deficits from neurotoxic exposures, and especially from lead and PBDEs. More research is needed to examine the nuanced sex-specific effects found for postnatal exposures to toxic chemicals.

Reference:
Woodruff, T. J., & Sutton, P. (2014). The navigation guide systematic review methodology: A rigorous and transparent method for translating environmental health science into better health outcomes. Environmental Health Perspectives, 122(10), 1007–1014.
https://doi.org/10.1289/ehp.1307175

Categories: Drug/Toxin-Related Disorders (including Alcohol)
Keyword 1: neurotoxicity
Keyword 2: intellectual functioning
Keyword 3: prenatal factors
Correspondence: Carly V. Goodman, York University, cgoodman@yorku.ca

3 Fluoride Exposure and Hypothyroidism in Pregnant Women: A Potential Mechanism of Fluoride Neurotoxicity

Meaghan Hall[1], Bruce Lanphear[2], Jonathan Chevrier[3], Richard Hornung[1], Rivka Green[1,4], Carly Goodman[1], Pierre Ayotte[5], E. Angeles Martinez-Mier[6], Christine Till[1]
[1]York University, Toronto, ON, Canada. [2]Simon Fraser University, Burnaby, BC, Canada. [3]McGill University, Montreal, QC, Canada. [4]The Hospital for Sick Children, Toronto, ON, Canada. [5]Université Laval, Québec City, QC, Canada. [6]Indiana University, Indianapolis, IND, USA

Objective: Fluoride exposure has been associated with thyroid dysfunction, but fluoride's impact on thyroid function in pregnancy is unclear, especially during early gestation when the fetus is dependent on maternal thyroid hormone. We examined the potential thyroid-disrupting effects of maternal fluoride exposure in pregnancy and tested whether thyroid disruption in pregnancy mediates the association between maternal fluoride exposure and child intelligence quotient (IQ) among Canadian mother-child dyads living in areas with optimal fluoridation.

Participants and Methods: We measured fluoride concentrations in drinking water and in spot urine samples collected in each trimester from pregnant women enrolled in the Maternal-Infant Research on Environmental Chemicals study. We also measured thyroid hormone (thyroid stimulating hormone [TSH], free thyroxine [FT4], and total thyroxine [TT4]) levels during the first trimester of pregnancy and categorized women as euthyroid (n=1301), subclinical hypothyroid (n=100), or primary hypothyroid (n=28). Those categorized as primary hypothyroid were combined with an additional 79 women who reported clinical diagnoses at time of study enrolment (total n=107). In a sample of 1508 women, we used logistic regression to estimate the association between fluoride exposure and risk of either subclinical or primary hypothyroidism, separately, and linear regression to estimate associations between fluoride exposure and women's thyroid hormone levels (TSH, FT4, TT4). We tested effect modification by child sex and thyroid peroxidase (TPO) antibody status. In a subsample of 439 mother-child pairs, we measured child Full-Scale IQ (FSIQ) at 3-4 years of age using the Wechsler Preschool and Primary Scale of Intelligence. We used linear regression to test associations between maternal hypothyroidism or thyroid hormone levels, and children's FSIQ scores. Finally, mediation analysis in the counterfactual framework was used to estimate the proportion of the effect of maternal fluoride exposure on child FSIQ mediated by maternal hypothyroidism, through evaluation of the natural direct (not through hypothyroidism) and indirect (through hypothyroidism) effects.
Results: Using categorical measures of thyroid status, a 0.5 mg/L increase in water fluoride concentration was associated with a 1.64 (95% confidence interval [CI], 1.04 to 2.58) increased odds of primary hypothyroidism. This association was stronger among women with normal TPO antibody levels (< 5.61 IU/mL) (odds ratio, 2.80; 95% CI, 1.24 to 6.36). In contrast, we did not find a significant association between maternal urinary fluoride and hypothyroidism. For continuous measures of thyroid hormone levels, a 1 mg/L increase in maternal urinary fluoride was associated with a 35% (p=0.01) increase in TSH among women pregnant with a female fetus. In our subsample analyses, children born to women with primary hypothyroidism had lower FSIQ than children of euthyroid women, especially among boys (B, -

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8.78; 95% CI, -16.78 to -0.79). In contrast, maternal TSH, FT4, and TT4 levels were not significantly associated with child FSIQ scores. Maternal primary hypothyroidism did not significantly mediate the relationship between maternal water fluoride concentration and child FSIQ (p natural indirect effect= .35).
Conclusions: Fluoride in drinking water may increase the risk of hypothyroidism in pregnancy. Thyroid dysfunction in pregnancy may be one mechanism underlying developmental neurotoxicity of fluoride.

