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Perfluoroalkane Acids and Fetal Growth

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In the November issue of *Environmental Health Perspectives*, Apelberg et al. (2007) reported an inverse relationship between umbilical cord blood concentrations of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) and ponderal index and head circumference in children delivered vaginally in Baltimore, Maryland. In the same issue, Fei et al. (2007) reported an inverse relationship between first trimester maternal blood PFOA (but not PFOS) concentration and birth weight in Danish infants born to normal-weight women. Although these studies do not necessarily support one another (Fei et al. also collected cord blood but did not report these results), they raise the important question of whether low-level exposure to perfluoroalkane acids might affect fetal growth. In both articles, the authors called attention to the inconsistency between these findings and those in experimental animal studies, in which fetal growth effects occur only at blood concentrations several orders of magnitude higher than were measured in human umbilical cord or maternal blood. The question was reasonably posed by both groups whether a confounder could be responsible for the observed associations. The Baltimore group (Apelberg et al. 2007) identified two candidate confounders that may explain their findings: diet and plasma volume.

Perfluoroalkanesulfonamides, which may be metabolized to PFOS, have been used in grease- and water-repellant packaging for foods, particularly pizza, french fries, and other fried foods. The Canadian Total Diet Study (Tittlemier et al. 2006) detected perfluoroalkanesulfonamides in all foods tested, but the highest concentrations were found in pizza, microwave popcorn, egg breakfast sandwiches, french fries, chicken nuggets, and fish burgers. Fluorotelomer alcohols, which can be converted to the corresponding alkane acids, have been used in coatings for paper, including microwave popcorn bags. 8-2 Fluorotelomer alcohol can be converted atmospherically and metabolically to PFOA, and gavage treatment of pregnant mice with 8-2 fluorotelomer alcohol results in the appearance of PFOA in fetuses (Henderson and Smith 2007). Both 8-2 fluorotelomer alcohol and PFOA have been found in popcorn bags and in the vapor produced after cooking microwave popcorn (Begley et al. 2005; Sinclair et al. 2007).

The pregnancies studied by Fei et al. (2007) occurred in 1996–2002, a period during which perfluorinated compounds were commonly used in fast-food packaging. The use of perfluorinated compounds in food packaging decreased some years before 2004–2005, the study period of Apelberg et al. (2007); however, PFOS and PFOA have long half-lives and may still have been present as markers of a high intake of fast-food. A high intake of fast food may in turn be a marker of poor nutrition. The Danish National Birth Cohort (Fei et al. 2007) included a food frequency questionnaire. It would be interesting to know if a relationship between nutrition and maternal blood perfluoroalkane acid concentration was detected.

PFOA and PFOS repel fat and are distributed in body water, particularly plasma. Women with a reduced plasma or body water volumes would distribute the same body burden of perfluoroalkane acids in a smaller space, producing higher perfluoroalkane acid concentrations. Fat-free body mass and total body water volumes are important predictors of birth weight (Butte et al. 2003; Lederman et al. 1999; Mardones-Santander et al. 1998; Sanin Aguirre et al. 2004), giving rise to the possibility that higher maternal blood (and therefore fetal blood) concentrations of PFOS and PFOA are markers of reduced plasma or total body water volumes, producing an apparent inverse association between the perfluoroalkane acid concentrations and fetal growth.

A reasonable next step in addressing the question of whether perfluoroalkane acids (at current human blood concentrations) play a role in fetal growth will be studies in which maternal nutrition and body composition, as opposed to body weight, are considered as possible confounders.

A.R.S. has been a consultant for 3M and has testified in litigation involving PFOA and PFOS.

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References

Apelberg BJ, Witter FR, Herbstman JB, Calafat AM, Halden RU, Needham LL, et al. 2007. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. Environ Health Perspect 115:1670–1676.

Begley TH, White K, Honigfort P, Twaroski ML, Neches R, Walker RA. 2005. Perfluorochemicals: potential sources of and migration from food packaging. Food Addit Contam 22:1023–1031.

