



## Disclosure Statement

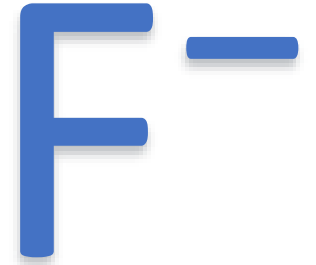
- I do not have any conflicts of interest or disclosures related to the material in this presentation

# Today's Presentation

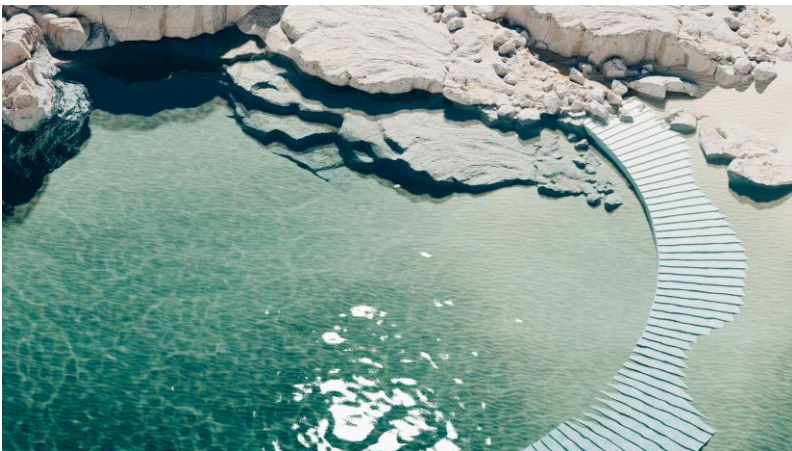
- **Fluoride and fluoridation additives**
- **Impacts of fluoride on health**
  - Bone and pineal gland
- **Fluoride and neurodevelopment**
  - The current state of the science shows that chronic fluoride exposure in early life is associated with worse child neurodevelopment, even at US levels

# What is Fluoride?

- A mineral that naturally occurs in rock and soil
- Can leach and naturally occur in drinking water



(NRC,2006; ATSRD, 2014)



# Community Water Fluoridation

- Began in the United States (US) in 1945 for preventing dental cavities (ATSDR, 2014)
- Approximately 72% of the US population on community water systems receives fluoridated water (CDC, 2022)
- The recommended concentration in drinking water is 0.7 mg/L
  - Previously 0.7-1.2 mg/L but lowered in 2015 (US Public Health Service, 2015)

# Dental Fluorosis

- An outward manifestation of excess fluoride exposure
- Prevalence of **70%** among US children and adolescents in NHANES 2015-2016

Normal teeth



Mild fluorosis



Moderate fluorosis



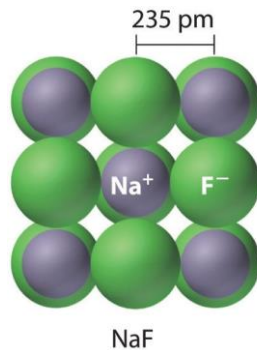
Severe fluorosis



(Dong et al., 2021)

# What is Added to Drinking Water?

- Fluorosilicic acid
- Sodium fluorosilicate
- Sodium fluoride



# Fluoridation Chemical Mixtures

➤ [Int J Occup Environ Health](#). 2014 Apr-Jun;20(2):157-66. doi: 10.1179/2049396714Y.0000000062.  
Epub 2014 Mar 20.

## **A new perspective on metals and other contaminants in fluoridation chemicals**

[Phyllis J Mullenix](#)

PMID: 24999851   PMCID: [PMC4090869](#)   DOI: [10.1179/2049396714Y.0000000062](#)



# Fluoridation Chemical Mixtures

- **Hydrofluorosilic Acid:**
  - Arsenic (4.9-56 ppm)
  - Lead (<10-10.3 ppm)
  - Aluminum (212-415 ppm)
- **Sodium Fluoride:**
  - Barium (13.3-18 ppm)
  - Aluminum (3312-3630 ppm)

# Fluoridation Chemicals

➤ [Neurotoxicology](#). 2007 Sep;28(5):1023-31. doi: 10.1016/j.neuro.2007.06.006. Epub 2007 Jun 30.

