The following are 19 studies, published from 2017 to 2021, reporting an association of fluoride exposure to lower IQ in children. 10 studies from China, 3 from Mexico, 2 from Canada, one each from Egypt, India, Kenya and Sudan.

Paul Connett, November 22, 2021.

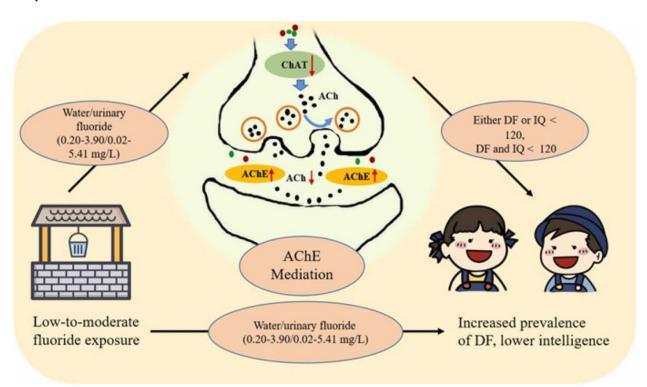
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#### 1. 2021- China. 709 resident children in Tianjin, China, ages 6-13.

Wang S, Zhao Q, Li G, Wang M, Liu H, Yu X, Chen J, Li P, Dong L, Zhou G, Cui Y, Wang M, Liu L, Wang A. 2021. <u>The cholinergic system, intelligence, and dental fluorosis in school-aged children with low-to-moderate fluoride exposure</u>. *Ecotoxicology and Environmental Safety*.

**Conclusions:** "... Our findings suggest low-to-moderate fluoride exposure was associated with dysfunction of cholinergic system for children. AChE may partly mediate the prevalence of DF and lower probability of having superior and above intelligence."

#### **Graphical abstract:**



### 2. 2021- Mexico. 103 mother-infant pairs, tested at 12 months and 24 months. Funded by NIH & NIEHS.

Cantoral A, Téllez-Rojo MM, Malin AJ, Schnaas L, Osorio-Valencia E, Mercado A, Martínez-Mier EA, Wright RO, Till C. 2021. <u>Dietary fluoride intake during pregnancy and neurodevelopment in toddlers: A prospective study in the progress cohort. NeuroToxicology.</u>

**Conclusions:** "In this prospective cohort study, higher exposure to fluoride from food and beverage consumption in pregnancy was associated with reduced cognitive outcome, but not with language and motor outcome in male offspring over the first two years of life."

#### 3. 2021 - China. 952 resident children, 7 to 13 years old.

Yu X, Xia L, Zhang S, Zhou G, Li Y, Liu H, Hou C, Zhao Q, Dong L, Cui Y, Zeng Q, Wang A, Liu L. 2021. <u>Dietary fluoride intake during pregnancy and neurodevelopment in toddlers: A prospective study in the progress cohort. Environment International 155:106681.</u>

**Conclusions:** "Our study suggests that fluoride is inversely associated with intelligence. Moreover, the interactions of fluoride with mitochondrial function-related SNP-set, genes and pathways may also be involved in high intelligence loss."

#### 4. 2021 - China. 567 children, 6-11 years old.

Zhao L, Yu C, Lv J, Cui Y, Wang Y, Hou C, Yu J, Guo B, Liu H, Li L. 2021. <u>Fluoride exposure, dopamine relative gene polymorphism and intelligence</u>: A cross-sectional study in China. *Ecotoxicology and Environmental Safety* 209:111826. [Epub ahead of print].

**Conclusions:** "Our study examined the association between excessive fluoride exposure in prenatal and childhood periods and the intelligence of school-age children. We found that prenatal excessive fluoride exposure could cause lower IQ scores, especially the decreased odds of developing excellent intelligence. Meanwhile, a negative association between fluoride exposure and children's IQ scores was observed in children without prenatal exposure."

### 5. 2020 – China. 99 children, 8–12 years. 55 in dental fluorosis group (none with moderate or severe dental fluorosis, but all with mild) and 44 students without dental fluorosis.