Butte NF, Ellis KJ, Wong WW, Hopkinson JM, Smith EO. 2003. Composition of gestational weight gain impacts maternal fat retention and infant birth weight. Am J Obstet Gynecol 189:1423–1432.

Fei C, McLaughlin JK, Tarone RE, Olsen J. 2007. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. Environ Health Perspect 115:1677–1682.

Henderson WM, Smith MA. 2007. Perfluorooctanoic acid and perfluorononanoic acid in fetal and neonatal mice following in utero exposure to 8-2 fluorotelomer alcohol. Toxicol Sci 95(2):452–461.

Lederman SA, Paxton A, Heymsfield SB, Wang J, Thornton J, Pierson RN Jr. 1999. Maternal body fat and water during pregnancy: do they raise infant birth weight? Am J Obstet Gynecol 180(1 Pt 1): 235–240.

Mardones-Santander F, Salazar G, Rosso P, Villarroel L. 1998. Maternal body composition near term and birth weight. Obstet Gynecol 91:873–877.

Sanin Aguirre LH, Reza-Lopez S, Levario-Carrillo M. 2004. Relation between maternal body composition and birth weight. Biol Neonate 86:55–62.

Sinclair E, Kim SK, Akinleye HB, Kannan K. 2007. Quantitation of gas-phase perfluoroalkyl surfactants and fluorotelomer alcohols released from nonstick cookware and microwave popcorn bags. Environ Sci Technol 41:1180–1185.

Tittlemier SA, Pepper K, Edwards L. 2006. Concentrations of perfluorooctanesulfonamides in Canadian total diet study composite food samples collected between 1992 and 2004. J Agric Food Chem 54:8385–8389.

Perfluoroalkane Acids: Apelberg et al. Respond

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We thank Scialli for his interest in our study (Apelberg et al. 2007). As he notes, we recognize that several factors could be responsible for the relationships observed between cord serum concentrations of perfluorooctane sulfonate/perfluorooctanoate (PFOS/PFOA) and birth weight, head circumference, and ponderal index in our study. Although diet may be a source of exposure (including consumption of polyfluoroalkyl compounds used in fast-food packaging), we are not aware of any evidence that such diets are associated with smaller size at birth. In fact, they may be related to obesity, which is associated with larger birth size (Surkan et al. 2004). Despite existing knowledge gaps on exposure pathways and the role of dietary intake, we do know that in our study, adjusting for body mass index of the mother had little impact on the associations observed.

Scialli posits that there may be a role of reduced plasma or body water volume on the associations observed. As we described in our article (Apelberg et al. 2007), both preeclampsia and pregnancy-induced hypertension (PIH) are associated with poor maternal plasma volume expansion (Salas et al. 2006), as is placental weight (Salas et al. 1993). However, cord concentrations of PFOS and PFOA were not elevated among mothers with preeclampsia or PIH, and adjustment for these conditions did not appreciably alter the observed associations.

Likewise, adjustment for placental weight, which may be associated with plasma volume of the infant, did not alter these associations. Despite theoretical considerations, we have not found support for this hypothesis. Further research is needed to better understand the pathways of human exposure and the role that pharmacokinetics of these compounds in the human body may play in the observed associations.

The authors declare they have no competing financial interests.

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References

Apelberg BJ, Witter FR, Herbstman JB, Calafat AM, Halden RU, Needham LL, et al. 2007. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. Environ Health Perspect 115:1670–1676.

Salas SP, Marshall G, Gutierrez BL, Rosso P. 2006. Time course of maternal plasma volume and hormonal changes in women with preeclampsia or fetal growth restriction. Hypertension 47:203–208.

Salas SP, Rosso P, Espinoza R, Robert JA, Valdes G, Donoso E. 1993. Maternal plasma volume expansion and hormonal changes in women with idiopathic fetal growth retardation. Obstet Gynecol 81:1029–1033.