## Effects of fluoridation and disinfection agent combinations on lead leaching from leaded-brass parts

Richard P Maas <sup>1</sup>, Steven C Patch, Anna-Marie Christian, Myron J Coplan

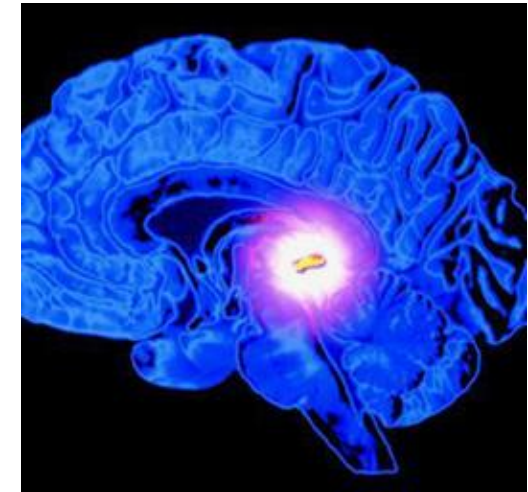
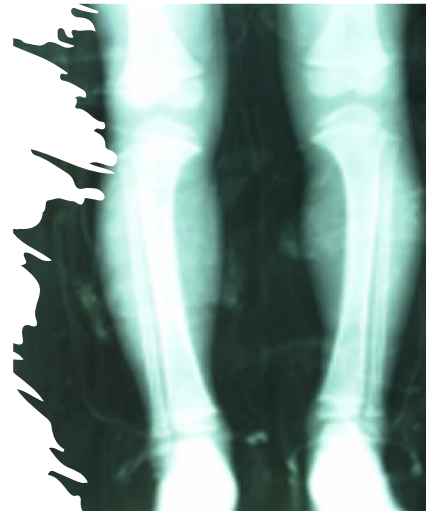
Affiliations + expand

PMID: 17697714 DOI: [10.1016/j.neuro.2007.06.006](#)



# Fluoride and Health

- Fluoride is beneficial for cavity prevention, particularly when applied to teeth
- When ingested, fluoride accumulates in bones, teeth and other calcium containing organs and glands, including the pineal gland and developing brain



# Fluoride and Bone Health

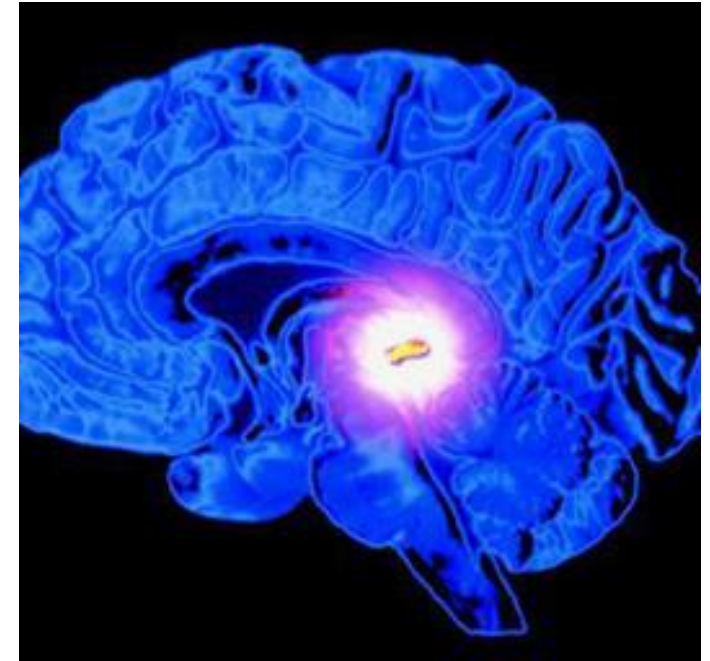
- Increases bone mineral density (BMD)
  - Trabecular bone
- Changes in bone quality
  - Bone weakness and increased risk of fracture
  - Even at levels similar to the United States



(Aaron et al., 1991; Grynpas, 1990; Helte et al., 2021; NRC, 2006; Riggs et al., 1990)

# Fluoride and Pineal Gland Health

- Accumulates highly in the pineal gland
  - Small gland at the base of the brain
  - Produces melatonin, a hormone that regulates sleep
- Associated with pineal gland calcification
  - Sleep disturbances and neurological problems
    - Alzheimer's Disease, schizophrenia, pediatric brain tumor, multiple sclerosis





Pergamon

Neurotoxicology and Teratology, Vol. 17, No. 2, pp. 169-177, 1995  
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0892-0362(94)00070-0

# Neurotoxicity of Sodium Fluoride in Rats

PHYLLIS J. MULLENIX,\*†<sup>1</sup> PAMELA K. DENBESTEN,‡ ANN SCHUNIOR\*  
AND WILLIAM J. KERNAN§

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*§Veterinary Diagnostic Laboratory, Iowa State University, Ames, IA 50011*