Lou D, Luo Y, Liu J, Zheng D, Ma R, Chen F, Yu Y, Guan Z. 2020. <u>Refinement Impairments of Verbal-Performance Intelligent Quotient in Children Exposed to Fluoride Produced by Coal Burning</u>. *Biological Trace Element Research*.

**Conclusions:** "In conclusion, we believe that reducing fluoride intake with the assistance of the government can reduce fluorosis as well as the severity of intellectual impairment caused by fluorosis. Fluorosis in children can cause IQ impairment, especially the VIQ that is represented by language learning and vocabulary comprehension."

#### 6. 2020 - Canada. 398 Mother-Offspring pairs. Fetus and Infants up to 3-4 year-olds. Funded by NIEHS.

Till C, Green R, Flora D, Hornung R, Martinez-Miller EA, Blazer M, Farmus L, Ayotte P, Muckle G, Lanphear B. 2020. Fluoride exposure from infant formula and child IQ in a Canadian birth cohort. Environment International 134:105315. (Published in November 2019)

**Conclusions:** "In summary, fluoride intake among infants younger than 6 months may exceed the tolerable upper limits if they are fed exclusively with formula reconstituted with fluoridated tap water. After adjusting for fetal exposure, we found that fluoride exposure during infancy predicts diminished non-verbal intelligence in children..."

## 7. 2019 – China. 571 children, ages 7-13, randomly selected from endemic and non-endemic fluorosis areas in Tianjin.

Wang M, Liu L, Li H, Li Y, Liu H, Hou C, Zeng Q, Li P, Zhao Q, Dong L, Zhou G, Yu X, Liu L, Guan Q, Zhang S, Wang A. 2019. <u>Thyroid function, intelligence, and low-moderate fluoride exposure among Chinese school-age children</u>. *Environment International* 134:105229. [Epub ahead of print].

**Conclusions:** The study suggests low-moderate fluoride exposure is associated with alterations in childhood thyroid function that may modify the association between fluoride and intelligence. In the current work, results demonstrated clearly that, across the full range of water and urinary fluoride concentrations and using a measure to focus on children's IQ scores, higher fluoride levels were associated with lower IQ scores."

# **8. 2019 – Canada. 512 Mother-Child pairs between the ages 3 and 4 years at testing. Funded by NIEHS.** Green R, Lanphear B, Hornung R, Flora D, Martinez-Mier EA, Neufeld R, Ayotte P, Muckle G, Till C. 2019. Association Between Maternal Fluoride Exposure During Pregnancy and IQ Scores in Offspring in Canada. *JAMA Pediatrics*.

**Conclusions:** "In this study, maternal exposure to higher levels of fluoride during pregnancy was associated with lower IQ scores in children aged 3 to 4 years. These findings indicate the possible need to reduce fluoride intake during pregnancy." <u>Listen to discussion of JAMA editors on their process to publish this study.</u>

### **9. 2018 -China.** 323 children, ages 7 – 12 years. Urine fluoride levels and age-specific IQ scores in children were measured at the enrollment.

Cui Y, Zhang B, Ma J, Wang Y, Zhao L, Hou C, Yu J, Zhao Y, Zhang Z, Nie J, Gao T, Zhou G, Liu H. 2018. Dopamine receptor D2 gene polymorphism, urine fluoride, and intelligence impairment of children in China: A school-based cross-sectional study. *Ecotoxicology and Environmental Safety,* Sept 11;165:270-277.

**Conclusions:** "Strengths of our study include using urine fluoride as an internal exposure index and thus minimizing the measurement error of exposure, adjusting up to 30 potential confounding covariates including child age and gene polymorphismin regressing IQ on urine fluoride in children, and careful modeling with applications of cross-validation, bootstrap techniques, and sensitivity analysis. "In the overall participants, by LOWESS, the IQ decreased in a roughly linear manner as the log-urine fluoride increased (Fig. 1A).

