Status report: Association of perfluorinated compounds with Attention Deficit/Attention Deficit Hyperactivity Disorder and Learning Disorder among children aged 5 – 18 years with elevated community exposure to PFOA

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This report summarizes the findings relating PFOA (C8), PFOS (C8S), PFHxS (C6S), and PFNA (C9) in the serum of 5 – 18 year old participants in the C8 Health Project, which was carried out in 2005 – 2006 in the Mid-Ohio Valley, and report of doctor diagnosed Attention Deficit/Attention Deficit Hyperactivity Disorder (ADD/ADHD) or Learning Disorder. A full report of these findings will be submitted to two scientific conferences and a peer-reviewed scientific journal.

Background: Perfluorooctanoic acid (PFOA, also known at C8), perfluorooctane sulfonate (PFOS, also known as C6S), perfluorohexane sulfonic acid (PFHxS, also known as C6S), and perfluorononanoic acid (PFNA, also known as C9) are fluorocarbons, chemicals that do not occur in nature, but have been widely used in chemical production for some time and remain in the environment. They are found in the blood of most Americans at levels of around 4 ng/mL (nanogram/milliliter) for PFOA, 21 ng/mL for PFOS, 2 ng/mL for PFHxS, and 1 ng/mL for PFNA. One study has looked at the levels of these four chemicals in children's blood and looked at whether a doctor told the parent the child had Attention Deficit/Attention Deficit Hyperactivity Disorder (ADD/ADHD). This previous study found that children with higher levels of these chemicals in their blood were more likely to have ADD/ADHD. ADD/ADHD is a very common neurobehavioral disorder. The United States Centers for Disease Control and Prevention estimates that 9.5% of children aged 4 – 17 years old have ADD/ADHD, and 4.8% have ADD/ADHD and currently take medication for treatment. Children with ADD/ADHD have trouble paying attention, controlling impulsive behaviors (acting without thinking about the results), and sometimes are overly active. There have not yet been any studies looking at the association between these chemicals and a Learning Disorder diagnosis. A Learning Disorder refers to different types of specific learning disabilities, such as disabilities in listening, speaking, basic reading skills, reading comprehension, written expression, mathematical calculation, and mathematical reasoning.

Methods: We conducted a study 10,546 children aged 5 – 18 years old who participated in the C8 Health Project to examine the relationship between PFOA and parent's report of ADD/ADHD or learning disorders. We also examined the relationship between ADD/ADHD or Learning Disorder and the other fluorocarbons PFOS, PFHxS, and PFNA. A parent's report of a medical diagnosis of ADD/ADHD is commonly used in research studies and national surveys. The C8 Health Project enrolled community residents in Ohio and West Virginia who lived or worked in six water districts contaminated with PFOA from a chemical plant. In 2005 – 2006 the participants provided blood specimens that were used to measure PFOA, PFOS, PFHxS, and PFNA in the serum (the clear liquid part of the blood after blood cells have been taken out) and answered questions about their health. We examined these four chemicals because these are the chemicals that were detected in 100% of blood samples, plus these are the chemicals that were examined in the previous study of perfluorinated compounds and ADD/ADHD. We included children aged 5 – 18 years old because most children are not diagnosed with ADD/ADHD or a Learning Disorder until they start school. We used multiple regression

techniques to adjust for the child's age and sex, which could influence ADD/ADHD diagnosis. The results are presented in terms of odds ratios that reflect the relative risk, i.e., the risk of the problem in more exposed children divided by the risk in less exposed children. An odds ratio above 1.0 indicates an increased risk of ADD/ADHD or Learning Disorder in the more exposed group versus the less exposed group. An odds ratio from 0 – 0.99 indicates a decreased risk of ADD/ADHD or Learning Disorder in the more exposed group versus the less exposed group. We also present 95% confidence intervals, which are a measure of how precise the estimates are, with a range of plausible values taking chance into account.

Results: The average serum PFOA in the children was 66.3 ng/mL and the median (middle value) was 28.2 ng/mL. The average PFOS concentration was 22.9 ng/mL and the median was 20.2 ng/mL. The average PFHxS concentration was 9.3 ng/mL and the median was 5.2 ng/mL. The average PFNA concentration was 1.7 ng/mL and the median was 1.5 ng/mL. Of the children aged 5 – 18 years, 12.4% (n=1,303) were reported to have had a diagnosis with ADD/ADHD and 5.1% (n=542) were reported to have had a diagnosis with ADD/ADHD plus current use of a medication commonly used to treat ADD/ADHD. 12.1% (n=1,281) of children were reported to have had a Learning Disorder diagnosis. We examined ADD/ADHD and Learning Disorder separately, although there may be some children who have both conditions.

As levels of PFOA in the blood increased, reports of ADD/ADHD decreased slightly. The odds ratio to compare PFOA exposure above the 50th percentile to below the 50th percentile was 0.80 (95% confidence interval 0.67, 0.95) for ADD/ADHD.

As levels of PFHxS in the blood increased, report of ADD/ADHD increased slightly. The odds ratio to compare PFHxS exposure above the 50th percentile to below the 50th percentile was 1.33 (95% confidence interval 1.11, 1.59) for ADD/ADHD.

There was no clear pattern between levels of PFOS or PFNA in the blood and ADD/ADHD. Overall, the associations for a diagnosis with ADD/ADHD and a diagnosis with ADD/ADHD plus medication use were similar.

There appears to be no association between PFOA, PFOS, or PFHxS and reports of Learning Disorder. For PFNA, as levels of PFNA in the blood increased, report of Learning Disorder decreased slightly. The odds ratio to compare PFNA exposure above the 50^{th} percentile to below the 50^{th} percentile was 0.83 (95% confidence interval 0.73, 0.93).

Conclusion: Overall our results do not provide a clear indication of an association between PFOA and either ADD/AHDH or Learning Disorder. Higher PFOA levels were associated with fewer ADD/ADHD diagnoses. However, because there is no biological explanation for why increased levels of PFOA could protect children against ADD/ADHD, we think that this finding is related to how PFOA exposure varied in the region, how the characteristics of the population vary across the region, and how different schools and health care providers in the region may be more or less likely to make ADD/ADHD diagnoses. We will continue to study these data to examine how bias and confounding may be causing the negative association we see between PFOA and ADD/ADHD. We also found little support for a possible relationship between the other fluorocarbons and ADD/ADHD or Learning Disorder. Higher PFHxS levels were associated with more ADD/ADHD diagnoses. However, the elevation in risk with PFHxS was small, and the finding may be due to chance.