Surkan PJ, Hsieh CC, Johansson AL, Dickman PW, Cnattingius S. 2004. Reasons for increasing trends in large for gestational age births. Obstet Gynecol 104:720–726.

Carcinogenicity of Aspartame in Rats Not Proven

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In their article on lifetime exposure to aspartame in rats, Soffritti et al. (2007) purported that their study demonstrated increased carcinogenic effects in female rats as a result of exposure beginning during prenatal life.

We believe that this article (Soffritti et al. 2007) has methodologic and conceptual weaknesses that require exposition. First, although the study was a toxicology study, the most important element—the reported doses—are not correct. The doses are "estimates" based on assuming constant food consumption of 20 g/day and constant body weights of 400 g for each rat from *in utero* (fetal day 12) to death. These assumptions are unrealistic and inaccurate. The doses during the early growth phase of rats would be much higher because, as is well known, rats consume more food per gram of body weight during the rapid growth phase. Food consumption and body weight were reportedly measured throughout the experiment; however, Soffritti et al. (2007) presented only data beginning 16 weeks postpartum, when rats reached adult body weight. Therefore the authors' conclusions are built on the exposure period for which they provide no data.

Second, for a study allegedly designed to assess prenatal exposure, Soffritti et al. (2007) did not address important details, such as *a*) pregnancy history and ages of breeders; *b*) number of pregnant dams per dose group; *c*) growth and food consumption of mothers during pregnancy and lactation; *d*) pregnancy outcomes; *e*) disposition of pups from all mothers and each litter; *f*) the origin of the 70 pups; and *g*) body weight of pups at birth and during lactation. These details are typically required to allow other scientists to assess the appropriateness of the study design and to repeat the study, if desired.

The findings are of questionable biological significance for a number of reasons. The lymphoma/leukemia incidences in the high-dose group, which were the only significant differences from control, were within or near the reported historical control ranges. Similarly, the mammary gland carcinoma incidence in high-dose females (again, the only significant difference from control) was similar to historical controls. In their article, Soffritti et al. (2007) stated that their study disproved the conclusions of the European Food Safety Authority (EFSA 2006) that the incidences of lymphomas/leukemias observed in the first report (Soffritti et al. 2006) were "unrelated to aspartame given the high background incidence of chronic inflammatory changes in the lungs …" (EFSA 2006). The U.S. Food and Drug Administration (FDA 2007) agreed with the EFSA assessment. It is not clear to us how this study disproved the EFSA's conclusions. Soffritti et al. (2007) indicated that the lung was often the site of lymphoma again in this study, which is not surprising because they used the same infected colony. Studies in the 1960s demonstrated that the progression of chronic pneumonia in rats resulted in lymphoid neoplasmas, and elimination of chronic respiratory disease in rat colonies reduced the incidence of pulmonary lymphoid neoplasias to near zero (Cotchin and Roe 1967). Rats with pulmonary infections developed lesions in multiple sites earlier than rats free from pulmonary disease (Cotchin and Roe 1967). The establishment of pathogen-free animal suppliers for toxicity research was impelled for this reason. Therefore, we believe it is highly likely that the present findings are due to infection and not aspartame consumption.

Data do not support the conclusions of Soffritti et al. (2007) that aspartame has carcinogenic potential at doses near the human level of exposure. The authors observed no significant effects at the low-diet level, and the actual dose is unknown. Also, no data were provided on *in utero* exposure. Aspartame is completely digested in the gastrointestinal tract into two amino acids (phenylalanine and aspartic acid) and methanol, which is subsequently metabolized to carbon dioxide and water. In human clinical studies (reviewed by Stegink and Filer 1996), oral doses equal to or exceeding the amount that would represent the 99th percentile of aspartame intake did not increase plasma aspartate or phenylalanine levels in adults or children, or in breast milk from lactating women beyond normal postprandial concentrations. Ratios of fetal/maternal plasma amino acids and transport across the placental membrane were unchanged in pregnant rabbits that received 1,600 mg aspartame/kg/day (Ranney et al. 1975). Thus, a biologically plausible explanation is lacking for Soffritti et al.'s (2007) contention that prenatal exposure to aspartame increases cancer risk.

