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C8 Science Panel

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C8 Study Results

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Below are listed 3 Status Reports submitted to the Wood County Court in Parkersburg West Virginia under the C8 Settlement. Each report is a concise summary of the key findings of this work. More detailed reports are being submitted to a peer-reviewed journal for publication. When they are accepted and published details for accessing them will be provided here. Right-click on the title and save or open the document (pdf format). These three reports arise from work in one of the Science Panel studies "Cholesterol, diabetes, uric acid, and C8 levels among participants in the C8 Health Project"

1. [Status report: Factors associated with PFOA levels in a community surrounding a chemical plant](#)
2. [Status report: Association of perfluorooctanoic acid \(PFOA\) and perfluorooctanesulfonate \(PFOS\) with lipids among adults in a community with high exposure to \(PFOA\)](#)
3. [Status report: A Cross-Sectional Analysis of Type II Diabetes in a Community with Exposure to Perfluorooctanoic acid \(PFOA\)](#)

Procedure for release of Study Results

The Science Panel is planning to complete a series of reports on various health measures and C8 over the coming months and years that

will contribute important knowledge regarding the potential health effects of C8 exposure. We explain here our process for making available these results: to the Court, to the public and the media, and through scientific journals. For a number of these results we are working in collaboration with West Virginia University. When we complete the analysis and interpretation of the data on a specific issue, the following will occur:

1. We will prepare a summary of our findings for the Court and a general audience, and that document will be submitted to the Court and posted here on the Science Panel website once the Court has received it.
2. We will make ourselves available to respond to requests from the media regarding the implications of our findings or other issues of interest.
3. We will prepare a detailed scientific report on the same results, that includes detailed information on the study and its findings for a scientific audience and submit that paper for review and publication by a medical/scientific journal. When the publication is accepted and published we will include a link here so people can locate the full text. We will be able to respond to further press queries at that time.
4. In addition, we will come to the mid-Ohio Valley periodically to meet with interested groups to present and discuss our findings and interpretation in person.

It should be noted that this only concerns release of results from individual studies, not the announcement of the Science Panel's Findings regarding a probable link between C8 exposure and any disease. That determination will require putting together all the evidence and will be handled exclusively through the Court. This is explained on another page on this

website: click on "The Science Panel" on the menu.

Status report: Factors associated with PFOA levels in a community surrounding a chemical plant

The C8 Science Panel (Kyle Steenland, Tony Fletcher, David Savitz)

Oct 7, 2008

This report summarizes the overall pattern of C8 levels measured in the blood serum of the participants in the C8 Health Project carried out in 2005-2006 in the Mid-Ohio Valley population. The extent to which the C8 levels vary in relation to the water district of residence, participants' age and other individual characteristics is explored by statistical models. A full report of these findings will be submitted to a peer-reviewed scientific journal.

Background: Perfluorooctanoic acid (PFOA, also known as C8) is a fluorocarbon which is present in the serum of most Americans at low levels (about 4-5 ng/ml), although the routes of exposure remain unknown. Here we examine factors associated with PFOA in a large population of mid-Ohio valley residents living near a chemical plant, which until recently released large quantities of PFOA into environment, contaminating drinking water.

Methods: The study population was 69,030 community residents living in six water districts contaminated by PFOA, who participated in a 2005-2006 survey (the C8 Health Project) involving a questionnaire and blood sample. Of these, 64,251 had complete data on PFOA blood level and other key information for the analysis. Additional analyses were conducted on a subset (71%) of subjects for whom we had occupational history. Median levels (middle value) of PFOA were calculated in relation to many different factors, like residence in a specific water district, working at Dupont, gender, age, etc. Median levels are a better indication of average levels than the actual arithmetic mean when a relatively small portion of the population has very high levels (which is the case here), skewing the arithmetic mean toward high levels. Linear regression models were also run to determine which factors were associated with serum PFOA levels, after adjusting for other factors.

Results: The arithmetic mean PFOA level of the entire population was 83 ng/ml, with a range from 0.25 to 22,412. The 75th percentile was 71, while the 25th percentile was 13. The median, or 50 percentile, was 28.

The most important predictor variables (in order) were current and past residence in a contaminated water district, and current or former employment at the chemical plant. Without adjusting for other factors, the median levels of PFOA for those currently (at time of survey) living in any of the six water districts was 38 ng/ml. Blood C8 levels for those currently living in

Little Hocking, Lubeck, Belpre, Tupper Plains, Pomeroy, and Mason were 224, 70, 35, 37, 12, and 12 ng/ml, respectively. Sixty-three percent of the population was currently living in one of these districts at the time of the C8 Health Project. Those currently living in water districts further from the plant had lower levels, as would be expected. Adjustment for other factors did not change these values very much.