RESEARCH

Open Access

# Exposure to fluoridated water and attention deficit hyperactivity disorder prevalence among children and adolescents in the United States: an ecological association

Ashley J Malin\* and Christine Till

**“Parents reported higher rates of medically-diagnosed ADHD in their children in states in which a greater proportion of people receive fluoridated water from public water supplies. The relationship between fluoride exposure and ADHD warrants future study.”**





# Prenatal Fluoride Exposure and Cognitive Outcomes in Children at 4 and 6–12 Years of Age in Mexico

 This article accompanies [LOW PRENATAL EXPOSURES TO FLUORIDE: ARE THERE NEUROTOXIC RISKS FOR CHILDREN?](#).

**Authors:** [Morteza Bashash](#), [Deena Thomas](#), [Howard Hu](#), [E. Angeles Martinez-Mier](#), [Brisa N. Sanchez](#), [Niladri Basu](#), [Karen E. Peterson](#), ... [SHOW ALL](#) ..., and [Mauricio Hernández-Avila](#) | [AUTHORS INFO & AFFILIATIONS](#)

**Publication:** Environmental Health Perspectives • Volume 125, Issue 9 • CID: 097017 • <https://doi.org/10.1289/EHP655>

JAMA Pediatrics | [Original Investigation](#)

## Association Between Maternal Fluoride Exposure During Pregnancy and IQ Scores in Offspring in Canada

Rivka Green, MA; Bruce Lanphear, MD; Richard Hornung, PhD; David Flora, PhD; E. Angeles Martinez-Mier, DDS; Raichel Neufeld, BA; Pierre Ayotte, PhD; Gina Muckle, PhD; Christine Till, PhD

**Each 1 mg/L increase in maternal urinary fluoride across pregnancy is associated with a 4-5-point IQ reduction in children**





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## Environment International

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)



### Prenatal fluoride exposure and attention deficit hyperactivity disorder (ADHD) symptoms in children at 6–12 years of age in Mexico City



Morteza Bashash<sup>a,\*</sup>, Maelle Marchand<sup>a</sup>, Howard Hu<sup>a,1</sup>, Christine Till<sup>b</sup>, E. Angeles Martinez-Mier<sup>c</sup>, Brisa N. Sanchez<sup>d</sup>, Niladri Basu<sup>e</sup>, Karen E. Peterson<sup>d,f,g</sup>, Rivka Green<sup>b</sup>, Lourdes Schnaas<sup>h</sup>, Adriana Mercado-García<sup>i</sup>, Mauricio Hernández-Avila<sup>i</sup>, Martha María Téllez-Rojo<sup>i</sup>

RESEARCH

Open Access

# Urinary fluoride levels and metal co-exposures among pregnant women in Los Angeles, California



Ashley J. Malin<sup>1\*</sup>, Howard Hu<sup>2</sup>, E. Angeles Martínez-Mier<sup>3</sup>, Sandrah P. Eckel<sup>2</sup>, Shohreh F. Farzan<sup>2</sup>, Caitlin G. Howe<sup>4</sup>, William Funk<sup>5</sup>, John D. Meeker<sup>6</sup>, Rima Habre<sup>2</sup>, Theresa M. Bastain<sup>2</sup> and Carrie V. Breton<sup>2</sup>

# Prenatal Fluoride Exposure in North America

NeuroToxicology 59 (2017) 65–70



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Contents lists available at ScienceDirect

NeuroToxicology



Full Length Article

## In utero exposure to fluoride and cognitive development delay in infants



L. Valdez Jiménez<sup>a</sup>, O.D. López Guzmán<sup>b</sup>, M. Cervantes Flores<sup>b</sup>, R. Costilla-Salazar<sup>c</sup>, J. Calderón Hernández<sup>a</sup>, Y. Alcaraz Contreras<sup>d</sup>, D.O. Rocha-Amador<sup>d,\*</sup>

<sup>a</sup>Coordinación para la Innovación y Aplicación de la Ciencia y la Tecnología (CIACYT), Universidad Autónoma de San Luis Potosí, San Luis Potosí, Mexico

<sup>b</sup>Facultad de Ciencias Químicas, Universidad Juárez del Estado de Durango (Unidad Durango), Victoria de Durango, Mexico

<sup>c</sup>División de Ciencias de la Vida, Universidad de Guanajuato, Guanajuato, Mexico

<sup>d</sup>División de Ciencias Naturales y Exactas, Universidad de Guanajuato, Guanajuato, Mexico

