG MICHIGAN WORKERS

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Abstract
We evaluated serum levels of 5 selected dioxin, furan and PCB congeners among 412 workers at a Midland, Michigan plant that manufactured trichlorophenol (TCP), pentachlorophenol (PCP) and formulated chlorophenol-based products. We examined indicators of exposure to dioxins, furans and PCB congeners taking into account intrinsic factors such as age and body fat and potential exposure from consumption of local game and fish and other occupations. All 5 congeners were significantly associated with age and body fat. The workplace exposure metrics were strongly related to the three dioxins analyzed. Other factors such as fish and game consumption and jobs outside of the chlorophenol workplace had only a minor impact on dioxin and furan levels, although they were major determinants for PCB levels. Other than occupational exposure at Dow, age and body mass index were by far the most important determinants of serum levels of the dioxin, furan and PCB levels.

Introduction
2,4,5-Trichlorophenol (TCP) and pentachlorophenol (PCP) were produced and used at the Midland, Michigan manufacturing facility of The Dow Chemical Company from 1937 to 1980. As part of the ongoing epidemiology surveillance of this population, blood dioxin, furan and polychlorinated biphenyls (PCB) concentrations were collected in a sample of these workers. We evaluated certain individual factors since it has been reported that dioxin, furan, and PCB levels are related not only to occupational exposure;[1, 2, 3, 4] but other factors such as age, body fat, recent weight change, gender, diet, and cigarette smoking.[4, 5, 6, 7, 8, 9 ,10, 11]

Materials and Methods
We sampled 412 current and past employees who had worked at the Midland, Michigan plant between 1937 and 1980 and who were still living in the area. We collected approximately 80 ml of blood from each participant. Details and quality control procedures have been described.[12] All results were lipid-adjusted based on methods developed by the CDC.[13] A brief questionnaire was completed by each participant or his or her proxy that addressed smoking, weight change, general consumption of local fish and game in the past year, select occupations with potential for exposure to dioxins and PCBs, and their potential exposure as TCP, PCP and formulation workers. The focus of this paper is on the responses to the questionnaire and exposure metrics related to working in chlorophenol departments.

We limited the analysis of individual congeners to one marker of TCP exposure, (2,3,7,8 tetrachlorodibenzo-*p*-dioxin or TCDD), one marker of PCP exposure (1,2,3,6,7,8 hexachlordibenzo–*p*-dioxin or 1,6-HxCDD), another dioxin (1,2,3,7,8 pentachlorodibenzo-*p*-dioxin or 1-PeCDD), a furan (2,3,4,7,8 pentachlorodibenzofuran or 4-PeCDF) and a PCB (PCB126) We also calculated the total toxic equivalency quotient (TEQ) using the 2005 toxic equivalency factors (TEF) based on all seventeen 2,3,7,8-substituted dioxins and furans and four non-ortho substituted PCBs (PCB77, PCB81, PCB126 and PCB169).[14]

The independent variables representing occupational exposure to dioxins and furans were based on the company job records and exposure metrics defined in previous epidemiology studies of the entire chlorophenol cohort. These included cumulative duration of TCP exposure alone (years), cumulative duration of PCP exposure alone (years), cumulative duration of mixed PCP or TCP exposure (years), cumulative estimated exposure of TCDD (sum of intensity days for each exposed job), and cumulative estimated exposure of hexachlorodibenzo and octachlorodibenzo dioxins (H/OCDD; sum of intensity days for each exposed job). Medically documented cases of chloracne were also noted. Other exposure related factors included “ever worked in a TCP job”, “ever worked in a

PCP job", number of years employed at Dow regardless of years worked in chlorophenol jobs, and number of years from employment termination to the date of the blood draw.

The questionnaire collected information on other sources of dioxin exposure or factors related to dioxin elimination or storage within the body. We evaluated smoking as current smoker (yes, no) and ever smoked (yes, no). Since the information on current smoking provided higher adjusted R^2 in the exploratory analyses, we used only current smoking in the multivariate regressions. Participants were asked about recent weight change. The number of pounds lost and number of pounds gained were evaluated in the regression models.

Information on diet was limited to consumption of specific fish caught in two local rivers or the Great Lakes and game hunted from the county where the plant is located. The fish and game listed by participants were overwhelmingly walleye, in the local rivers (31 of 33 responses), salmon in the Great Lakes (107 of 114), and deer in the local county (76 of 82). Two summary variables were created to reflect recently eating local or Great Lakes fish, and eating local game and/or fowl.

