

Comments on a Study Published in Environmental Health Perspectives
Prenatal Fluoride Exposure and Cognitive Outcomes in Children at 4 and 6-12 Years of Age in Mexico
November 27, 2017

The National Fluoridation Advisory Committee (NFAC) of the American Dental Association (ADA) Council on Advocacy for Access and Prevention has prepared the following comments on the study released in September 2017 by Bashash et al. NFAC members participating in the development of the comments included Valerie Peckosh, DMD, chair; Robert Crawford, DDS; Jay Kumar, DDS, MPH; Steven Levy, DDS, MPH; Howard Pollick, BDS, MPH; Brittany Seymour, DDS, MPH and Leon Stanislav, DDS.

Bashash, M., Thomas, D., Hu, H., et al. Prenatal Fluoride Exposure and Cognitive Outcomes in Children at 4 and 6–12 Years of Age in Mexico. *Environ Health Perspect.* 2017;125(9):097017-1-12.

The complete study is available at <https://ehp.niehs.nih.gov/ehp655/>.

Study Summary

The participants of this study were part of a number of long term studies in Mexico City that make up the Early Life Exposures in Mexico to Environmental Toxicants (ELEMENT) project. The 299 mother-child pairs in this study were recruited from three Mexico City hospitals that serve low-to-moderate income populations and were enrolled in one of two portions of the ELEMENT project; the first looked at prenatal lead exposure and neurodevelopment outcomes while the second looked at the effect of calcium supplementation during pregnancy on maternal blood lead levels. While not originally designed to examine prenatal fluoride exposure, the investigators used archived urine samples, data collected about the participants and scores on tests that looked at children's cognitive abilities at age 4 and full-scale intelligence quotients (IQ) at age 6–12. Sources of fluoride identified included fluoridated salt (250 ± 50 ppm) and naturally occurring fluoride in water (range 0.15 to 1.38 mg/L). Fluoride intake levels for participants were not reported in this study. The authors concluded that higher levels of maternal urinary fluoride during pregnancy (which served as a proxy for prenatal fluoride exposure) were associated with lower scores on tests of cognitive function of children at 4 and 6-12 years of age. No effect was seen up to a threshold of 0.8 mg/L urinary fluoride (which cannot be translated to fluoride exposure levels) while a negative association was seen at levels above that threshold. The authors noted a number of study limitations and stated that their findings must be confirmed in other study populations. They also noted that additional research is needed particularly on how the urine fluoride concentrations measured in this study are related to fluoride exposures.

Discussion

Study Strengths:

- To date, it is the largest, long-term study that looks at prenatal fluoride exposures and children's cognitive abilities.
- There is a large amount of data available about the study participants.
- Cognitive performance was assessed using recognized tools and protocols
- The procedure for urine analysis of fluoride levels was conducted using recognized protocols.

Study Limitations:

- The total number of participants in the study is a small convenience sample – 299 mother and child pairs.
- The study participants come from low to moderate income populations living in Mexico City at the time of the study whose characteristics may not be generalizable to the general population.
- The tool used to determine the quality of the children's individual home environments was not available in the early period of the study, so it was completed for only 124 of the 299 children studied.
- Sources of fluoride identified in the study are limited to fluoridated salt (250 ± 50 ppm) and naturally occurring fluoride in water (range 0.15 to 1.38 mg/L).
- No data regarding the levels of fluoride exposure (intake) are reported in the study.
- Pregnant women participants were asked to provide urine from only the second morning void instead of the preferred 24-hour collection protocol at least once during each of the three trimesters of pregnancy. Measuring urine fluoride levels under this protocol may not accurately reflect long term fluoride exposure.
- Of the urine samples examined, a majority had fluoride levels less than or equal to 1.5 mg/L with notably fewer samples above 1.5 mg/L. Since there are very few samples above 1.5 mg/L, there is a lower level of confidence in how prenatal urinary fluoride levels above the 1.5 mg/L level affect cognitive/IQ scores. (Care should be taken not to equate the urine fluoride levels with total fluoride intake due to the limited knowledge base about how fluoride exposure affects urine fluoride levels.)
- While a number of possible factors that could affect the study outcomes were examined:
 - There is no information on the iodine in salt which could modify the association between fluoride and cognitive abilities.