## Dietary fluoride intake during pregnancy and neurodevelopment in toddlers: A prospective study in the progress cohort

Alejandra Cantoral<sup>a</sup>, Martha M. Téllez-Rojo<sup>b,\*</sup>, Ashley J. Malin<sup>c</sup>, Lourdes Schnaas<sup>d</sup>, Erika Osorio-Valencia<sup>d</sup>, Adriana Mercado<sup>b</sup>, E. Ángeles Martínez-Mier<sup>e</sup>, Robert O. Wright<sup>c</sup>, Christine Till<sup>f</sup>

Fluoride exposure during pregnancy from a community water supply is associated with executive function in preschool children: A prospective ecological cohort study



Deborah Dewey<sup>a,b,c,d,\*</sup>, Gillian England-Mason<sup>a,b</sup>, Henry Ntanda<sup>b</sup>, Andrea J. Deane<sup>a,b</sup>, Mandakini Jain<sup>e</sup>, Nadia Barnieh<sup>b</sup>, Gerald F. Giesbrecht<sup>a,b,c,f</sup>, Nicole Letourneau<sup>a,b,c,g,h</sup>, APrON Study Team

Published in final edited form as:

*Environ Res.* 2022 August ; 211: 112993. doi:10.1016/j.envres.2022.112993.

## Domain-specific effects of prenatal fluoride exposure on child IQ at 4, 5, and 6–12 years in the ELEMENT cohort

Carly V. Goodman<sup>a</sup>, Morteza Bashash<sup>b</sup>, Rivka Green<sup>a</sup>, Peter Song<sup>c</sup>, Karen E. Peterson<sup>c</sup>, Lourdes Schnaas<sup>d</sup>, Adriana Mercado-García<sup>e</sup>, Sandra Martínez-Medina<sup>d</sup>, Mauricio Hernández-Avila<sup>f</sup>, Angeles Martinez-Mier<sup>g</sup>, Martha M. Téllez-Rojo<sup>e,\*</sup>, Howard Hu<sup>b</sup>, Christine Till<sup>a</sup>

Environmental Research 200 (2021) 111315



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Contents lists available at ScienceDirect

Environmental Research

journal homepage: [www.elsevier.com/locate/envres](http://www.elsevier.com/locate/envres)



## Critical windows of fluoride neurotoxicity in Canadian children



Linda Farmus<sup>a</sup>, Christine Till<sup>a,\*</sup>, Rivka Green<sup>a</sup>, Richard Hornung<sup>b</sup>, E. Angeles Martinez Mier<sup>c</sup>, Pierre Ayotte<sup>d,e</sup>, Gina Muckle<sup>d,f</sup>, Bruce P. Lanphear<sup>g,h</sup>, David B. Flora<sup>a</sup>

# Fluoride Exposure Assessment

- Urinary fluoride level (Valdez Jiménez, 2017; Bashash, 2017,2018; Green, 2019)
- Water fluoride (Dewey et al., 2023; Green et al., 2019)
- Dietary fluoride intake (Cantoral et al., 2021)

# What About Infant Exposures?

Environment International 134 (2020) 105315



ELSEVIER

Contents lists available at ScienceDirect

Environment International

journal homepage: [www.elsevier.com/locate/envint](http://www.elsevier.com/locate/envint)



## Fluoride exposure from infant formula and child IQ in a Canadian birth cohort

Christine Till<sup>a,\*</sup>, Rivka Green<sup>a</sup>, David Flora<sup>a</sup>, Richard Hornung<sup>b</sup>, E. Angeles Martinez-Mier<sup>c</sup>, Maddy Blazer<sup>a</sup>, Linda Farmus<sup>a</sup>, Pierre Ayotte<sup>d,e</sup>, Gina Muckle<sup>d,f</sup>, Bruce Lanphear<sup>g,h</sup>