Those no longer residing in contaminated water districts had lower levels than current residents (median 19 ng/ml). We grouped those not currently living in an exposed water district by the water district they listed as their 'qualifying water district', used to qualify for participating in the C8 Health Project. Participants were required to have lived, worked, or gone to school in their qualifying water district for at least a year. Most of these had lived previously in their 'qualifying water district'. For those not currently living in a contaminated water district, their median levels based on qualifying water district of Little Hocking, Lubeck, Belpre, Tupper Plains, Pomeroy, and Mason were 34, 28, 17, 14, 11, and 11 ng/ml, respectively.

Based on the 71% of the population for whom we had an occupational history, 5% had ever worked at Dupont (2% current, 3% former). The median serum level of PFOA was 148 for current Dupont workers, 75 for former Dupont workers, and 24 for those who had never worked at Dupont.

PFOA was higher for men vs women; median 34 vs 24 ng/ml. Levels were somewhat higher for young people and old people, compared to those in between.

Conclusions: PFOA levels in this population vary with distance of residence from the plant and employment at the plant. The effect of age and gender reflected prior findings. Effects of other demographic and lifestyle covariates are relatively weak.

Status report: Association of perfluorooctanic acid (PFOA) and perfluorooctanesulfonate (PFOS) with lipids among adults in a community with high exposure to (PFOA)

The C8 Science Panel (Kyle Steenland, Tony Fletcher, David Savitz)

Oct 8, 2008

This report summarizes the findings of the statistical analysis of the relationship between C8 levels measured in the blood serum of the participants in the C8 Health Project, and cholesterol and other lipids in their serum. A detailed report will be submitted to a peer-reviewed journal for publication.

Summary

Background: Serum perfluorooctanoic acid (PFOA) has been associated with total cholesterol and other lipids in some studies of exposed workers. Here we examine the association of PFOA and a related chemical, perfluorooctanesulfonate (PFOS), with lipids in a large population of adults in the mid-Ohio valley. Many in this population have high levels of serum PFOA due to drinking water contaminated from a nearby chemical plant.

Methods: The study population was 46,294 community residents age 18 and above living in six water districts contaminated by PFOA, who were not taking cholesterol-lowering medication, and who participated in a large health survey in 2005-2006. Participants in the health survey (the C8 Health Project) were required to have lived, worked, or gone to school in one of the contaminated water districts for at least one year. The relationship between PFOA and PFOS with total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), the ratio of total cholesterol to HDL, and triglycerides was examined via linear and logistic regression, after adjustment for other variables which affect lipids.

Results: The average level of PFOA in the serum was 80 ng/ml, while the median or most common value was 27 ng/ml. These levels are much higher than the US population average level of about 5 ng/ml. The average level of PFOS was 22 ng/ml, while the median was 20 ng/ml, both similar to the average level for the US population. In multivariate models adjusting for other factors (age, body mass index, sex, education, smoking, alcohol, regular exercise) all lipid outcomes except HDL were higher when serum PFOA and PFOS levels were higher. The positive trends were statistically significant in all cases, again with the exception of HDL. The predicted increase in cholesterol from lowest to highest decile of either PFOA or PFOS was 11-12 mg/dl, for example an increase from 199 to 210 in mg/dl cholesterol. PFOA and PFOS were

moderately correlated ($r=0.32$). The association between each chemical and cholesterol was maintained, although slightly moderated, when both chemicals were included in regression models. The risk for high cholesterol (total cholesterol ≥ 240 mg/dl) was measured via odds ratios in logistic regression models. The odds ratios, by increasing quartile of PFOA, were 1.00, 1.21 (95% confidence interval 1.12-1.31), 1.33 (95% CI 1.23-1.43), and 1.40 (95% CI 1.29-1.51). The corresponding adjusted odds ratios by quartile of PFOS were 1.00, 1.13 (95% CI 1.04-1.22), 1.28 (95% CI 1.19-1.39), and 1.51 (95% CI 1.40-1.64). These odds ratios indicate those with serum levels in the top 25% of the two chemicals had a 40%-50% increased risk of having high cholesterol compared to those in the lowest 25%.

Although PFOA and PFOS showed an association with cholesterol and other lipids, other factors were more strongly associated. The most important variables associated with cholesterol were age, gender, and body mass index.