"The authors also determined a safety threshold of urine fluoride on intelligence impairment in the subgroup TT as 1.73 mg/L urine fluoride with a 95% CI of (1.51 mg/L, 1.97 mg/L)."

#### 10. 2018 - Egypt. 1,000 children, 495 children, 4.6 - 11 years old.

El Sehmawy AAEW, Hammouda SM, Ibrahim GE, Barghash SS, Elamir RY. 2018. Relationship between Drinking Water Fluoride and Intelligence Quotient in Egyptian School Children. Occupational Medicine & Health Affairs, Aug 13: 6:3.

**Results:** "In this study there's a highly significant decrease in average IQ level in group of children with high fluoride level more than 1.5 mg /dL than the group of children with low fluoride level less than 1.5 mg /dL with the mean IQ was  $(96.25 \pm 19.63)$  and  $(103.11 \pm 28.00)$  for both groups respectively with p value (p<0.001), the graphical representation of the observation is shown in Figure 2."

#### 11. 2018 - Kenya. 269 school children, 13-15 years

Induswe B, Opinya G, Khasakhala LI, Owino R. 2018. <u>The Auditory Working Memory of 13-15-Year-Old Adolescents Using Water with Varying Fluoride Concentrations from Selected Public Primary Schools in North Kajiado Sub County</u>. *American Journal of Medicine and Medical Sciences*, Jan; 8(0):274-290. **Conclusions:** "In conclusion, low fluoride in the water seemed to enhance the AWM (Auditory Working Memory). However, the AWM declined with an increase in the fluoride concentration in water."

#### 12. 2018 - Sudan. 775 primary students, 315 boys and 460 girls from 27 schools.

Mustafa DE, Younis UM, Elhag SA. (2018). <u>The relationship between the fluoride levels in drinking water and the schooling performance of children in rural areas of Khartoum State, Sudan</u> (pdf). *Fluoride* 51(2):102–113.

**Results:** "Negative correlation coefficients were found for the average score for all the subjects and for the overall score, with the result being statistically significant in five out of the eight subjects and in the overall score (Tables 4 and 5). ... significant correlations undoubtedly exit between the drinking water F

level and the schooling performances in all the subjects except for one, technology, which might be due to the nature of the subject."

### 13. 2018 – China. 268 children, 8 -12 years of age: 134 children each from endemic fluorosis area and non-endemic fluorosis areas.

Pang H, Yu L, Lai X, Chen Q. 2018. <u>Relation Between Intelligence and COMT Gene Polymorphism in Children Aged 8-12 in the Endemic Fluorosis Area and Non-Endemic Fluorosis Area</u>. *Chinese Journal of Control of Endemic Diseases* 32(2):151-152. Study in Chinese translated into English.

**Conclusions:** "This study found that there was a great difference in the level of intelligence between children in the endemic fluorosis area and those in the non-endemic fluorosis area and such difference was statistically significant (P < 0.05).

"The rate of mental retardation (IQ < 69) in children in the endemic fluorosis area was significantly higher than that in the non-endemic fluorosis area, and the difference was statistically significant (P < 0.05)."

#### 14. 2018 - China. 2,886 resident children, 7 to 13 years.

Yu X, Chen J, Li Y, Liu H, et al. (2018). <u>Threshold effects of moderately excessive fluoride exposure on children's health:</u> A potential association between dental fluorosis and loss of excellent intelligence. *Environment International*, Jun 2; 118:116-124.

**Conclusions:** "In conclusion, chronic exposure to excessive fluoride, even at a moderate level, was inversely associated with children's dental health and intelligence scores, especially excellent intelligence performance, with threshold and saturation effects observed in the dose-response relationships. Additionally, DF severity is positively associated with the loss of high intelligence, and may be useful for the identification of individuals with the loss of excellent intelligence."