# Till et al. 2020

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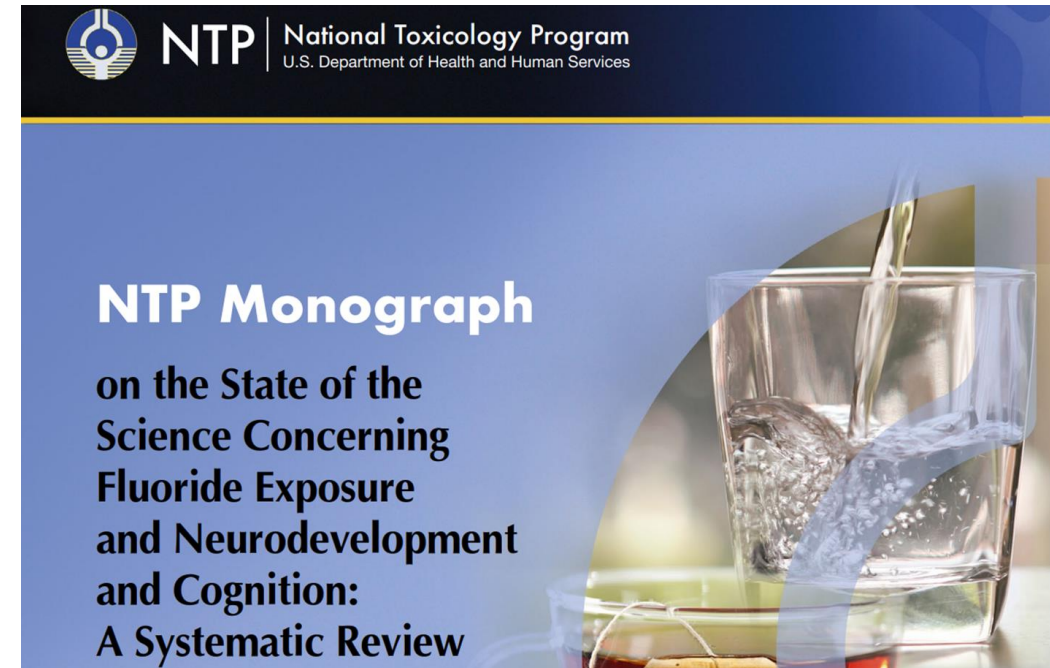
- An increase of 0.5 mg/L in water fluoride concentration in infancy was associated with:
- A 9.3-point decrement in Performance IQ (PIQ) among formula-fed children (95% CI: -13.77, -4.76)
- A 6.2-point decrement in PIQ among breast-fed children (95% CI: -10.45, -1.94)





# National Toxicology Program (NTP) Report

- Comprehensive systematic review on early life fluoride exposure and child neurodevelopment
- Included studies published by 2023
- 72 total studies on fluoride and IQ
  - 64 found that higher fluoride was associated with lower child IQ
- 19 high quality studies
  - 18 found that higher fluoride was associated with lower child IQ



(NTP, 2024)



## NTP Report

- “there is **moderate confidence** in the body of evidence that estimated fluoride exposure is **inversely associated with IQ in children**”
- “the moderate confidence in the inverse association between fluoride exposure and children’s IQ is **relevant to some children living in the United States**, including at a minimum those living in areas where fluoride in drinking water is known to be at or above 1.5 mg/L”

(NTP, 2024)

# NTP Report

- Associations between drinking water fluoride levels below 1.5 mg/L and children's IQ remain “**unclear**”
- It is plausible that pregnant women and children living in optimally fluoridated communities could have a total fluoride intake at or above the level of those living in a community with a water fluoride level of 1.5 mg/L or higher.

(NTP, 2024)

# NTP Meta-Analysis



Research

JAMA Pediatrics | [Original Investigation](#)

## Fluoride Exposure and Children's IQ Scores A Systematic Review and Meta-Analysis

Kyla W. Taylor, PhD; Sorina E. Eftim, PhD; Christopher A. Sibrizzi, MPH; Robyn B. Blain, PhD; Kristen Magnuson, MESM; Pamela A. Hartman, MEM;  
Andrew A. Rooney, PhD; John R. Bucher, PhD

# NTP Meta-Analysis

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- **Urinary fluoride concentrations *below* 1.5 mg/L are consistently associated with lower child IQ**
  - When considering all studies or only the high-quality ones
- The findings show that a **dose-response relationship** between higher fluoride exposure and lower child IQ exists

- The NTP report highlighted a need for more US-based studies on fluoride and neurodevelopment



Original Investigation | Public Health

## Maternal Urinary Fluoride and Child Neurobehavior at Age 36 Months

Ashley J. Malin, PhD; Sandrah P. Eckel, PhD; Howard Hu, MD, MPH, ScD; E. Angeles Martinez-Mier, PhD, DDS, MSD; Ixel Hernandez-Castro, PhD; Tingyu Yang, MS; Shohreh F. Farzan, PhD; Rima Habre, ScD; Carrie V. Breton, ScD; Theresa M. Bastain, PhD

Higher prenatal fluoride exposure is associated with more neurobehavioral problems (anxiety, temper tantrums, symptoms of autism, and headaches/stomach aches) among 3-year-old children in Los Angeles, California.



