

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

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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  $\geq 240$  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.