### 15. 2017 -Mexico. 299 Mother-Offspring pairs. Tests at age 4 and 6–12 years. Funding from NIH, NIEHS, and EPA.

Bashash M, Thomas D, Hu H, Martinez-Mier EA, Sanchez BN, Basu N, Peterson KE, Ettinger AS, Wright R, Zhang Z, Liu Y, Schnaas L, Mercado-García A, Téllez-Rojo MM, Hernández-Avila M. 2017. <a href="Perenatal-Prenatal-Linearing-Invironmental-Prenatal-Linearing-Invironmental-Prenatal-Prenatal-Linearing-Invironmental-Prenatal-Linearing-Invironmental-Prenatal-Linearing-Invironmental-Prenatal-Linearing-Invironmental-L

**Conclusions:** "In this study, higher prenatal fluoride exposure, in the general range of exposures reported for other general population samples of pregnant women and nonpregnant adults, was associated with lower scores on tests of cognitive function in the offspring at age 4 and 6–12 y."

### 16. 2017 – Mexico. 65 Mother-Offspring infant pairs, aged 3–15 months, in an endemic hydrofuorosis

Valdez Jiménez L, López Guzmán OD, Cervantes Flores M, Costilla-Salazar R, Calderón Hernández J, Alcaraz Contreras Y, Rocha-Amador DO. 2017. <u>In utero exposure to fluoride and cognitive development delay in infants</u>. *Neurotoxicology* Mar;59:65-70.

**Results:** "In this study near to 60% of the children consumed contaminated water and the prevalence of children with IQ below 90 points was 25% in the control group (F urine 1.5 mg/g creatinine) in comparison with the 58% of children in the exposed group (F urine >5 mg/g creatinine) (OR = 4.1, CI 95% 1.3–13.2) (data unpublished).

"Only 66.2% of the babies were at term. "We found higher levels of F in urine across trimester in premature compared with full term 2.4 vs 1.6 mg/l (1st); 2.3 vs 1.8 mg/l (2nd); and 4.1 vs 2.8 mg/l (3rd) (data not shown)."

#### 17. 2017 - China. 118 newborns, 68 newborns to 12 months of age, from coal-burning fluorosis areas.

Chang A, Shi Y, Sun H, Zhang L. 2017. <u>Analysis on the Effect of Coal-Burning Fluorosis on the Physical Development and Intelligence Development of Newborns Delivered by Pregnant Women with Coal-Burning Fluorosis</u>. *Chinese Journal of Control of Endemic Diseases*, 32(8):872-873.

Conclusions: "Comparison of the mental development index (MDI) and psychomotor development index (PDI) (assessed using the Standardized Scale for the Intelligence Development of Children formulated by the Children Development Center of China [CDCC]) of newborns in the two groups at 3, 6, 9 and 12 months after birth showed that both the MDI and the PDI in the observation group were significantly lower than those in the control group (P< 0.05), which suggests that maternal fluorosis have a significant impact on the intelligence development of newborns."

### 18. 2017 - China. 284 children, 8 – 12 years: 167 were from coal burning-related endemic fluorosis areas and 117 were the control.

Jin T, Wang Z, Wei Y, Wu Y, Han T, Zhang H. (2017). <u>Investigation of Intelligence Levels of Children of 8 to 12 Years of Age in Coal Burning-Related Endemic Fluorosis Areas</u>. *Journal of Environment and Health* 34(3):229-231.

**Conclusions:** "The intelligence of the 12-year-old group in the endemic area was lower than that of the control area, with the difference having statistical significance (Z = 3.244, P = 0.001)."

### 19. 2017 – India. 219 children, 12-14 year olds: 75 from low F area, 75 medium F area, and 69 from high F area.

Razdan P, Patthi B, Kumar JK, Agnihotri N, Chaudhan P, Prasad M. (2017). Effect of fluoride concentration in drinking water on intelligence quotient of 12–14-year-old children in Mathura District: A cross-sectional study. Journal of International Society of Preventive & Community Dentistry 7(5):252-258.

**Conclusions:** "Concentration of Fluoride in the ingested water was significantly associated with the IQ of children. Outcome measures revealed that exposure to higher levels of F determined by dental fluorosis status of child inferred higher IQ deficit."