Interpretation: Interpretation of these data is made difficult by the cross-sectional design of our study, which prohibits knowing whether an increase in cholesterol may have followed or preceded an increase in PFOA or PFOS. The mechanism by which these chemicals might be related to cholesterol in humans is not known. It is possible that both cholesterol and the two chemicals are all correlated with a third unknown substance which increases with increased lipids, for example, or even that increased lipids could lead to increased retention of PFOA/PFOS in the blood, ie, exhibiting “reverse causality”. The fact that both PFOA and PFOSs were associated with lipids may indicate an association with this chemical class (perfluorinated compounds) in general, rather than specifically either PFOA or PFOS. Despite difficulty in interpretation, our findings are a cause for concern, given the fact that high cholesterol is known to be related to heart disease. Longitudinal (follow-up) studies of PFOA

and PFOS in relation to heart disease are needed, in which it will be clear that exposure to the chemicals preceded any disease. We are conducting such studies.

**Status report: A Cross-Sectional Analysis of Type II Diabetes in a Community with
Exposure to Perfluorooctanoic acid (PFOA)**

The C8 Science Panel (Kyle Steenland, Tony Fletcher, David Savitz)

Oct 8, 2008

Summary:

Background: An increased number of deaths from diabetes, compared to those expected, has been seen in an previous study of workers exposed to perfluorooctanoic acid (PFOA). To investigate this issue further, we analyzed the relationship between serum PFOA and self-reported type II diabetes in residents of six water districts in Ohio and West Virginia contaminated with PFOA. We also looked at the sub-group of participants for whom medical validation of their reported diabetes was available. Finally we also looked at the relationship between PFOA and fasting glucose levels, among those who did not have diabetes. High fasting glucose indicates an increased risk of future diabetes.

Methods: The study population included adults ≥ 20 years of age, who participated in a community health survey (the C8 Health Project) in 2005-2006 (N=54,468). Participants reported whether or not they had diabetes at that time, and if they did, their age at diagnosis. They also provided a blood sample in which serum PFOA and glucose levels were measured. We conducted a case-control analysis of prevalent type II (adult-onset) diabetes, in which the level of PFOA was compared between diabetics and non-diabetics. The primary analysis was restricted to long-time residents of contaminated water districts (≥ 20 years, n=13,922), to maximize the likelihood that serum PFOA levels in 2005-2006 reflected previous exposure. Diabetes cases (n=1,005) in this analysis were restricted to those with medical record validation and with a least ten years residence in a contaminated water district prior to their diagnosis. We also analyzed the entire population for diabetes prevalence, without regard to length of residence. Finally, we studied the association between serum PFOA and fasting glucose in 2005-2006. This analysis was restricted to adult subjects who reporting not having eaten for at least six hours

prior to their blood draw (N=21,642). In this last analysis we excluded those who reported having diabetes.

Results: Median (50th percentile) serum PFOA levels were 28 ng/ml among all subjects, and 49 ng/ml in long-term residents, compared to approximately 5 ng/ml in the general US population. There were 4,278 prevalent diabetes cases reported by C8 Health Project participants, of which 3,529 were medically verified. The prevalence of self-reported adult diabetes in this population (7.8%) was similar to age-adjusted prevalence in Ohio (7.8%) and W. Virginia (9.8%). In the analysis of long-term residents, after adjusting for other variables related to diabetes, we observed little association between serum PFOA in 2005-2006 and the prevalence of medically-verified type II diabetes. In an analysis using ten categories of PFOA, the risk of prevalent diabetes by increasing level serum PFOA did not show a consistent increase with increasing PFOA. Taking the lowest category of PFOA as baseline (risk of 1.00), the ratio of risks (odds ratios) by increasing category of PFOA were 0.71, 0.60, 0.72, 0.65, 0.65, 0.87, 0.58, 0.71, 1.25. While the last risk for the highest category was somewhat elevated, it was not statistically significant. We conducted further analyses including all adults in the C8 Health Project, without regard to length of residence in contaminated water districts. These also did not show any relation between level of PFOA and the proportion of people with diabetes (odds ratios 1.00, 0.74, 0.67, 0.62, 0.67, 0.69, 0.73, 0.68, 0.89, 0.91 for medically verified cases). Finally, there was also no consistent association between fasting serum glucose and serum PFOA.

Conclusions: Our findings do not demonstrate an association between PFOA and either type II diabetes or fasting glucose level. However, these data are limited by their cross-sectional nature, because we cannot be sure the serum level of PFOA in 2005-2006 correctly reflects the exposure level preceding the onset of diabetes. Therefore based on these data we cannot exclude the

possibility of a true relationship between PFOA and the occurrence of diabetes. Future work will include follow-up studies in which we will look at the occurrence of new diabetes and also estimate more precisely historical exposure to PFOA.