In summary, considering that there are no significant differences in cancer rates between high-dose groups and historical controls, plus the many deficiencies in the experimental design and data, Soffritti et al. (2007) failed to provide convincing evidence of aspartame carcinogenicity. Given the effort expended by many government review agencies to document shortcomings of the first article by this group (Soffritti et al. 2006), it is disappointing that the editor and reviewers of this paper (Soffritti et al. 2007) did not require the authors to address those problems that appear again in this study. Diligence is especially necessary on topics of great public interest and relevance because the public is relying upon the scientific community to assure that only high quality, well-documented, and controlled studies appear in peer-reviewed journals.

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References

Cotchin E, Roe JFC. 1967. Pathology of Laboratory Rats and Mice. Oxford, UK:Blackwell Scientific Publications.

EFSA (European Food Safety Authority). 2006. Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on a Request from the Commission Related to a New Long-term Carcinogenicity Study on Aspartame. EFSA J 356:1–44. Available: http://www.efsa.europa.eu/EFSA/Scientific_Opinion/afc_op_ej356_aspartame_en1,2.pdf [accessed 9 April 2008].

FDA (Food and Drug Administration). 2007. FDA Statement on European Aspartame Study. Available: http://www.cfsan.fda.gov/~lrd/fpaspar2.html [accessed 15 August 2007].

Ranney RE, Mares SE, Schroeder RE, Hutsell TC, Raczialowski FM. 1975. The phenylalanine and tyrosine content of maternal and fetal body fluids from rabbits fed aspartame. Toxicol Appl Pharmacol 32:339–346.

Soffriti M, Belpoggi F, Degli Esposti D, Lambertini L, Tibaldi E, Rigano A. 2006. First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats. Environ Health Perspect 114:379–385.

Soffritti M, Belpoggi F, Tibaldi E, Degli Esposti D, Lauriola M. 2007. Life-span exposure to low doses of aspartame beginning during prenatal life increases cancer effects in rats. Environ Health Perspect 115:1293–1297.

Stegink LD, Filer LJ. 1996. Effect of aspartame ingestion on plasma aspartate, phenylalanine, and methanol concentrations in potentially sensitive populations. In: The Clinical Evaluation of a Food Additive: Assessment of Aspartame (Tschanz C, Butchko HH, Stargel WW, Kotsonis FN, eds). Boca Raton, FL:CRC Press, 87–113.

Carcinogenicity of Aspartame: Soffritti Responds

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Magnuson and Williams's letter is substantially a repetition of the arguments set forth in a recent article (Magnuson et al. 2007), which was a "safety evaluation" sponsored entirely by Ajinomoto, the manufacturer of aspartame. Their article (Magnuson et al. 2007) and this letter contain numerous erroneous statements about the long-term carcinogenesis studies on aspartame conducted by the European Ramazzini Foundation (ERF).

First, Magnuson and Williams imply that our findings (Soffritti et al. 2007) should be discounted because the incidence of lymphomas/leukemias in the high-dose group "were within or near the reported historical control ranges." As reported in our study (Soffritti et al. 2007), the incidence of lymphomas/leukemias observed in both sexes treated with 2,000 ppm aspartame is nearly double the concurrent control (Soffritti et al. 2007). The suggestion that concurrent control data should be ignored is contrary to the widely accepted standard of good laboratory science.