## Maternal Urinary Fluoride and Child Neurobehavior at Age 36 Months

Ashley J. Malin, PhD; Sandra P. Eckel, PhD; Howard Hu, MD, MPH, ScD; E. Angeles Martinez-Mier, PhD, DDS, MSD; Ixel Hernandez-Castro, PhD; Tingyu Yang, MS; Shohreh F. Farzan, PhD; Rima Habre, ScD; Carrie V. Breton, ScD; Theresa M. Bastain, PhD

- Pregnant women whose **urinary fluoride levels were approximately 1.2 mg/L** had **children with nearly double the odds of exhibiting clinically relevant neurobehavioral problems** by age 3 when compared with pregnant women whose urinary fluoride levels were approximately 0.5 mg/L

(Malin et al., 2024)

# Mechanisms of Developmental Neurotoxicity

- Fluoride can readily cross the placenta
- Accumulates in brain regions implicated in **learning, memory, mood, attention** and **executive function**



(Bartos et al., 2018, 2022; Chen et al., 2003; Mullenix, 1995; Sun et al., 2018)



# Impacts on Neurochemistry at Low Levels

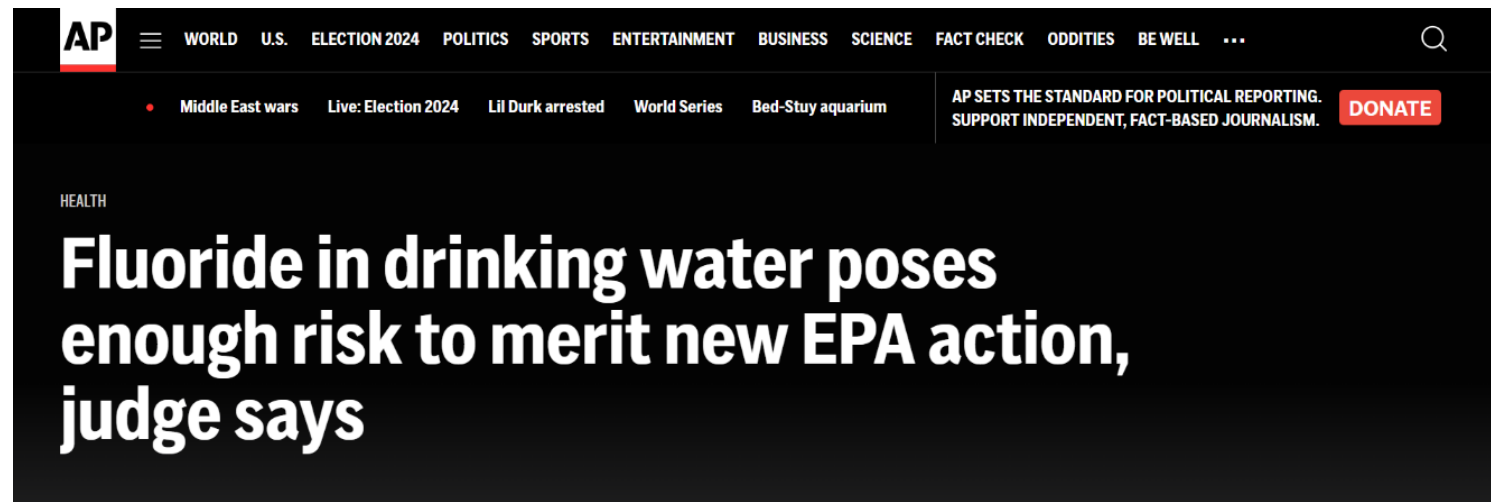
- Alters cholinergic activity
  - Important for attention, learning, memory
- Alters glutamate metabolism
- Contributes to mitochondrial dysfunction
- Increases oxidative stress



(Bartos et al., 2018, 2022; Chen et al., 2003; Liu et al., 2010; Mullenix, 1995; Sun et al., 2018)

## Criteria for Causality

- Strength of the association ✓
- Consistency ✓
- Temporality ✓
- Biological plausibility ✓
- Dose-response relationship ✓
- Coherence ✓
- Experimental evidence



- “the Court finds that fluoridation of water at 0.7 milligrams per liter (“mg/L”) – the level presently considered “optimal” in the United States – poses an **unreasonable risk of reduced IQ in children.**”
- “The scientific literature in the record provides a **high level of certainty that a hazard is present; fluoride is associated with reduced IQ.**”

(Case 3:17-cv-02162-EMC Document 445)