- There is a lack of information regarding known environmental neurotoxins, such as arsenic, which can be important factors in lower IQs.
- There is no information on the participants' primary water source (public water supply or other) nor are there any data available on the actual fluoride content of the water consumed by the individuals.
- There is the potential for uncontrolled confounding due to other factors, including diet, which could affect urinary fluoride excretion.

General Comments

While this one study adds to the science base, as the authors state, its findings need to be confirmed in other study populations and additional research is required on how the urinary fluoride levels are related to fluoride exposure.

This is an observational study that by definition can only show a possible association between fluoride exposure and IQ – not cause and effect. The association between fluoride and cognitive abilities observed as the result of this analysis should not be interpreted to mean that drinking fluoridated water during pregnancy causes IQ deficits in children.

Because not all potential confounders were adequately addressed in the study, there are other factors that might explain the association. There are many factors such as genetics, family, peer group, education, training and interventions, environmental enrichment, prenatal and postnatal nutrition, breast feeding, stress, maternal age, gestational age, birth weight, and exposure to lead, mercury, arsenic, iodine, alcohol, and drugs that affect IQ and other measures of cognitive ability.

There is very limited research on the pharmacokinetics (bodily absorption, distribution, metabolism and excretion) of fluoride during pregnancy, so the authors note that there is limited ability to draw conclusions about how the level of fluoride exposures in this study might impact the general population.

Limited literature suggests that urinary excretion is significantly decreased in pregnant women. Therefore, the urine fluoride levels in the pregnant women in this study most likely reflect much higher fluoride intake levels than in non-pregnant women or men.

There are no reference values for urinary fluoride in pregnant women in the United States and so it is not possible to compare the findings of this study from Mexico with fluoride exposures for pregnant women in the U.S.

This study from Mexico explores a number of environmental, socio-economic and cultural differences from conditions in the U.S. Of particular note is the availability of fluoridated salt in the study areas where the natural level of fluoride in the water supply ranges from 0.15 to 1.38 mg/L. Only one systemic source of fluoride is recommended for each country. The U.S. has chosen water fluoridation and so salt fluoridation is not available. Recommendations developed by the Pan American Health Organization, a division of the World Health Organization, state that fluoridated salt should be consumed only in areas where the naturally-occurring fluoride levels are low or moderate. Areas with optimal and high fluoride concentrations need to be monitored to prevent fluoridated salt from being sold in those areas.

At the time the data were collected, regulations in Mexico called for salt to be fluoridated at a level of 250±50 ppm. However, a study that analyzed fluoridated salt in Mexico in 2008 found that less than 7% of the samples met Mexican regulations with fluoride levels in samples ranging from 0 to 485 ppm. Additionally, consumption of salt in Mexico is known to be high.

Since 2015, the U.S. Public Health Service has recommended 0.7 mg/L as the optimal fluoride concentration in public water supplies to provide the best balance of protection from tooth decay while limiting the risk of dental fluorosis. According to the latest data from 2014, nearly 75% of the U.S. population on public water supplies receives fluoridated water (at the recommended fluoride level of 0.7 mg/L). Fluoridated salt is not available in the U.S.

In reviewing studies from countries with conditions more similar to those in the U.S., a 2014 observational (risk factor) study from New Zealand followed nearly 1,000 individuals from the area of Dunedin who grew up with and without fluoridated water (and where fluoridated salt is unavailable). Participants' IQs were measured a number of times between the ages of 7-13 years through age 38. After controlling for a number of possible confounding factors, the researchers found no significant differences (no association) in IQ between those who grew up in fluoridated areas versus those who grew up in nonfluoridated areas.

Following the a review of this study, the American Congress of Obstetricians and Gynecologist reaffirmed its recommendation that pregnant women drink fluoridated water – a recommendation shared by the ADA and numerous other health organizations and agencies as detailed in the 2011 Oral Health Care During Pregnancy: A National Consensus Statement available at https://www.mchoralhealth.org/materials/consensus_statement.php.

The ADA's support for community water fluoridation is based on a body of scientific evidence developed over nearly 75 years of research. The ADA continues to welcome additional research and looks forward to additional information that will add to the body of evidence on prenatal fluoride exposure and cognitive outcomes in children.