Second, Magnuson and Williams attribute our findings (Soffritti et al. 2007) to some kind of bias (i.e., infection) that would affect only treated animals but not the controls. We have responded in detail to this hypothesis in our article (Soffritti et al. 2007) and in an earlier letter (Soffritti 2006). To support their assertion, Magnuson and Williams mislead readers by stating that "the lung was often the site of lymphoma again in this [second] study." However, we actually reported that

> we observed the diffusion of neoplastic tissue not only in the lung but also concurrently in various organs (liver, spleen, mediastinal and other lymph nodes). (Soffritti et al. 2007)

Infection as a mode of action for induction of rat lymphoma has been recently examined by a group of scientists at the National Center for Environmental Assessment of the U.S. Environmental Protection Agency; Caldwell et al. (2008) found that

> a careful examination of available information does not support the hypothesis that the observed lymphomas/leukemias in the ERF bioassays are a general effect from infection. The reports of chemically-induced lymphomas/leukemias by the ERF seem to be chemical specific.

Third, the idea that we must provide a "biologically plausible explanation" for human or rodent carcinogens is a time-honored approach to postpone or prevent the application of regulatory measures to minimize carcinogenic risks. The reality is that this explanation is quite often unknown, as is, in general, the mode of action behind the carcinogenic process.

I regard the other questions raised by Magnuson and Williams as trivial. For example, whatever the doses at various ages and weights, the finding of any effect should be a cause for concern. Likewise, the authors' observation that some methodologic details were omitted from the publication certainly does not change the oncologic results of this research.

Magnuson and Williams express disappointment that *Environmental Health Perspectives* would publish original scientific research by the ERF after regulatory agencies went through so much trouble to review our first aspartame study (Soffritti 2006) only to disagree with our conclusions. It is the obligation of the agencies responsible for food safety to review any new scientific data available and to make their opinion available to the public. The Food and Drug Administration (FDA) did not make public the contents of their review, but rather they issued a short press release a full year after the European Food Safety Authority (EFSA) concluded its evaluation, and coincidently, just days before I presented new aspartame data in a lecture at the Mount Sinai School of Medicine in New York (FDA 2007).

I find it unfortunate that some scientists have such a low tolerance for original, independent scientific research; however, I welcome continued discussion and more importantly, additional long-term experimental studies on aspartame and other artificial sweeteners. We at the ERF stand behind our results, and we remain convinced that a review of the current regulations governing the use of aspartame is necessary to better protect public health.

The author declares he has no competing financial interests.

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References

Caldwell J, Jinot J, DeVoney D, Gift JS. 2008. Evaluation of evidence for infection as a mode of action for induction of rat lymphoma. Environ Mol Mutagen 49:155–164.

FDA (Food and Drug Administration). 2007. FDA Statement on European Aspartame Study. Available: http://www.cfsan.fda.gov/~lrd/fpaspar2.html [accessed 12 January 2008].

Magnuson BA, Burdock GA, Doull J, Kroes RM, Marsh GM, Pariza MW, et al. 2007. Aspartame: a safety evaluation based on current use levels, regulations, and toxicological and epidemiological studies. Crit Rev Toxicol 37:629–727.

Soffritti M. 2006. Acesulfame potassium: Soffritti responds [Letter]. Environ Health Perspect 114:A516–A519.

Soffritti M, Belpoggi F, Tibaldi E, Degli Esposti D, Lauriola M. 2007. Life-span exposure to low doses of aspartame beginning during prenatal life increases cancer effects in rats. Environ Health Perspect 115:1293–1297.

Food Additives and Hyperactivity

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In the December 2007 Forum article on the links between food additives and hyperactivity, Barrett (2007) offered a somewhat distorted perspective on the public health implications of these additives. Barrett described a clinical trial testing the proposition that consumption of a blend of artificial food flavors and sodium benzoate induces changes in children's behavior (McCann et al. 2007). The results of that study support such a claim.