## Federal Ruling Implications

- There is not enough of a margin of safety between the hazard level (i.e., 1.5 mg/L) and exposure level (i.e., 0.7 mg/L) of fluoride in drinking water for dental cavities prevention
- The EPA's default standard is for there to be at least a **factor of 10** between the hazard level and exposure level

## Federal Ruling Implications

- According to the EPA's default standard:

The fluoride concentration in drinking water would need to be **0.15 mg/L or lower** to provide enough of a margin of safety **to protect child IQ**

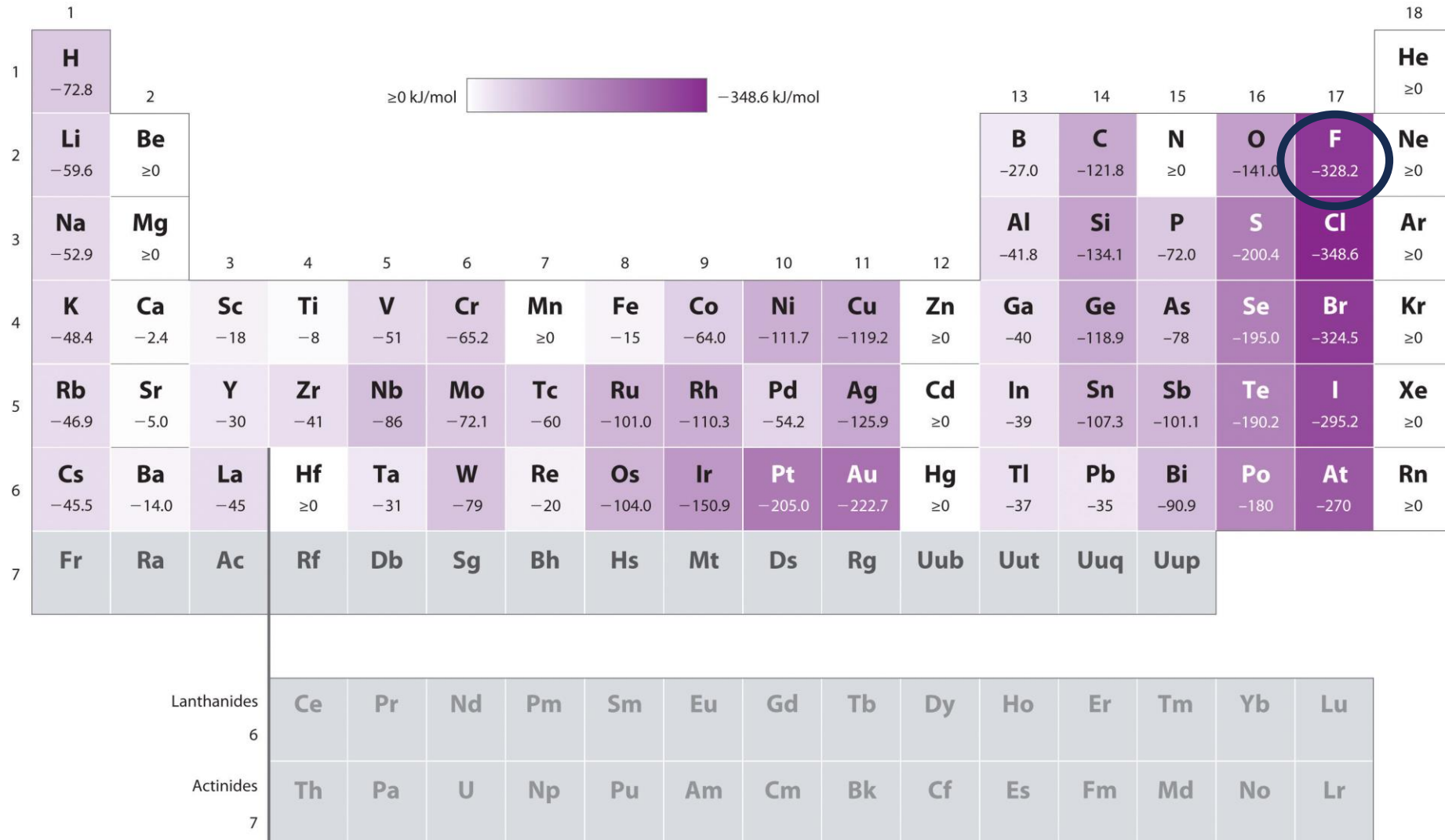


Questions:  
[ashleymalin@ufl.edu](mailto:ashleymalin@ufl.edu)