There were 10 questions on specific jobs with a potential for exposure to dioxins, furans and PCBs. There was evidence of misinterpretation in some of the other job questions. Most problematic was the question "Have you ever been employed in the professional application of the herbicide 2,4-D or 2,4,5-T?" Nearly all the affirmative responses were among Dow workers with jobs in the *manufacture* or *formulation* of these herbicides. We concluded that workers misunderstood the intent of this question, and, therefore, we did not use their responses in the subsequent analyses. Also, we did not use "working in right of way clearance" in the analyses for the same reason. Conversely, jobs in lawn care, farming, foundry and auto working were jobs rarely held within the company by the study participants. No participants reported working in sod production. The remaining occupations with opportunity to use herbicides (farming, lawn care, and forestry) were grouped into a single variable.

Backwards linear regression was used to model serum dioxin congeners as functions of occupational exposure, health (self reported weight change and smoking) and self-reported occupation and diet. Covariates remained in each model if the p value was less than 0.10. Logistic regression models were also used to evaluate the associations of the independent variables with serum levels being above or below the 75 percentile. The categorical results were similar to those with linear regression and are not discussed further.

Results and Discussion

In the multivariate models the personal factors of body mass index (BMI) and age, and self-reported eating local game and working with hazardous waste were correlated with serum levels for all 5 congeners and the TEQ. The self-reported jobs in a foundry or automobile plant (jobs external to Dow) were negatively correlated for all congeners except PCB126. The company chlorophenol exposure metrics created for past epidemiology studies based upon job descriptions were consistent with serum measures.

In general, the available information on diet, occupation, and personal factors contributed to less than half of the variability in the serum levels for the dioxins, the furan and TEQ (Table 1). Further, the self-reported information explained less than 5% of any dioxin or furan variability. PCB levels were largely influenced by self-reported diet. Since the factors related to working at a foundry or an automobile plant were negatively correlated with dioxin or furan serum levels, this is more likely to be a measure of shorter time employed at Dow than exposure outside of Dow. Most important in understanding these specific dioxin and furan congeners were BMI, age and the job exposure metrics from the Dow work history.

Table 1. Partial contribution to the adjusted R^2

Congener	Overall	Dow job metrics	BMI and age	Self-reported diet*	Self-reported job**	Self-reported smoking and weight change
TCDD	0.41	0.16	0.25	0.00	0.01	0.01
PeCDD	0.35	0.16	0.14	0.01	0.02	0.01
1,6-HxCDD	0.47	0.36	0.08	0.01	0.01	0.01
4-PeCDF	0.19	0.03	0.11	0.02	0.02	0.01
PCB126	0.18	0.00	0.04	0.09	0.00	0.04
TEQ05	0.41	0.18	0.19	0.02	0.02	0.01

*Diet includes eating fish from Saginaw or Great Lakes; game and fowl from Midland County.
** job categories external to Dow

We found little impact from diet upon the specific dioxins or the furan. This finding is similar to the recent community study.[20] The only significant finding was for PCB126 where half of explained variance was attributable to eating fish. The Great Lakes fish study concluded that the type of fish (trout and salmon) and source (Lake Michigan) were also significant predictors for PCB exposure.[5] We did observe a relationship with the 5 congeners and with the TEQ for eating game, primarily deer, in the last 12 months. However, this effect was very small and contributed very little relative to other exposures, age and amount of body fat.

We also discovered some limitations with the questionnaire. It was clear that participants did not understand some of the survey questions. In addition, the dietary section of the questionnaire may not have accurately captured opportunity for exposure. The question we used only addressed recent consumption. It is likely that most, if not all, respondents who said they ate local fish, game or fowl in the last 12 months, have done so on a regular basis for many years in the past. This could even reflect overall differences in diet, such as consuming more meat overall.

The current serum study is the largest industrial group ever examined for serum dioxin and furan levels. We were able to distinguish different dioxin profiles among former TCP and PCP workers. The workplace exposure metrics were strongly related to the three dioxins analyzed. As a result of the many years since chlorophenol exposure, changes in body weight, metabolism and energy expenditure likely had a considerable impact upon the congener elimination rate and the levels currently observed.[16, 17] The job exposure metric might have been a stronger predictor of congener levels had the sera been collected closer to the time of exposure. Other factors such as fish and game consumption and jobs outside of the chlorophenol workplace had only a minor impact on dioxin and furan levels, although they were major determinants for PCB levels. Other than occupational exposure at Dow, age and BMI were by far the most important determinants of serum levels of the dioxin, furan and PCB levels.

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