Barrett (2007) fumbled the significance of the trial (McCann et al. 2007) for environmental health. The Forum article emphasized how food additives might contribute to the clinical diagnosis of attention deficit/hyperactivity disorder rather than on the more significant finding that food

additives, particularly synthetic colors at levels prevailing in the diet, induce adverse behavioral responses. This is hardly a novel finding. In 1980, such effects were documented in two different groups of subjects with two different experimental designs (Swanson and Kinsbourne 1980; Weiss et al. 1980). Many later publications have confirmed their results. I briefly reviewed the data in *Environmental Health Perspectives* (Weiss 2000).

According to Barrett (2007), a Food and Drug Administration (FDA) official, Mike Herndon, maintains that the agency sees "… no reason at this time to change our conclusions that the ingredients that were tested in this study that currently are permitted for food use in the United States are safe for the general population." This is a rather baffling statement. In fact, our study (Weiss et al. 1980) was funded by the FDA, and its results, along with a number of others from that period, definitively demonstrated adverse behavioral effects of synthetic food colors (Weiss 1982). During the intervening years, with a plethora of confirmations, the FDA has remained blindly obstinate. It continues to shield food additives from testing for neurotoxicity and apparently believes that adverse behavioral responses are not an expression of toxicity.

Herndon and the FDA should seriously consider what the late Philip Handler said about balancing risks and benefits:

> A sensible guide would surely be to reduce exposure to hazard whenever possible, to accept substantial hazard only for great benefit, minor hazard for modest benefit, and no hazard at all when the benefit seems relatively trivial. (Handler 1979)

The FDA has never clarified the health benefits of artificial food colors.

The author declares he has no competing financial interests.

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References

Barrett JR. 2007. Hyperactive ingredients? Environ Health Perspect 115:A578.

Handler P. 1979. Some comments on risk. In: The National Research Council in 1979; Current Issues and Studies. Washington, DC:National Academy of Sciences, 3–24.

McCann D, Barrett A, Cooper A, Crumpler D, Dalen L, Grimshaw K, et al. 2007. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. Lancet 370:1560–1567.

Swanson JM, Kinsbourne M. 1980. Food dyes impair performance of hyperactive children on a laboratory learning test. Science 207:1485–1487.

Weiss B. 1982. Food additives and environmental chemicals as sources of childhood behavior disorders. J Am Acad Child Psychiatry 21:144–152.

Weiss B. 2000. Vulnerability of children and the developing brain to neurotoxic hazards. Environ Health Perspect 108(suppl 3):375–381.

Weiss B, Williams JH, Margen S, Abrams B, Caan B, Citron LJ, et al. 1980. Behavioral responses to artificial food colors. Science 207:1487–1489.

Editor's note—Weiss correctly points out that several investigators, including himself, have reported links between food additives and hyperactivity in children. He is also correct in stating that food additives appear to exacerbate existing hyperactive behavior in children, rather than contribute to the clinical diagnosis of attention deficit/hyperactivity disorder (ADHD). The study by McCann et al. [Lancet 370:1560–1567 (2007)] supports that conclusion, as described in Barrett's December 2007 Forum article [Environ Health Perspect 115:A578 (2007)].

We believe it was important to mention ADHD because hyperactivity and clinically defined ADHD are often conflated in the science news press. The point of referring to ADHD and therein clarifying the relationship between ADHD and hyperactivity was to put the import of the findings by McCann et al. (2007) into proper perspective.

Errata

Fox et al. [Environ Health Perspect 116:618–625 (2008)] inadvertently used the wrong calibration unit in the text and Figure 3 of their article. Candela-seconds per square meter (cd-sec/m^2) should have been Trolond-seconds (td-sec) throughout.

The authors regret the error.

In the statistical analysis section of "Hypertension and Exposure to Noise Near Airports: the HYENA Study" [Environ Health Perspect 116:329–333 (2008)], Jarup et al. erroneously named Biostat International (Tampa, FL) as the manufacturer of the meta-analysis software used in the study. The software is actually produced by Biostat (Englewood, NJ).

The authors regret the error.