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# Chemical Properties





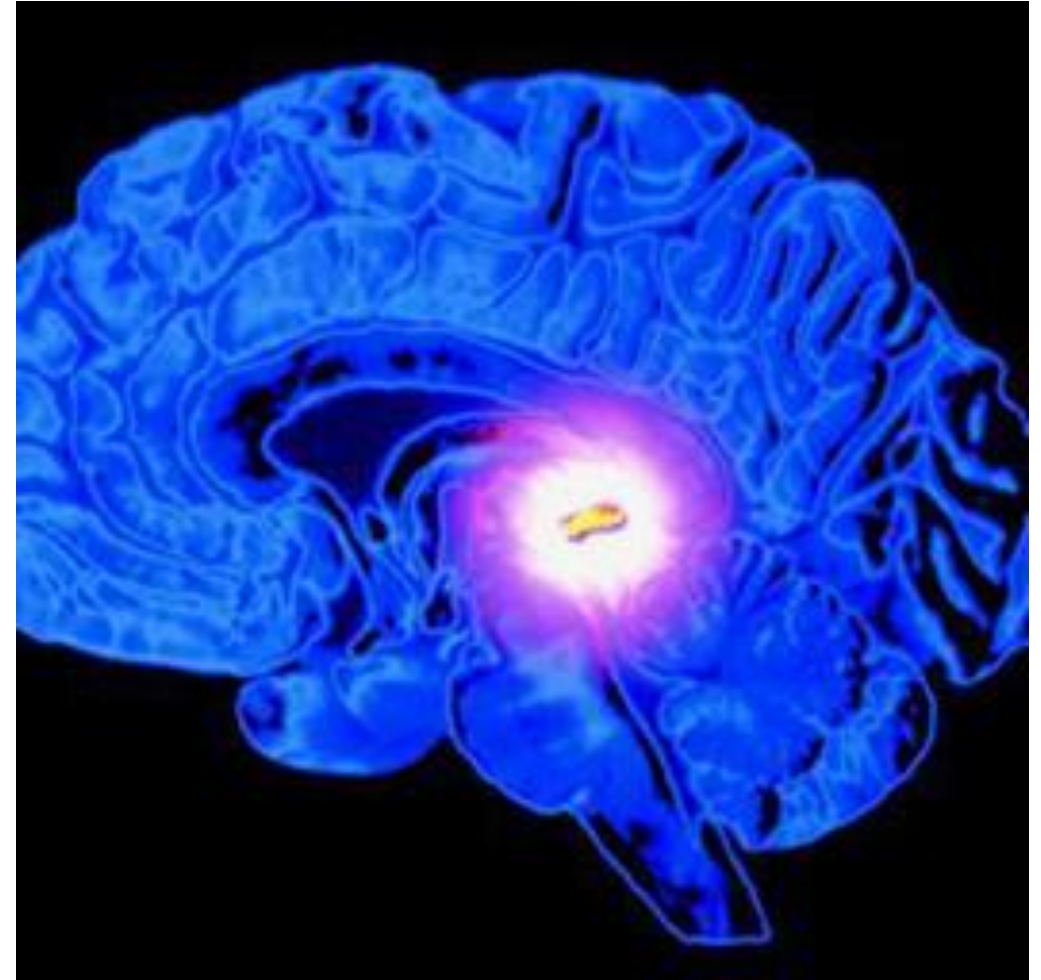
# Complex effects on the skeletal system:

- **Increases bone mineral density (BMD)**
  - Trabecular bone
  - Redistribution from cortical bone
- **Changes in bone quality**
  - Delayed initiation and rate of bone mineralization
  - Reduced bone elasticity and surface area
- **Bone weakness and increased risk of fracture**



# Effects on the Pineal Gland

- “fluoride is likely to cause decreased melatonin production and to have other effects on normal pineal gland function, which in turn could contribute to a variety of effects in humans” (NRC, 2006)



[Environ Health Perspect.](#) 2012 Oct; 120(10): 1362–1368.

PMCID: PMC3491930

Published online 2012 Jul 20. doi: [10.1289/ehp.1104912](https://doi.org/10.1289/ehp.1104912)

PMID: [22820538](https://pubmed.ncbi.nlm.nih.gov/22820538/)

## Developmental Fluoride Neurotoxicity: A Systematic Review and Meta-Analysis

[Anna L. Choi](#),<sup>1</sup> [Guifan Sun](#),<sup>2</sup> [Ying Zhang](#),<sup>3</sup> and [Philippe Grandjean](#)<sup>1,4</sup>

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**Conclusion:** *“The results support the possibility of an adverse effect of high fluoride exposure on children's neurodevelopment”*