Categories: Drug/Toxin-Related Disorders (including Alcohol)
Keyword 1: neurotoxicity
Keyword 2: endocrine disorders
Keyword 3: intelligence
Correspondence: Meaghan Hall; Faculty of Health, York University, Toronto, ON, Canada; mkhall@yorku.ca

4 Urinary Fluoride Levels and Metal Co-Exposures Among Pregnant Women in Los Angeles, California

Ashley J Malin[1], Howard Hu[2], E. Angeles Martinez-Mier[3], Sandrah P Eckel[2], Shohreh Farzan[2], Rima Habre[2], Theresa M Bastain[2], Carrie V Breton[2]
[1]University of Florida, Gainesville, FL, USA. [2]University of Southern California, Los Angeles, CA, USA. [3]Indiana University, Indianapolis, IN, USA

Objective: Approximately 73% of the United States (US) population on public water systems receives fluoridated water for tooth decay prevention. In Los Angeles (LA) County, 89% of cities are at least partially fluoridated. Drinking water is the primary source of fluoride exposure in the US. Studies conducted in Mexico and Canada suggest that prenatal fluoride exposure, at levels relevant to the US, may contribute to poorer neurodevelopment in offspring. However, data on biomarkers and patterns of fluoride exposure among US pregnant women are scarce. This study examined urinary fluoride levels according to sociodemographic factors and metal co-exposures among pregnant women in the US.
Participants and Methods: Participants were from the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) cohort based in Los Angeles, California. There were 293 and 490 women with urine fluoride measured during the first and third trimesters of pregnancy, respectively. An intra-class correlation coefficient examined consistency of specific gravity-adjusted maternal urinary fluoride (MUFsg) between trimesters. Kruskal-Wallis and Mann-Whitney U tests examined associations of MUFsg with sociodemographic variables. Spearman correlations examined associations of MUFsg with blood and urine metals within and between trimesters. A False Discovery Rate (FDR) correction accounted for multiple comparisons. The criterion for statistical significance was an alpha of 0.05.
Results: Participants were approximately 29 years old on average, and 80% were Hispanic or Latina. Median (IQR) MUFsg during trimesters one and three was 0.65 (0.5) mg/L and 0.8 (0.59) mg/L, respectively. MUFsg levels were moderately consistent between trimesters (N=292, ICC = 0.46, 95%CI: 0.32,0.57). Maternal age was positively associated with MUFsg during first ($\rho = 0.16$, $p = 0.006$) and third ($\rho = 0.18$, $p < 0.001$) trimesters. MUFsg differed by race/ethnicity during first and third trimesters (N = 293, H (3) = 7.99, $p = 0.046$; N = 486, H (3) = 25.31, $p < 0.001$, respectively). Specifically, MUFsg was higher for White, Non-Hispanic participants (first trimester Median (IQR) =1.03 (1.31) mg/L; third trimester Median (IQR) = 1.32 (1.24) mg/L) than for Hispanic participants in both trimesters (first trimester Median (IQR) =0.64 (0.48) mg/L; third trimester Median (IQR) = 0.76 (0.55) mg/L). Additionally, during trimester three, MUFsg was higher for White, Non-Hispanic participants than for Black Non-Hispanic participants (Median (IQR) = 0.82 (0.49) mg/L). MUFsg also differed by education during trimester one (N = 293, H (4) = 10.61, p = 0.031), and was higher for participants with some graduate training than for those with high school or some college/technical school education (ps = 0.03 and 0.04, respectively). After FDR correction, MUFsg was associated with blood lead (N =91, $\rho = 0.29$, $p = 0.024$) and urinary cadmium (N =279, $\rho = 0.19$, $p = 0.042$), copper (N=279, $\rho = 0.16$, $p = 0.042$), and tungsten (N=279, $\rho = 0.16$, $p = 0.049$) during trimester three.
Conclusions: Consistent with studies conducted in Canada and Mexico, MUFsg

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